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Section I

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Chapter 1

Embryology and Anatomy

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EMBRYOLOGY

The central nervous system is developed from the neural groove which invaginates to form the neural tube running longitudinally down the dorsal surface of the embryo. At either side from the lateral aspect of the anterior portion of this structure, which is the precursor of the forebrain, a thickening appears at an early stage,(the *optic plate)* which then grows outwards as a diverticulum towards the surface to form the *primary optic vesicle* (Tig. 1.1 A and B). From this pair of diverticula from the sides of the forebrain and the mesodermal and ectodermal structures in contact with it, the two eyes develop.

After it meets the surface ectoderm, the primary optic vesicle invaginates from below (the *optic cup),* the line of invagination remaining open for some time as the embryonic fissure (Fig. 1.1C). The inner layer of the cup forms the main structure of the retina, the nerve fibres from which eventually grow backwards towards the brain. Its outer layer remains as a single layer of pigment epithelium; between the two lies a narrow space representing the original optic vesicle; and from its anterior border develop parts of the ciliary body and iris (Fig. 1.1E). At the point where the neural ectoderm meets the surface ectoderm, the latter thickens to form the *lens Dials,* invaginates to form th*e lens vesicle* (Fig. 1.1C) and then separates to form the lens (Fig 1.1D) The hyaloid artery enters the optic cup through the embryonic fissure and grows forwards to meet the lens, bringing temporary nourishment

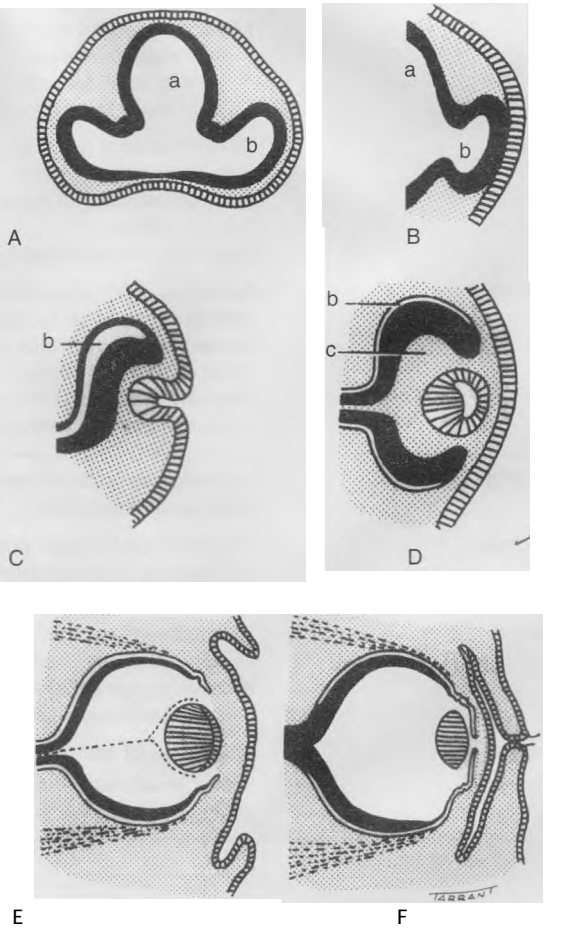


Fig. 1.1 The development of the eye. In each case the solid black is the neural ectoderm, the hatched layer is the surface ectoderm and its derivatives, the dotted area is the mesoderm: a, cavity of the forebrain; b, cavity of the optic vesicle; c, cavity of the optic cup (or secondary optic vesicle) formed by invagination. (A) Transverse section through the anterior part of the forebrain and optic vesicles of a 4mm human embryo. (B) The primary optic vesicle. (C) The formation of the optic cup by invagination at the embryonic fissure and invagination of the surface epithelium. (D) The optic cup and lens vesicle. (E) The formation of the ciliary region and iris, the anterior chamber, the hyaloid artery and the lid folds. The lens is formed from the posterior cells of the lens vesicle. (F) The complete eye.

Table 1.1 Summary of ocular embryogenesis

Period after conception	Major milestone	
3 weeks	Optic groove appears	
4th week	Optic pit develops into optic vesicle Lens plate forms Embryonic fissure develops	Fig. 1.1 A–D
1 st month	Lens pit and then lens vesicle form Hyaloid vessels develop	
1Vi months	Closure of embryonic fissure Differentiation of retinal pigment epithelium Proliferation of neural retinal cells Appearance of eyelid folds and nasolacrimal duct	
7th week	Formation of embryonic nucleus of the lens Sclera begins to form Migration of waves of neural crest First wave: formation of corneal and trabecular endothelium Second wave: formation of corneal stroma Third wave: formation of iris stroma	Fig. 1.1E
3rd month	Differentiation of precursors of rods and cones Anterior chamber appears Fetal nucleus starts to develop Sclera condenses Eyelid folds lengthen and fuse	
4th month	Formation of retinal vasculature begins Hyaloid vessels begin to regress Formation of physiological optic disc cup and lamina cribrosa Canal of Schlemm appears Bowman's membrane develops Formation of major arterial circle and sphincter muscle of iris	
5th month	Photoreceptors differentiate Eyelid separation begins	
6th month	Differentiation of dilator pupillae muscle Nasolacrimal system becomes patent Cones differentiate	Fig. 1 .IF
7th month	Rods differentiate Myelination of optic nerve begins Posterior movement of anterior chamber angle Retinal vessels start reaching nasal periphery	
8th month	Completion of anterior chamber angle formation, hyaloid vessels disappear	
9th month	Retinal vessels reach temporal periphery, pupillary membrane disappears	
After birth	Macular region of the retina develops further	

to the developing structures before it eventually atrophies and disappears; as it does so, its place is taken by a clear jelly (the vitreous) largely secreted by the surrounding neural ectoderm.

While these ectodermal events are taking place, the mesoderm surrounding the optic cup differentiates to form the coats of the eye and the orbital structures; that between the lens and the surface ectoderm becomes hollowed to form the anterior chamber, lined by mesodermal condensations which form the anterior layers of the iris, the angle of the anterior chamber and the main structures of the cornea; while the surface ectoderm remains as the corneal and conjunctival epithelium. In the surrounding region folds grow over in front of the cornea, unite and separate again to form the lids (Fig. 1.1E and F). Summary of ocular embryogenesis is given in Table 1.1.

In summary, the eye is essentially formed from both ectoderm and mesoderm. The ectoderm is of two types: (i) the neural ectoderm derived from the neural tube and (ii) the surface ectoderm on the side of the head (Table 1.2).

Table 1.2 Primordial tissue and its derivatives

Precursor	Derivatives
Neural ectoderm	Smooth muscle of the iris
	Optic vesicle and cup
	Iris epithelium
	Ciliary epithelium
	Part of the vitreous
	Retina
	Retinal pigment epithelium
	Fibres of the optic nerve
Surface ectoderm	Conjunctival epithelium
	Corneal epithelium
	Lacrimal glands
	Tarsal glands
	Lens
Mesoderm	Extraocular muscles
	Corneal stroma
	Sclera
	Iris
	Vascular endothelium of eye and orbit
	Choroid
	Part of the vitreous
Neural crest*	Corneal stroma, keratocytes and endothelium
	Sclera
	Trabecular meshwork endothelium
	Iris stroma
	Ciliary muscles
	Choroidal stroma
	Part of the vitreous
	Uveal and conjunctival melanocytes
	Meningeal sheaths of the optic nerve
	Ciliary ganglion
	Schwann cells of the
	Orbital bones
	Orbital connective tissue
	Connective tissue sheath and muscular layer of the ocular and orbital blood vessels

*During the folding of the neural tube, a ridge of cells comprising the neural crest develops from the tips of the converging edges and migrates to the dorsolateral aspect of the tube. Neural crest cells from this region subsequently migrate and give rise to various structures within the eye and the orbit.
The structures are listed from anterior to posterior.

ANATOMY

The wall of the globe is composed of a dense, imperfectly elastic supporting membrane (Fig. 1.2). The anterior part of the membrane is transparent—the cornea and the remainder is opaque—the sclera. The anterior part of the sclera is covered by a mucous membrane—the conjunctiva—which is reflected from its surface onto the lids.

The *cornea* consists of three layers: the epithelium, the substantia propria or stroma and Descemet's membrane with its endothelium. The epithelium, which is stratified, may be regarded as the continuation of the conjunctiva over the cornea. Its basal cells lie on a lamina of the substantia propria, called Bowman's membrane. The substantia propria may be regarded as the continuation forwards of the sclera.

The stroma, forming 90% of the total corneal thickness, is composed of regularly arranged thin fibrils of collagen ensheathed by acid mucopolysaccharides and set in a ground substance. They form ribbon-like bundles and give the stroma a laminated appearance. The collagen fibrils are circular on transverse section and are spaced equidistantly. They lie in staggered rows to form a hexagonal lattice.

Transparency of the cornea is related to the regularity of the stromal components. The lattice theory proposes that the stromal collagen fibrils are of regular diameter, arranged as a lattice with an interfibrillar spacing of less than a wavelength of light so that tangential rows of fibres act as a diffraction grating resulting in destructive interference of scattered rays.

Descemet's membrane is a thin elastic membrane, covered on its posterior surface by endothelium. The primary mechanism controlling stromal hydration is a function of the corneal endothelium. Electrolytes are removed and water flows passively. The endothelium may be examined by a specular microscope at a magnification of 500 x. Endothelial cells become less in number with age and the residual individual cells may enlarge to compensate.

The cornea is set into the sclera like a watch glass so that the latter overlaps the cornea all round the periphery; the junction of the two tissues is known as the *limbus.* The cornea is very richly supplied with nerve fibres derived from the trigeminal nerve. It has no blood vessels with the exception of minute arcades, extending about 1 mm into the cornea at the limbus, so that it is dependent for its nourishment upon diffusion of tissue fluid from the vessels at its periphery and the aqueous humour.

Lining the inner aspect of the sclera are two structures: the highly vascular *uveal tract* concerned chiefly with the nutrition of the eye, and within this a nervous layer, the true visual nerve endings concerned with the reception and transformation of light stimuli, called the *retina.*

The uveal tract consists of three parts, of which the two posterior, the *choroid* and *ciliary body,* line the sclera while the anterior forms a free circular diaphragm, the *iris.* The plane of the iris is approximately coronal; the aperture of the diaphragm is the *pupil.* Situated behind the iris and in contact with the pupillary margin is the crystalline *lens.*

The *anterior chamber* is a space filled with fluid, the *aqueous humour;* it is bounded in front by the cornea, behind by the iris and the part of the anterior surface

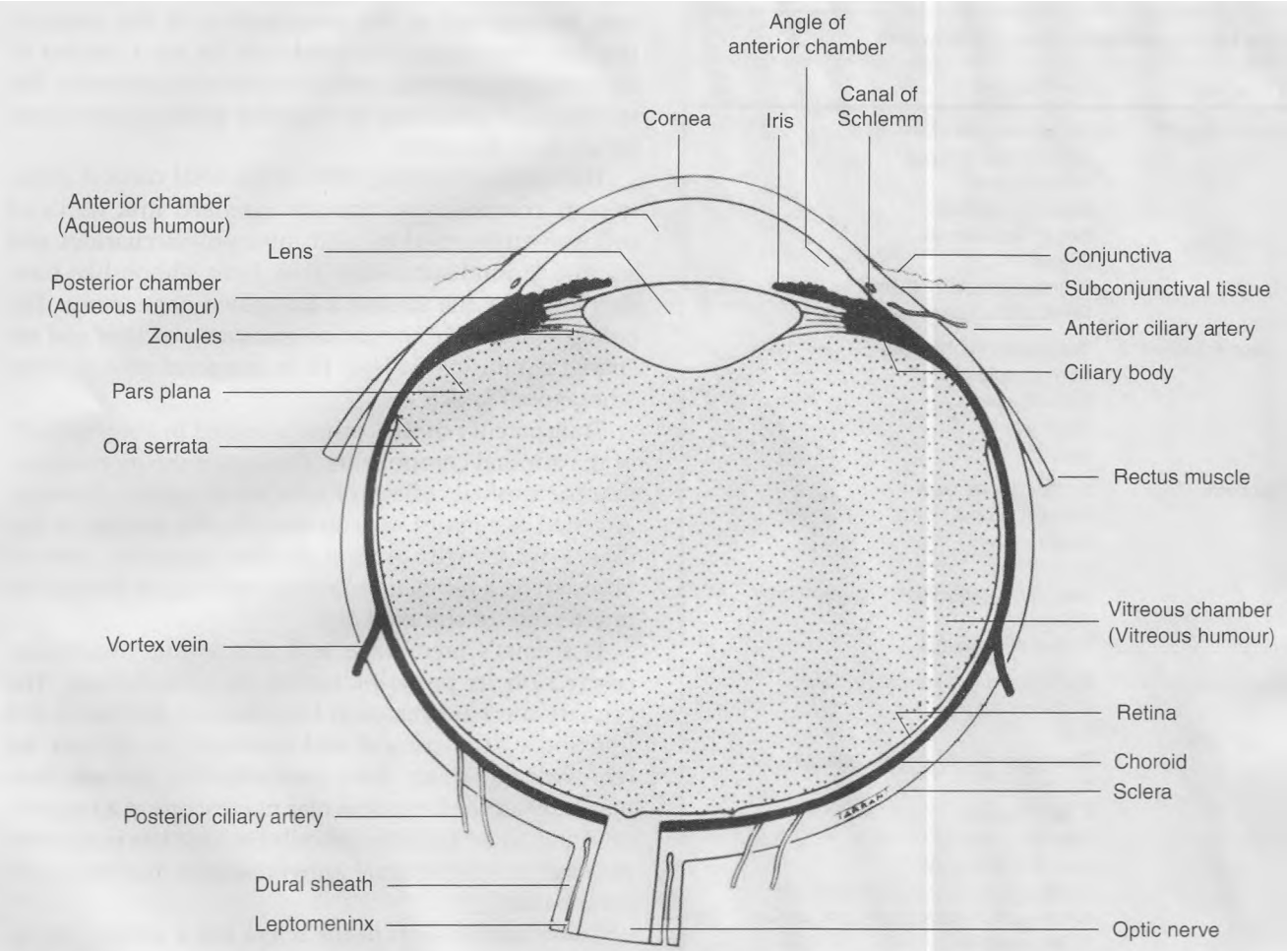


Fig. 1.2 Diagram of a longitudinal section of the eyeball.

of the lens which is exposed in the pupil. Its peripheral recess is known as the *angle of the anterior chamber*, bounded posteriorly by the root of the iris and the ciliary body and anteriorly by the corneosclera (Fig. 1.3). In the inner layers of the sclera at this part there is a circular venous sinus, sometimes broken up into more than one lumen, called the *canal of Schlemm*, which is of great importance for the drainage of the aqueous humour. At the periphery of the angle between the canal of Schlemm and the recess of the anterior chamber there lies a loosely constructed meshwork of tissues, the *trabecular meshwork*. This has a triangular shape, the apex arising from the termination of Descemet's membrane and the subjacent fibres of the corneal stroma and its base merging into the tissues of the ciliary body and the root of the iris. It is made up of circumferentially disposed flattened bands, each perforated by numerous oval stomata through which tortuous passages exist between the anterior chamber and Schlemm's canal. The extracellular spaces contain both a coarse framework (collagen and elastic components) and a fine framework (mucopolysaccharides) of extracellular materials, which form the probable site of greatest resistance to the flow of aqueous.

The endothelial cells of Schlemm's canal are connected to each other by junctions which are not 'tight' but this intercellular pathway accounts for only 1% of the aqueous drainage. The major outflow pathway appears to be a series of transendothelial pores, which are usually found in outpouchings of the endothelium called 'giant vacuoles' (Fig. 1.4A-C).

The anterior chamber is about 2.5 mm deep in the centre in the normal adult; it is shallower in very young children and in old people.

The *iris* is thinnest at its attachment to the ciliary body, so that if torn it tends to give way in this region (Fig. 1.3). It is composed of a stroma containing branched connective tissue cells, usually pigmented but largely unpigmented in blue irides, with a rich supply of blood vessels which run in a general radial direction.

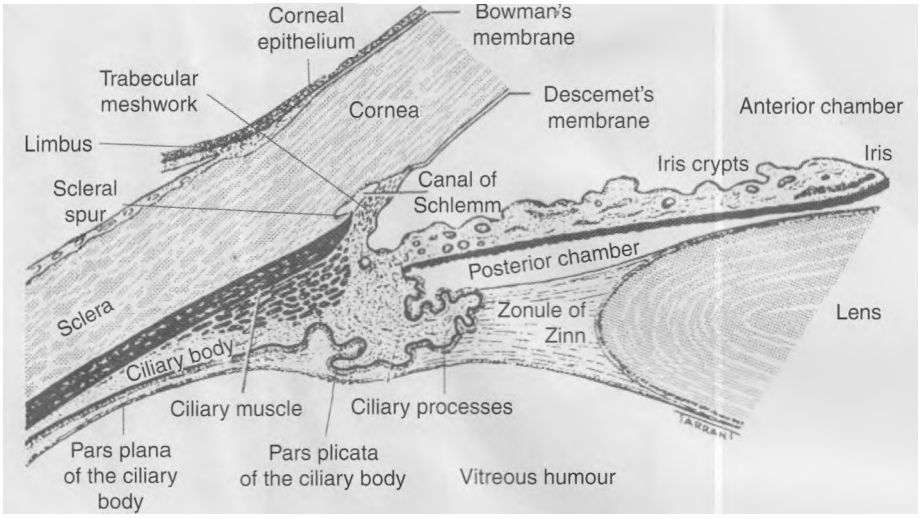


Fig. 1.3 The region of the angle of the anterior chamber.

The tissue spaces communicate directly with the anterior chamber through crypts found mainly near the ciliary border; this allows the easy transfer of fluid between the iris and the anterior chamber. The stroma is covered on its posterior surface by two layers of pigmented epithelium, which developmentally are derived from the retina and are continuous with each other at the pupillary margin. The anterior layer consists of flattened cells and the posterior of cuboidal cells. From the epithelial cells of the former, two unstriped muscles are developed which control the movements of the pupil, the *sphincter pupillae,* a circular bundle running round the pupillary margin, and the *dilator pupillae,* arranged radially near the root of the iris.

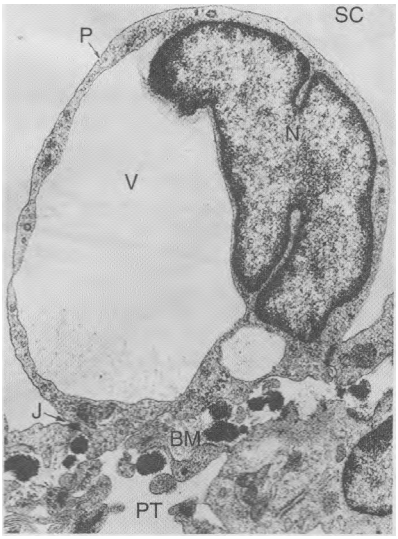
The anterior surface of the iris is covered with a single layer of endothelium, except at some minute depressions or crypts which are found mainly at the ciliary border; it usually atrophies in adult life.

The iris is richly supplied by sensory nerve fibres derived from the trigeminal nerve. The sphincter pupillae is supplied by parasympathetic autonomous secretomotor nerve fibres derived from the oculomotor nerve, while the motor fibres of the dilator muscle are derived from the cervical sympathetic chain.

The *ciliary body* in anteroposterior section is shaped roughly like an isosceles triangle, with the base forwards. The iris is attached about the middle of the base, so that a small portion of the ciliary body enters into the posterior boundary of the anterior chamber at the angle (Fig. 1.3). The chief mass of the ciliary body is composed of unstriped muscle fibres, the *ciliary muscle.* This consists of three parts with a common origin in the ciliary tendon, a structure which runs circumferentially round the globe blending with the 'spur' of the sclera and related to the trabecular mesh work. The greater part of the muscle is composed of meridional fibres running anteroposteriorly on the inner aspect of the sclera to find a diffuse insertion into the suprachoroid. Most of the remainder of the fibres run obliquely in interdigitating V-shaped bundles so as to give the impression of running in a circle round the ciliary body, concentrically with the base of the iris. The third portion of the muscle is composed of a few tenuous iridic fibres arising most internally from the common origin and finding insertion in the root of the iris just anterior to the pigmentary epithelium in close relation to the dilator muscle.

The inner surface of the ciliary body is divided into two regions; the anterior part is corrugated with a number of folds running in an antero-posterior direction while the posterior part is smooth. The anterior part is, therefore, called the *pars plicata,* the posterior, the *pars plana.* About 70 plications are visible around the circumference macroscopically, but if microscopic sections are examined, many smaller folds, the *ciliary processes,* will be seen between them. These contain no part of the ciliary muscle, but consist essentially of tufts of blood vessels, not unlike the glomeruli of the kidney. They are covered upon the inner surface by two layers of epithelium, which belong properly to the retina, and are continuous with similar layers in the iris; the outer layer, corresponding to the anterior in the iris, consists of flattened cells, the inner of cuboidal cells, but only the outer layer in the ciliary body is pigmented.

The ciliary body extends backward as far as the *ora serrata,* at which point the retina proper begins abruptly; the transition from the ciliary body to the choroid, on the other hand, is gradual, although this line is conveniently



Fig, 1.4 (A) Electron micrograph of a typical macrovacuoiar configuration as seen normally in the endothelial cells lining the trabecular wall of Schlemm's canal. The vacuole (V), bound by a smooth unit membrane, is in fact formed by a basal invagination of the cell surface and eventually opens on the luminal aspect, thus constituting a transient transcellular channel that allows the bulk outflow of the aqueous humour. Owing to the vacuolar configuration of the channel, which has small basal and apical openings, these openings are rarely encountered together in a single plane of section. The nucleus (N) is displaced to one side to accommodate the macrovacuole that contains aqueous humour. For comparison of the size of the macrovacuole, a micropinocytotic vesicle (100nm) is denoted with p. J, junctional complex of lining endothelial cells; BM, patchy basal lamina seen beneath the endothelial lining of Schlemm's canal; PT, loosely organized pericanalicular tissue of the trabecular wall of Schlemm's canal (SC) (x18720).

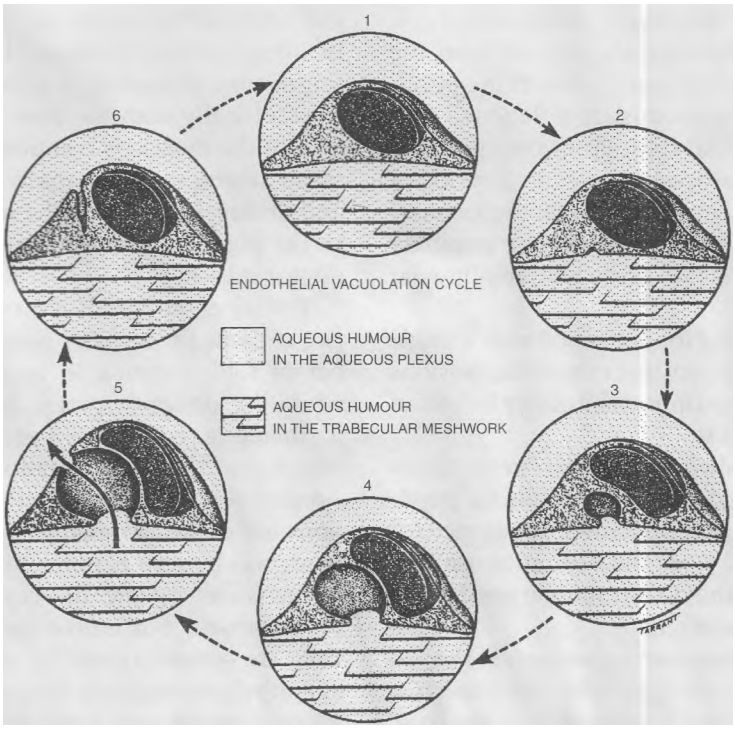


Fig. 1.4 (B) Diagrammatic representation of the cyclical sequence of events in the formation of vacuolar transcellular channels that constitute a dynamic system of pores, and the mechanism of the bulk outflow of the aqueous humour across the endothelial barrier of Schlemm's canal. Initially, the vacuolar configuration is formed by a membranous depression or infolding on the basal aspect of the cell surface (Stage 2). A progressive enlargement of this infolding leads to the formation of a macrovacuoiar structure (Stages 3 and 4) which eventually opens on the luminal aspect of the cell's surface (Stage 5), thus forming a temporary vacuolar transcellular channel (continuous arrow). The bulk outflow of aqueous humour takes place down a pressure gradient (i.e. from the trabecular meshwork into the lumen of the canal of Schlemm) via such vacuolar transendothelial channels which also act as one-way valves. After a certain time interval, the basal infolding is occluded and the cell returns to its non-vacuolated state (Stage 1).

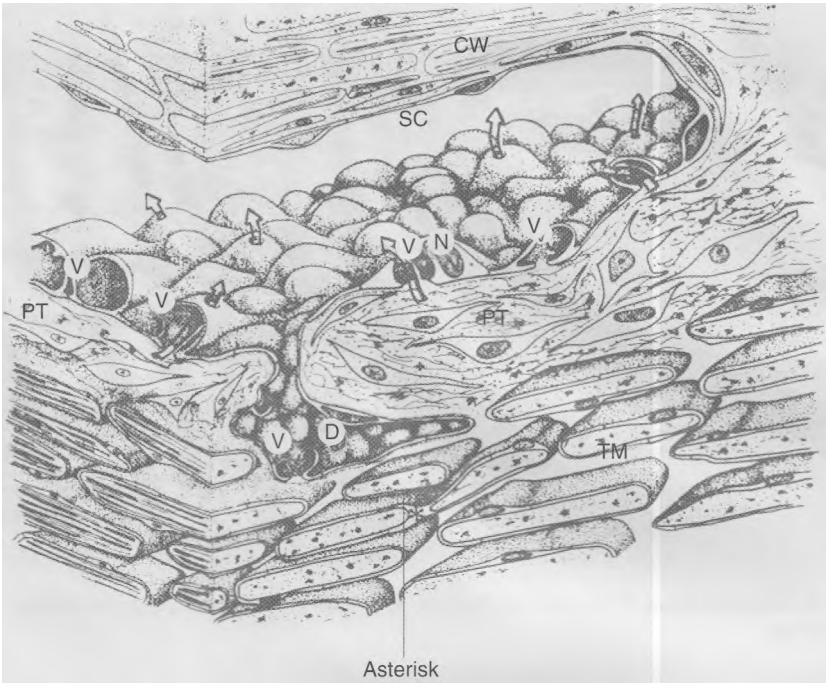


Fig. 1.4 (C) Semidiagrammatic representation of the walls of Schlemm's canal (SC) and adjacent trabecular meshwork (TM) in a composite sectional and three-dimensional view. The endothelial lining of the trabecular wall of Schlemm's canal is very irregular and normally the cells show luminal bulges corresponding to cell nuclei (N) and macrovacuoiar configuration (V), the latter representing cellular invaginations beginning from the basal aspect and eventually opening on the apical aspect of the cell to form transcellular channels (arrows) through which aqueous humour flows down a pressure gradient. The sequence of events in this process is illustrated in Fig 1.4 (B). A diverticulum (D) on the inner wall of Schlemm's canal is seen with its endothelial lining being continuous with that of the canal and contains macrovacuoiar configurations. Such blind, tortuous diverticula course for a variable distance into the trabecular meshwork but remain separated from the open spaces of the meshwork by their continuous endothelial lining. The endothelial lining of the trabecular wall is supported by an interrupted, irregular basement membrane and a zone of pericanalicular connective tissue (PT) of variable thickness; the cellular element predominates in this zone and the fibrous elements, especially elastic fibres, are irregularly arranged in a net-like fashion, and the open spaces are narrower than the trabecular meshwork. The corneoscleral trabecular sheets show frequent branching and the endothelial covering (asterisk) may be shared between adjacent trabecular sheets. The corneoscleral wall (CW) of Schlemm's canal is more compact than the trabecular wall, with a predominance of lamellar arrangement of collagen and elastic tissue. (By courtesy of RC Tripathi)

accepted as the limit of the two structures. The ora serrata thus circles the globe, but is slightly more anterior on the nasal than on the temporal side.

The ciliary body is richly supplied with sensory nerve fibres derived from the trigeminal nerve. The ciliary muscle is supplied with motor fibres from the oculomotor and sympathetic nerves.

The *choroid* is an extremely vascular membrane in contact everywhere with the sclera, although not firmly adherent to it, so that there is a potential space between the two structures—the *epichoroidal or suprachoroidal space* (Fig. 1.5). On the inner side, the choroid is covered by a thin elastic membrane, the *lamina vitrea* or *membrane of Bruch.*

The blood vessels of the choroid increase in size from within outwards, so that immediately beneath the membrane of Bruch there is a capillary plexus of fenestrated vessels, *the choriocaptilaris* (Fig. 1.6). Upon this is the layer of medium-sized vessels, while most externally are the large vessels, the whole being held together by a stroma consisting of branched pigmented connective tissue cells (Fig. 1.5). The choroid is supplied with sensory nerve fibres from the trigeminal as well as autonomic nerves, presumably of vasomotor function.

The *retina* corresponds in extent to the choroid, which it lines, although the same embryological structure is continued forwards as a double layer of epithelium as far as the pupillary margin. If the two layers of epithelium are traced backwards, the anterior layer in the iris is found to be continuous with the outer layer in the ciliary body, and this again is continued into the pigment epithelium of the retina as a single layer of hexagonal cells lying immediately adjacent to the membrane of Bruch. Similarly the posterior layer in the iris, although pigmented, passes into the inner unpigmented layer of the ciliary body, and this suddenly changes at the ora serrata into the highly complex visual retina.

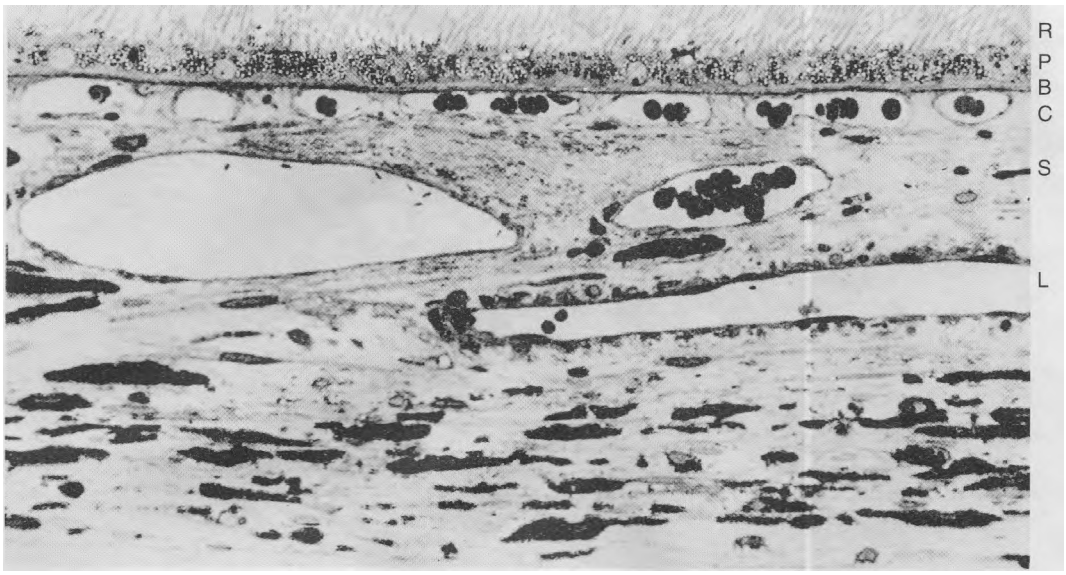


Fig. 1.5 Normal choroid: R, rods and cones; P, pigment epithelium; B, Bruch's membrane; C, choriocapillaris; S, small vessels; and L, large vessels. (By courtesy of Garner)

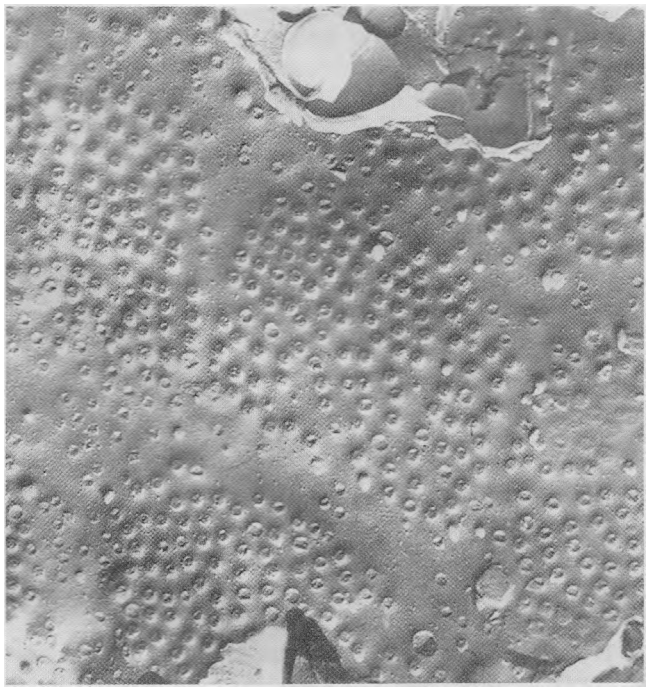


Fig. 1.6 Freeze-fractioned replica of endothelial cell membrane from the choriocapillaris of the rabbit to show groups of fenestrations separated by smooth cytoplasmic areas. (By courtesy of S Melamed)

The retina consists of a number of layers (Fig. 1.7A and B) formed by three strata of cells and their synapses—the visual cells (lying externally), a relay layer of bipolar cells (lying intermedially) and a layer of ganglion cells (lying internally), the axons of which run into the central nervous system.

Most externally, in contact with the pigment epithelium, is a neural epithelium, the rods and cones, which are the end-organs of vision (Fig. 1.8). The microanatomy of the rods and cones reveals the transductive region (outer segment), a region for the maintenance of cellular homoeostasis (inner segment), a nuclear region (outer nuclear layers) and a transmissive region (the outer plexiform or synaptic layer).

When the outer segments of the rods are sectioned parallel to their long axes, they are seen by the electron microscope to consist of a boundary or cell membrane, which encloses a stack of membrane systems. The discs in the rods of many species are continuously renewed throughout life. New discs are formed in the region of the inner segment and are progressively displaced towards the pigment epithelium. Rod discs have a limited life and are eventually lost to the pigment epithelium.

At the junction of the inner and outer segments, the cell body of both rods and cones constricts. The electron microscope reveals a connecting cilium which is always eccentric and provides the only link between the inner and outer segments.

The pigment epithelium consists of a single layer of hexagonal cells lying between the photoreceptor outer segment and Bruch's membrane. They assist the metabolism of the retina by transporting selected substances to the receptor cells. Products of metabolism are freely exchanged between the receptor cells and the pigment epithelium.

The most striking inclusions in the pigment epithelium are the organelles responsible for its colour, the melanin granules. Most of the light which passes through

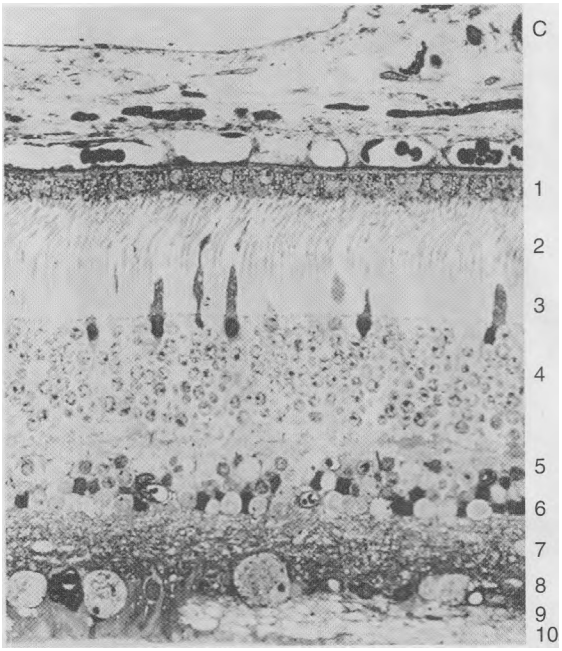


Fig. 1.7 (A) Section of the human retina: C, choroid; 1, pigment epithelium; 2, layer of rods and cones; 3, external limiting membrane; 4, outer nuclear layer; 5, outer plexiform layer; 6, inner nuclear layer; 7, inner plexiform layer; 8, ganglion cell layer; 9, nerve fibre layer; and 10, internal limiting membrane. (By courtesy of Garner)

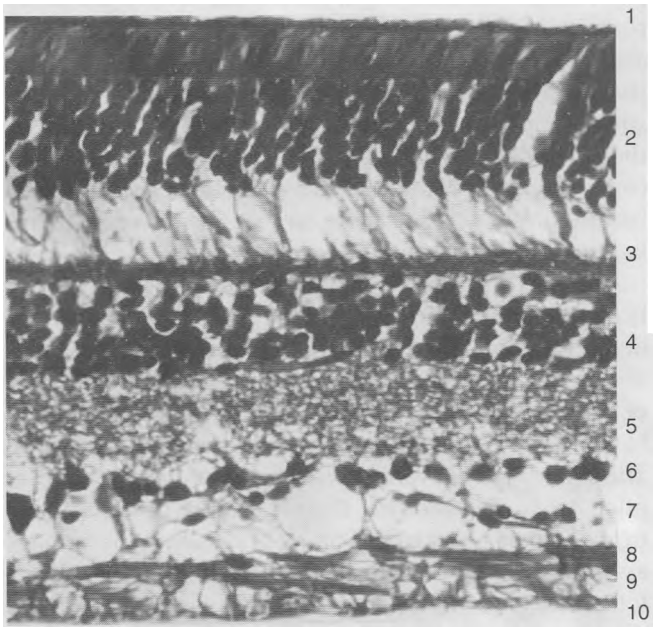


Fig. 1.7 (B) Section stained with haematoxylin and eosin of the normal human retina. (By courtesy of S Kashyap)

the retina and is not absorbed by the photopigments in the photoreceptor outer segments is absorbed by these granules. Phagosomes are known to be discarded rod

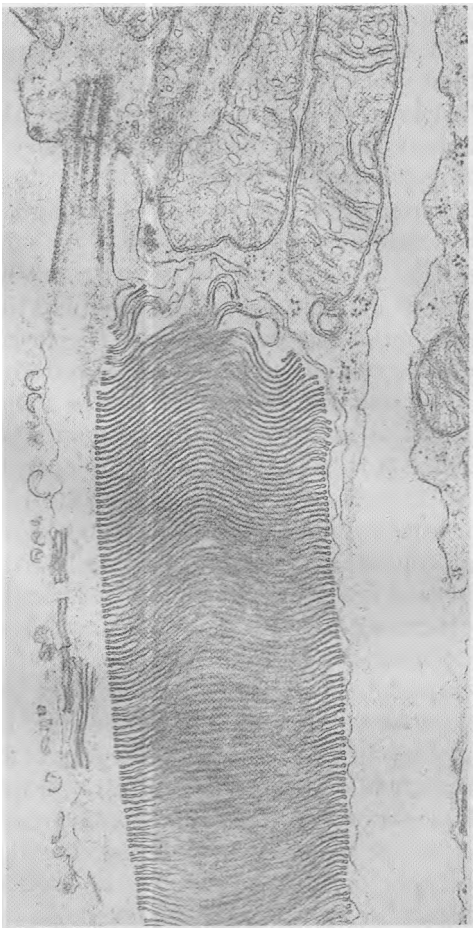


Fig. 1.8 Electron micrograph of a longitudinal section of a human rod cell at the junction of the inner and outer segments: OS, outer segment; IS, inner segment and C, cilium. (By courtesy of Marshall and Pedler)

discs that have been engulfed by the pigment epithelium. The phagocytic capacity of the pigment epithelium is demonstrated in the response of the retina to injury as by laser irradiation, when the number of phagosomes in the underlying epithelial cells increases significantly.

Inner to the retinal pigment epithelium, in order from without inwards, lie the outer nuclear layer (the nuclei of the rods and cones), the outer plexiform layer consisting of synapses, the inner nuclear layer (the nuclei of the bipolar cells), the inner plexiform layer (again synaptic), the ganglion cell layer and finally lying innermost, the nerve fibre layer composed of the axons of ganglion cells running centrally into the optic nerve. These special nervous constituents are bound together by neuroglia, the better developed vertical cells being called the fibres of Muller, which in addition to acting as a supportive framework, have a nutritive function. The structure is completed by two limiting membranes, the outer perforated by the rods and cones, and the inner separating the retina from the vitreous.

To excite the rods and cones, incident light has to traverse the tissues of the retina but this arrangement allows these visual elements to approximate the opaque pigmented layer to form a functional unit, and their source of nourishment is the choriocapillaris.

At the posterior pole of the eye, which is situated about 3 mm to the temporal side of the optic disc, a specially differentiated spot is found in the retina, the *fovea centrali,* a depression or pit, where only cones are present in the neuro-epithelial layer and the other layers are almost completely absent. The fovea is the most sensitive part of the retina, and is surrounded by a small area, the *macula lutea,* or yellow spot which, although not so sensitive, is more so than other parts of the retina. It is here that the nuclear layers become gradually thinned out, while parts of the plexiform layers are especially in evidence. The ganglion cells too, instead of consisting of a single row of cells, are heaped up into several layers. There are no blood vessels in the retina at the macula, so that its nourishment is entirely dependent upon the choroid.

At the optic disc the fibres of the nerve fibre layer pass into the *optic nerve (see* Chapter 17), the other layers of the retina stopping short abruptly at the edge of the aperture in the scleral canal. This is spanned by a transverse network of connective tissue fibres containing much elastic tissue, the *lamina cribrosa,* through the meshes of which the optic nerve fibres pass; on the posterior side they suddenly become surrounded by medullary sheaths. The fibres, the axons of the ganglion cells of the retina, are, of course, afferent or centripetal fibres, but the optic nerve also contains a few efferent or centrifugal fibres.

The *lens* is a biconvex mass of peculiarly differentiated epithelium. It is developed from an invagination of the surface ectoderm of the fetus, so that what was originally the surface of the epithelium comes to lie in the centre of the lens, the peripheral cells corresponding to the basal cells of the epidermis. Just as the epidermis grows by the proliferation of the basal cells, the old superficial cells being cast off, so the lens grows by the proliferation of the peripheral cells. The old cells, however, cannot be cast off, but undergo changes (sclerosis) analogous to that of the stratum granulosum of the epidermis, and become massed together in the centre or nucleus; moreover, the newly formed cells elongate into fibres. The lens fibres have a complicated architectural form, being arranged in zones in which the fibres growing from opposite directions meet in sutures. Without going into details, it is important to bear in mind that the central nucleus of the lens consists of the oldest cells and the periphery or cortex the youngest (Fig. 1.9).

The fibres of the central *embryonic nucleus* meet around Y-shaped sutures. Outside this embryonic nucleus, successive nuclear zones are laid down as development proceeds, called, depending on the period of formation,

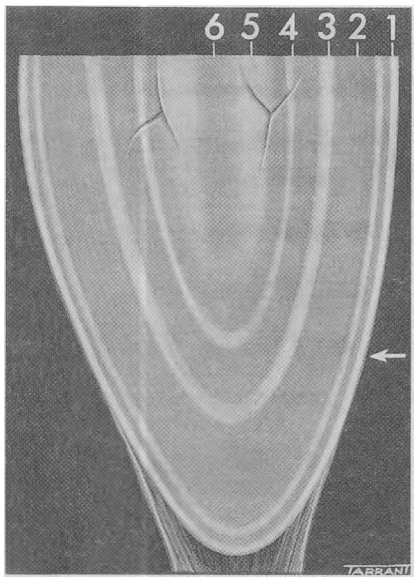


Fig. 1.9 The structure of the lens in an adult 40 years of age, as shown in the optical beam of the slit-lamp: 1, anterior capsule; 2, cortex; 3, adult nucleus; 4, infantile nucleus; 5, fetal nucleus; and 6, embryonic nucleus (see Fig. 18.3A).

the *fetal nucleus* (corresponding to the lens at birth), the *infantile nucleus* (corresponding to the lens at puberty), the *adult nucleus* (corresponding to the lens in early adult life), and finally and most peripherally, the *cortex* consisting of the youngest fibres. In this part of the lens also the fibres meet along the sutures with a general stellate arrangement. The mass of epithelium which constitutes the lens is surrounded by a hyaline membrane, the *lens capsule,* which is thicker over the anterior than over the posterior surface; it is a cuticular deposit secreted by the epithelial cells having on the outside a thin membrane, the *zonular lamella.*

The lens in fetal life is almost spherical; it gradually becomes flattened so as to assume a biconvex shape. It is held in place by the *suspensory ligament* or *zonule of Zinn.* This is not a complete membrane, but consists of bundles of strands which pass from the surface of the ciliary body to the capsule where they join with the zonular lamella. The strands pass in various directions so that the bundles often cross one another. Thus the most posterior arise from the pars plana of the ciliary body almost as far back as the ora serrata; these lie in contact with the ciliary body for a considerable distance and then curve towards the equator of the lens to be inserted into the capsule slightly anterior to the equator. A second group of bundles springs from the summits and sides of the ciliary processes, i.e. far forwards, and passes backwards to be inserted into the lens capsule slightly posterior to the equator. A third group passes from the summits of the processes almost directly inwards to be inserted at the equator.

It will be noticed that there is a somewhat triangular space between the back of the iris and the anterior surface of the lens, having its apex at the point where the pupillary margin comes in contact with the lens; it is bounded on the outer side by the ciliary body. This is the *posterior chamber* and contains aqueous humour.

Behind the lens is the large vitreous chamber, containing the *vitreous humour.* This is a jelly-like material chemically of the nature of an inert gel containing a few cells and wandering leucocytes. As in other gels the concentration of the micellae on the surface gives rise to the appearance of a boundary membrane in sections—the so-called *hyaloid membrane.*

The *vitreous body* is attached anteriorly to the posterior lens surface by the ligament of Wiegert. In the region of the ora the vitreous cortex is firmly attached to the retina and pars plana and this attachment is referred to as the vitreous base.

Posteriorly, the vitreous body is attached to the margin of the optic disc and to the macula forming a ring around each structure and also to the larger blood vessels. The primary vitreous is concentrated into the centre of the globe by the secondary vitreous and forms the canal of Cloquet which contains material less optically dense than the secondary vitreous.

The body of the vitreous has a loose fibrous framework of collagenous fibres whereas its cortex is made up of collagen-like fibres and protein.

THE BLOOD SUPPLY OF THE EYE

The arteries of the eye in man are all derived from the ophthalmic artery (Fig. 1.10A and B), which is a branch of the internal carotid artery. The ophthalmic artery has few anastomoses, so that on the arterial side the ocular circulation is an offshoot of the intracranial circulation. This does not apply in so marked a degree to the venous outflow from the eye. In man, most of the blood passes to the cavernous sinus by way of the ophthalmic veins, but they anastomose freely in the orbit, the superior ophthalmic vein communicating with the angular vein at the root of the nose and the inferior ophthalmic vein with the pterygoid plexus.

The retina is supplied by the central retinal artery, which enters the optic nerve on its lower surface, 15-20 mm behind the globe. The central artery divides on, or slightly posterior to, the surface of the disc into the main retinal trunks, which will be considered in detail later (Fig. 1.10A). The retinal arteries are end-arteries and have no anastomoses at the ora serrata. The only place where the retinal system anastomoses with any other is in the neighbourhood of the lamina cribrosa. The veins of the retina do not accurately follow the course of the arteries, but they behave similarly at the disc, uniting on, or slightly posterior to, its surface to form the central vein of the retina, which follows the course of the corresponding artery.

The blood supply of the optic nerve head in the region of the *lamina cribrosa* is served by fine branches from the arterial circle of Zinn but mainly from the branches of the posterior ciliary arteries (Fig. 1.11). The central retinal artery makes no contribution to this region. The *prelaminar region* is supplied by centripetal branches from the peripapillary choroidal vessels with some contribution from the vessels in the lamina cribrosa region. The central artery of the retina does not contribute to this region either. The surface layer of the *optic disc* contains the main retinal vessels and a large number of capillaries in addition to some small vessels. The capillaries on the surface of the disc are derived from branches of the retinal arterioles. In this part of the disc, vessels of choroidal origin derived from the adjacent prelaminar part of the disc may be seen usually in the temporal sector of the disc and one of them may enlarge to form a cilioretinal artery. The capillaries on the surface of the

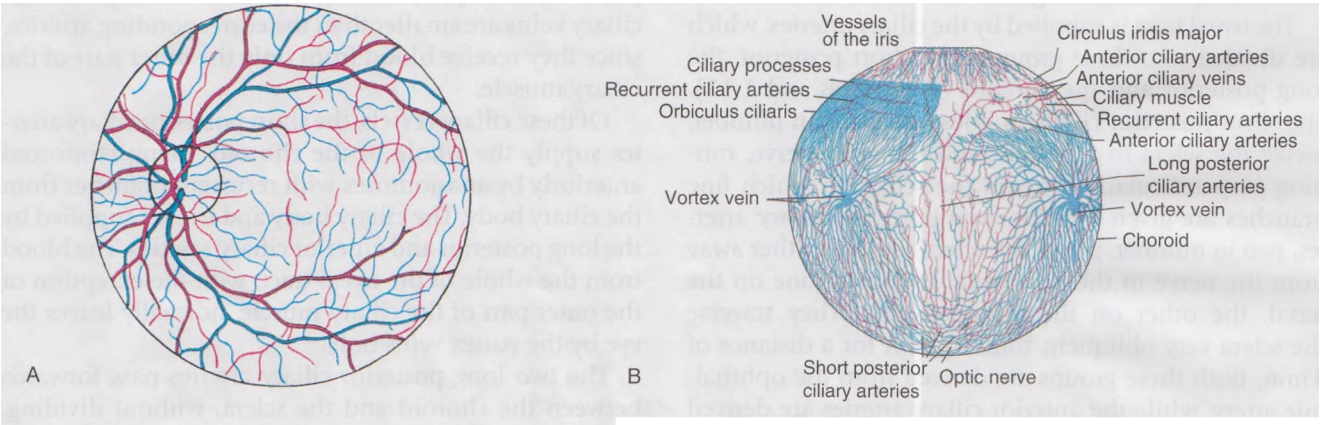


Fig. 1.10 (A) The retinal circulation; (B) the choroidal circulation.

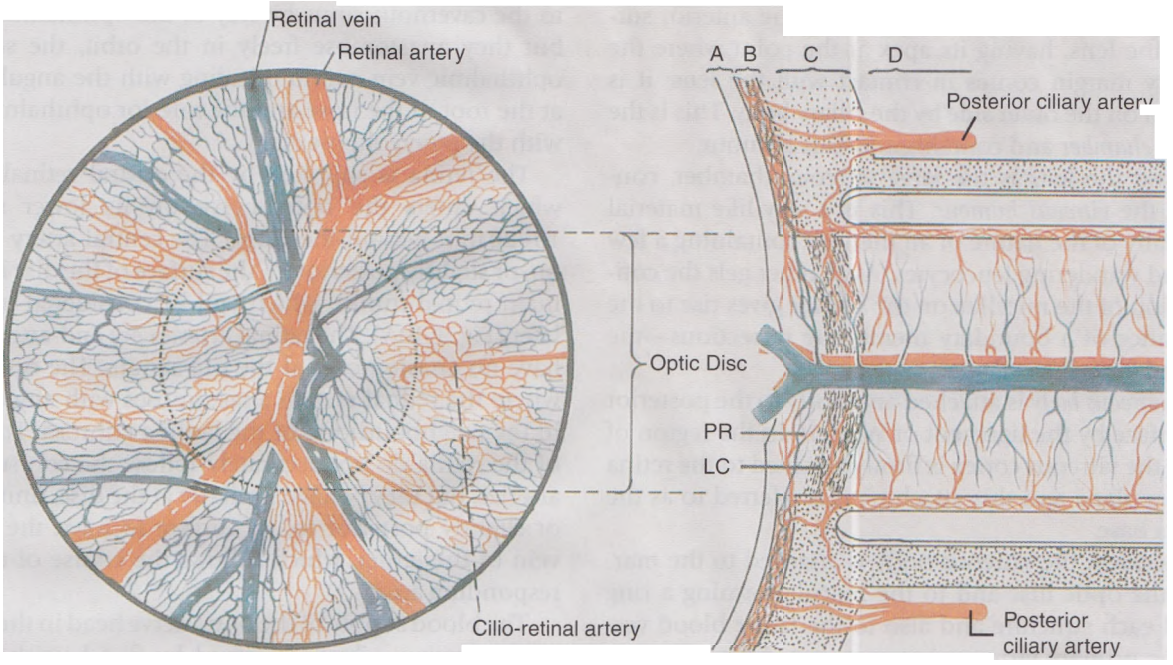


Fig. 1.11 Blood supply of the optic nerve. Region marked: A, represents the surface of the disc and peripapillary nerve fibre layer; B, portion anterior to the lamina cribrosa; C, portion related to the lamina cribrosa; D, portion behind the lamina cribrosa; LC, lamina cribrosa; and PR, prelaminar. (Reproduced with kind permission from Hayreh SS. *Arch Ophthalmology* 1977; 95:1560.)

disc are continuous with the capillaries of the peripapillary retina. These capillaries are mainly venous and drain into the central retinal vein. In the retrolaminar part of the optic nerve, blood is supplied by the intraneural centrifugal branches of the central artery of the retina with centripetal contributions from the pial branches of the choroidal arteries, circle of Zinn, central artery of the retina and the ophthalmic artery.

Venous drainage of the optic disc is mainly carried out by the central retinal vein. The prelaminar region also drains into the choroidal veins. There is no venous channel corresponding to the circle of Zinn. The central retinal vein communicates with the choroidal circulation in the prelaminar region.

The uveal tract is supplied by the ciliary arteries, which are divided into three groups—the short posterior, the long posterior and the anterior (Figs 1.10B and 1.12). The short posterior ciliary arteries, about 20 in number, pierce the sclera in a ring around the optic nerve, running perpendicularly through the sclera, to which fine branches are given off. The long posterior ciliary arteries, two in number, pierce the sclera slightly farther away from the nerve in the horizontal meridian, one on the nasal, the other on the temporal side. They traverse the sclera very obliquely, running in it for a distance of 4 mm. Both these groups are derived from the ophthalmic artery, while the anterior ciliary arteries are derived from the muscular branches of the ophthalmic artery to the four recti. They pierce the sclera 5 or 6 mm behind the limbus, or corneoscleral junction, giving off twigs to the conjunctiva, the sclera and the anterior part of the uveal tract.

The ciliary veins also form three groups—the short posterior ciliary, the vortex veins and the anterior ciliary. The short posterior ciliary veins are relatively unimportant; they do not receive any blood from the choroid; but only from the sclera. The vortex veins or venae vorticosae are the most important, consisting usually of four large trunks which open into the ophthalmic veins. They enter the sclera slightly behind the equator of the globe, two above and two below, and pass very obliquely through this tissue. The anterior ciliary veins are smaller than the corresponding arteries, since they receive blood from only the outer part of the ciliary muscle.

Of these ciliary vessels, the short posterior ciliary arteries supply the whole of the choroid, being reinforced anteriorly by anastomoses with recurrent branches from the ciliary body. The ciliary body and iris are supplied by the long posterior and anterior ciliary arteries. The blood from the whole of the uveal tract, with the exception of the outer part of the ciliary muscle, normally leaves the eye by the vortex veins only.

The two long posterior ciliary arteries pass forwards between the choroid and the sclera, without dividing, as far as the posterior part of the ciliary body. Here

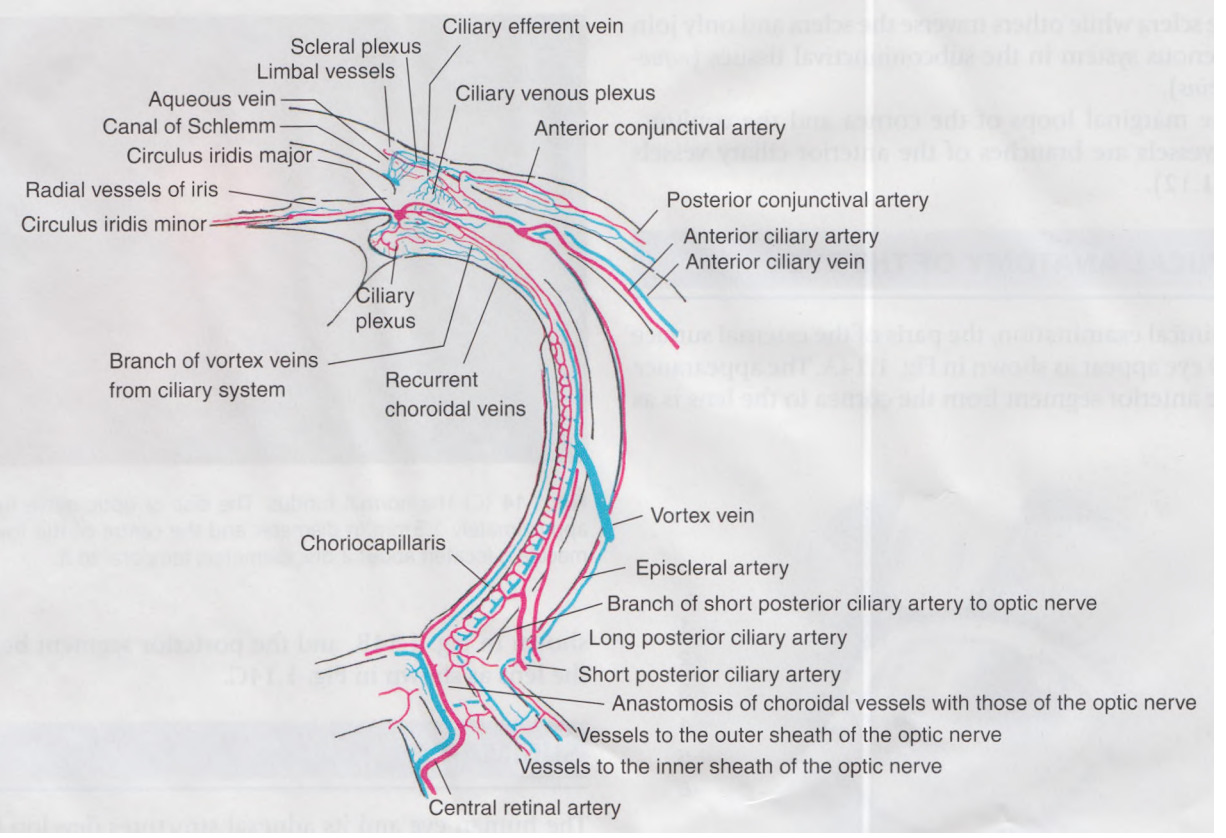


Fig. 1.12 The ciliary circulation.

each divides into two branches (Fig. 1.12); they run forwards in the ciliary muscle, and at its anterior part bend round in a circular direction, anastomosing with each other and thus forming the *circulus arteriosus iridis major*. This is situated in the ciliary body at the base of the iris; from it the ciliary processes and iris are supplied. Other branches from the major arterial circle run radially through the iris, dividing dendritically and ending in loops at the pupillary margin. A circular anastomosis takes place a little outside the pupillary margin, the *circulus arteriosus iridis minor*.

The tributaries of the vortex veins, which receive the whole of the blood from the choroid and iris, are arranged radially, the radii being bent, so as to give a whorled appearance—hence their name. The veins of the iris are collected into radial bundles which pass backwards through the ciliary body, receiving tributaries from the ciliary processes. Thus reinforced, they form an immense number of veins running backwards parallel to each other through the smooth part of the ciliary body. After reaching the choroid they converge to form the large anterior tributaries of the vortex veins.

The veins from the outer part of the ciliary body, on the other hand, pass forwards and unite with others to form a plexus (the *ciliary venous plexus*) which drains into the anterior ciliary veins and the episcleral veins. These vessels communicate directly with the canal of Schlemm which is intimately connected with the anterior chamber by means of numerous tortuous channels through the loose tissue of the trabecular meshwork (Fig. 1.4). From this canal the efferent channels form a complex system (Fig. 1.13); some ofthem drain into efferent ciliary veins

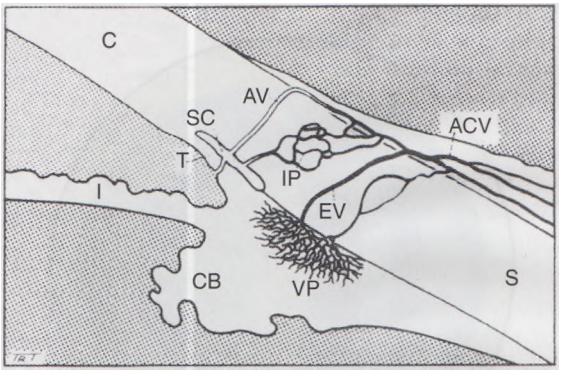


Fig. 1,13 The exit channels of the aqueous humour in man: C, cornea; S, sclera; I, iris; and CB, ciliary body. The primitive drainage channels of lower animals are seen in VP, the ciliary venous plexus, draining by EV, the ciliary efferent veins into ACV, and the anterior ciliary veins. Superimposed on this is the drainage system peculiar to primates, represented by T, the trabeculae; SC, the canal of Schlemm; IP, the intrascleral plexus; and AV, an aqueous vein emptying into the anterior ciliary veins.

in the sclera while others traverse the sclera and only join the venous system in the subconjunctival tissues (*aqueous veins).*

The marginal loops of the cornea and the conjunctival vessels are branches of the anterior ciliary vessels (Fig. 1.12).

CLINICAL ANATOMY OF THE EYE

On clinical examination, the parts of the external surface of the eye appear as shown i n Fig. 1.14A. The appearance of the anterior segment from the cornea to the lens is as shown in Fig. 1.14B, and the posterior segment behind the lens as shown in Fig. 1.14C.

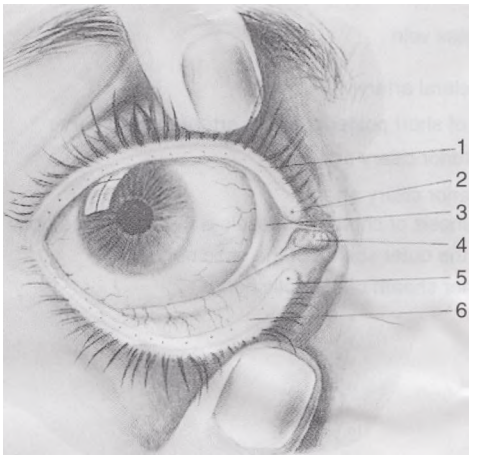


Fig. 1.14 (A) The surface anatomy of the lid margins and the conjunctival sac. The lids have been pulled aside to display their margins and expose the structures at the inner canthus. 1, intermarginal strip; 2, upper punctum; 3, plica semilunaris; 4, caruncle; 5, lower punctum; and 6, openings of the tarsal glands.

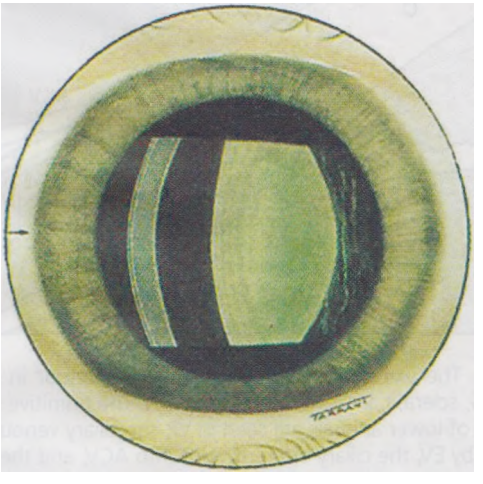


Fig. 1.14 (B) Optical section of the normal eye, as seen with the slit-lamp. The light (arrowed) comes from the left and, in the beam of the slit-lamp, the sections of the cornea and lens are clearly seen.

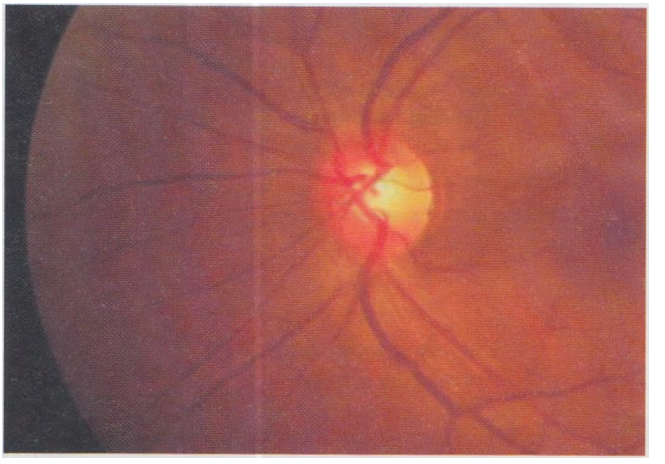


Fig. 1.14 (C) The normal fundus. The disc or optic nerve head is approximately 1.5 mm in diameter and the centre of the fovea or macula is located about 2 disc diameters temporal to it.

SUMMARY

The human eye and its adnexal structures develop from the neuroectoderm of the neural groove and the adjoining surface ectoderm, mesoderm and cells of neural crest origin. Though the development takes place by a predetermined sequence of events, local interactions and trophic influences affect the chain of interrelated processes which take place both simultaneously and sequentially. Teratogenic influences like intrauterine infections, noxious stimuli, maternal intake of drugs or alcohol, exposure to radiation, etc. can affect the normal course of development leading to abnormalities and congenital deformities. The milestones in embryological development are not absolute and are more representative of a time period than an actual finite time. Any disruption in that period will have an effect on the structures forming at that particular phase of development. As expected, abnormal developmental influences have a more severe impact if they occur early when the system is more immature and more prone to major developmental defects.

The eye is a complex anatomical structure consisting of delicate tissues. It is a sense organ which is designed to capture and focus light to form a retinal image which is translated into electrical signals and transmitted to the central nervous system via the optic nerve. The eye is protected from the environment by the eyelids, lashes and the orbital wall. The extraocular muscles function in a synchronized fashion to stabilize the globes, enable binocular vision and the full functional field of vision by allowing the full range of ocular movements. The blood supply of the eye and orbit is derived from the ophthalmic artery.

Overall the eye is a unique organ of the body as most of its anatomical structures are available for direct observation using appropriate optical devices such as the slit lamp and ophthalmoscope.

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2

Physiology of the Eye

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The human eye is a precise system which comprises components that must be optimally maintained so that a clear image is seen. Transparency, surface regularity and smoothness, and a stable ocular anatomy are important for sight. The constant shape of the eye is due to the structure of the sclera and a stable intraocular pressure, higher than the atmospheric pressure.

The anterior and posterior chambers of the eye are filled with aqueous humour, a fluid with an ionic composition very similar to blood plasma and with two main functions; to supply nutrients to the avascular structures of the eye—cornea and lens and to maintain intraocular pressure within its physiological range, because it is the volume of aqueous humour in the eye chambers that determines the IOP value.

NATURE AND FORMATION OF THE INTRAOCULAR FLUID

A two-way transference of fluid occurs through the capillary walls in all the organs of the body; allowing nutrients to be conveyed to the tissues and metabolites removed.

The capillaries in different tissues vary considerably in their permeability to suit local needs. The system of semipermeable membranes separating the blood from the ocular cavity is known as the blood-ocular barrier, the composition of which is shown in Fig. 2.1. The blood-aqueous barrier is formed in the posterior

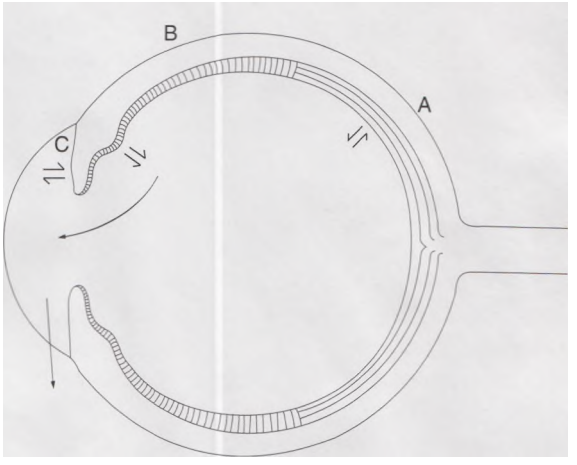


Fig. 2.1 The effective blood–ocular barrier. (A) In this zone the barrier is formed by retinal capillaries, Bruch's membrane and retinal pigment epithelium. (B) In this zone the barrier consists of the ectodermal layer formed by the anterior part of the retina and its prolongation as the ciliary epithelium. (C) In this zone the barrier is formed by the uveal capillaries only. The arrows indicate that in A and C, two-way traffic exists; in the ciliary region fluid traffic is essentially into the cavity of the eye, determining a circulation through the pupil and out at the angle of the anterior chamber.

segment of the globe by the walls of the retinal capillaries which, like those of the central nervous system, are nearly impermeable, and by Bruch's membrane and the retinal pigment epithelium. In the ciliary region it is formed by the two-layered ciliary epithelium, through which fluid must traverse before the posterior chamber is reached. In the iris it is formed by the walls of the capillaries in this tissue which are freely exposed to the anterior chamber through the crypts and spongy stroma.

For optical purposes, capillaries in the retina (like those in the central nervous system) are relatively impermeable so that practically no colloid molecules can pass into the cavity of the eye. Fluorescein in the blood stream is readily bound to albumin, making a larger molecular complex. The blood-retinal barrier, by preventing leakage of this dye in the physiological state, results in a clear outline

of retinal vessels of all calibres. In the choroidal circulation, fluorescein passes freely across the endothelium of capillaries to the extravascular spaces. There is, however, a physiological barrier to the passage of dye from these spaces across Bruch's membrane and the intact retinal pigment epithelium into the subretinal space.

The peculiar impermeability of the retinal capillaries and of the Bruch's membrane-pigment epithelial barrier, while necessary from the optical point of view, prevents the ready passage of large-sized molecules of any kind into the eye. Antibiotics, when administered systemically, are often of little value in ocular therapeutics. Substances with a high lipoid solubility, however, which easily penetrate living cells, traverse the barrier much more readily such as sulphonamides and chloramphenicol.

It is obvious that if the permeability of the capillaries is increased, large molecules will be able to pass through their walls, so that a turbid fluid rich in protein is formed—*plasmoid aqueous*. This increase in permeability may be brought about by vasodilator drugs, in inflammatory conditions such as iridocyclitis or choroiditis, and also if the capillary walls are mechanically stretched by suddenly lowering the intraocular pressure and removing their external support. This occurs when the globe is suddenly opened as by paracentesis or when the intraocular pressure is lowered by vigorous massage of the globe. Such a two-way transference of fluid across the capillary walls would lead to stagnation.

Formation of the aqueous humour (Fig. 2.2) is known to involve a number of mechanisms—ultrafiltration, diffusion and secretion. The secretory process is powered by the metabolic activity of the cells of the ciliary epithelium and probably accounts for some 95% of the total quantity of aqueous. The entire mechanism is not understood, but it is known that a watery fluid rich in sodium and containing small quantities of ascorbic acid and other substances is secreted into the posterior chamber.

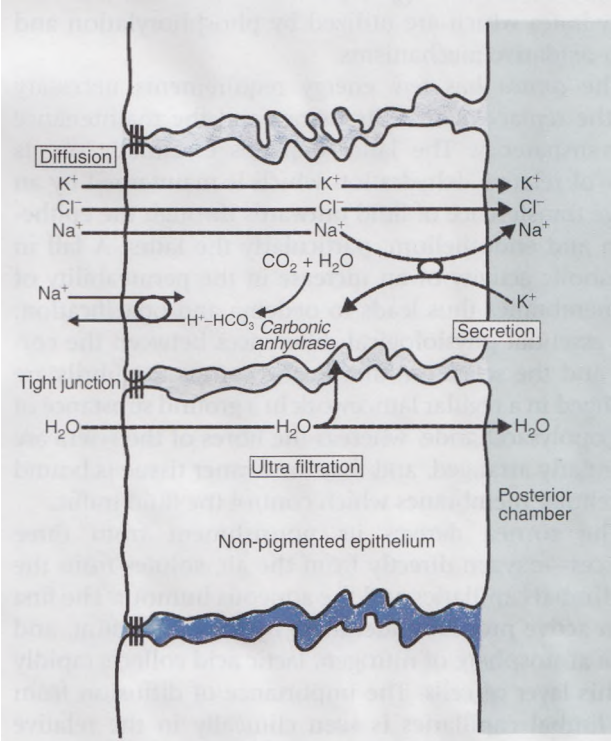


Fig. 2.2 Formation of aqueous humour.

Having this varied origin, the aqueous humour thus consists of a dilute solution of all the diffusible constituents of the plasma, in addition to the substances specifically secreted. Since entry into the eye across the blood-aqueous barrier is difficult and exit through the drainage channels is easy, many of the constituents of the aqueous humour are in deficit in comparison with the blood, with the exception of those secreted. There is, however, an excess of lactic acid in the aqueous compared with the blood due to the formation of this substance as an end-product of the metabolism of the lens.

CIRCULATION OF THE AQUEOUS HUMOUR

Circulation of aqueous is necessary both for metabolic purposes and to regulate the intraocular pressure. As the greater part of the fluid is formed in the ciliary region, it flows from the posterior chamber through the pupil into the anterior chamber and escapes through the drainage channels at the angle, i.e. trabecular meshwork, Schlemm's canal, collector channels and aqueous veins, and from there into the episcleral veins. In addition to this there is a second accessory exit (the *uveoscleral outflow)* through the ciliary body into the choroid and suprachoroid and into the episcleral tissue. Although a minor means of exit, this pathway assumes importance if the conventional outflow is impeded and in inflammatory conditions.

INTRAOCULAR PRESSURE

The major factors controlling intraocular pressure are the dynamic balance between aqueous humour production in the ciliary body and its elimination via the canal of Schlemm. Other factors like choroidal and vitreous blood volume and the extraocular muscle tone can also affect intraocular pressure, generally in the short term.

Prolonged changes in intraocular pressure are essentially caused by two factors: (i) an alteration in the forces determining the formation of the aqueous; and (ii) alterations in the resistance to its outflow. From the clinical point of view the latter is the more important. A rise in intraocular pressure may be caused either by a process which blocks the seepage of aqueous into the canal of Schlemm, such as sclerosis of the trabeculae or their obstruction by exudates or organized tissues, or by

an increase in pressure of the episcleral veins, into which the aqueous drains. In either event glaucoma is the result. If the drainage channels to the canal of Schlemm are blocked, the intraocular pressure does not chronically rise indefinitely. It cannot rise above the mean blood pressure since at that point the circulation will cease; moreover, some drainage of intraocular fluid will take place through the uveoscleral outflow.

While these are the principal factors determining prolonged changes in the intraocular pressure, other factors can exert more temporary effects.

1. *Variations in the hydrostatic pressure in the capillaries:* It is obvious that the pressure in the eye will follow all such variations; thus it follows faithfully the pulse and respiratory rhythms.
2. *An increase in permeability of the capillaries,* allowing the formation of a plasmoid aqueous with a high protein content, will increase its osmotic pressure relative to that of the blood and thus raise the pressure in the eye, a process accentuated if the drainage channels become clogged. This occurs particularly in inflammations.
3. A *change in the osmotic pressure of the blood* will be reflected in the intraocular pressure by altering the process of diffusion across the capillary walls, hypotonicity inducing a rise as in the water-drinking test and hypertonicity a fall. This can be demonstrated experimentally, and in clinical conditions such changes are induced by the use of glycerol by mouth or mannitol intravenously.
4. *Volumetric changes* within the globe should be immediately transformed into pressure changes owing to the indistensibility of the sclera; if extra fluid, such as a vitreous haemorrhage, were forced into the eye its tension would rise abruptly.
5. A *blockage of the circulation of aqueous,* on the other hand, has a profound effect in raising the ocular tension. Such a block may occur in two places: (i) at the pupil where the flow of fluid from the posterior to the anterior chamber may be impeded; and (ii) at the angle of the anterior chamber. Obstruction in situation (i) is usually due to one of two causes. The first arises in eyes with a shallow anterior chamber—a lax iris has a larger area of apposition to the anterior surface of the lens, causing the condition of 'relative pupillary block' with the aqueous being dammed in the posterior chamber. The iris billows forward to reach the cornea and blocks the angle of the anterior chamber, leading to an attack of primary angle-closure glaucoma. Obstruction in situation (ii) is due to organic changes when the iris becomes adherent to the anterior capsule of the lens in inflammatory conditions or fibrosis after neovascularization, when secondary glaucoma occurs.

Inefficiency of the drainage channels, on the other hand, causes either a cumulative rise of pressure or transient increments.

The intraocular pressure within the eye normally varies from 10 to 20 mm Hg. It is most accurately measured by *manometiy.* A small cannula is inserted into the anterior chamber and connected with a small-bore mercury or saline manometer. Such a technique is used experimentally on animals but its clinical application is obviously impossible. The sclera is only very slightly elastic and is rendered tense by the internal pressure, allowing the intraocular pressure to be measured by the degree to which it can be indented on the application of a standard weight or flattened by a measured pressure with considerable accuracy. Such a method is used clinically in *tonometry (see* p. 126). The result thus obtained (usually given also as mm Hg by standardization with a manometer on experimental animals) is referred to as the *intraocular pressure.*

METABOLISM OF THE OCULAR TISSUES

The vascularized tissues of the eye, particularly the uveal tract, differ in no respect in their general metabolism from other tissues in the body.

The non-vascularized tissues of the eye—the cornea and the lens—must obviously have a specialized metabolism, and so far as our present knowledge goes, they depend for their energy requirements essentially on carbohydrates which are utilized by phosphorylation and auto-oxidative mechanisms.

The *cornea* has few energy requirements necessary for the replacement of its tissues and the maintenance of transparency. The latter depends essentially on its state of relative dehydration which is maintained by an active transference of fluid outwards through the epithelium and endothelium, particularly the latter. A fall in metabolic activity or an increase in the permeability of its membranes thus leads to oedema and opacification. The essential physiological differences between the cornea and the sclera are that in the cornea the fibrils are arranged in a regular latticework in a ground substance of mucopolysaccharide, whereas the fibres of the sclera are irregularly arranged, and that the former tissue is bound by cellular membranes which control the fluid traffic.

The cornea derives its nourishment from three sources—oxygen directly from the air, solutes from the perilimbal capillaries and the aqueous humour. The first is an active process undertaken by the epithelium, and in *an* atmosphere of nitrogen, lactic acid collects rapidly in this layer of cells. The importance of diffusion from the limbal capillaries is seen clinically in the relative resistance of the peripheral parts of the cornea to degenerative changes, but, at the same time, if these vessels

are experimentally cut, corneal transparency is maintained. Similarly, if the aqueous is replaced by nitrogen, the cornea remains transparent; but it turns opaque if both these sources of nutrition are cut off. Metabolic activity which exhibits a high rate of aerobic glycolysis is maintained by the aid of enzyme systems, as occurs in the lens.

The *lens* derives its nourishment entirely from the aqueous humour in which it is immersed, the fluid traffic being regulated by the semipermeability of the capsule and the subcapsular epithelium. If this membrane is disrupted, the whole tissue, like the cornea, tends to adsorb fluid and turn opaque. Active transport takes place between the lens and the aqueous owing to the activity of the subcapsular epithelium. The capsule itself is freely permeable to water and electrolytes as well as colloids of small molecular size, the posterior part being more permeable than the anterior. The permeability of the capsule decreases with age.

The fact that the lens has a respiratory quotient ($C0_2/0_2$) of 1.0 shows that carbohydrate is its essential source of energy, a conclusion confirmed by the fact that the aqueous in the aphakic eye contains more glucose than in the normal eye. Chemical studies have shown that the initial stage in the breakdown of the sugar is its combination with phosphates (phosphorylation) in the production of pyruvic acid; and radioactive tracers have found this to occur particularly in the cortical layers. In all tissues this chemical process is effected by enzymes (such as hexokinase) which have been demonstrated in the lens; in this process oxygen is not required. For the further catabolism of pyruvate, oxygen is sometimes used. There is a small amount of oxygen in the aqueous derived from the blood, but by which enzymes it is used in the lens is not yet clear. The essential process is probably anaerobic and in the lens there are a number of enzymes which break down pyruvate to lactic acid and water. Lactic acid is found in considerable quantity in the aqueous humour when the lens is present; this is not so in the aphakic eye. Agents which appear to participate in this process are glutathione and ascorbic acid (vitamin C) which, reacting together, probably participate in an internal auto-oxidative system. The former, both as reduced and oxidized glutathione, occurs in very high concentration in the lens, particularly in the cortex; the latter is specially secreted by the ciliary body. Neither is present in cataract. The metabolic activity of the lens is largely confined to the cortex; the older nucleus is relatively inert.

The metabolism of the lens is fairly complex but can be simplified for presenting an overview. The energy requirements are met by various pathways of glucose metabolism, namely the glycolysis (Embden-Meyerhoff-Parnas [EMP]) pathway, pentose phosphate pathway and the tricarboxylic acid (TCA) cycle. Energy is stored in the form of adenosine triphosphate (ATP). Most of the glucose which enters the normal lens (90%-95%) is converted into glucose-6-phosphate by the enzyme hexokinase and a small quantity is converted by the enzyme aldose reductase into sorbitol and enters the sorbitol pathway. The latter pathway becomes more important when there is excess glucose in the lens as in diabetes. About 80% of the glucose is then metabolized by the EMP pathway which is the anaerobic pathway of glycolysis. Around 10% of glucose is utilized by the pentose phosphate pathway which, in addition to generating reduced nicotinamide adenine di-nucleotide phosphate (NADPH)—an important reducing substance required for the biosynthesis of many vital cellular components such as reduced glutathione—also generates the building blocks for synthesis of nucleic acids, proteins and components of cell membranes. As the oxygen content of the lens is low, only about 3% of glucose is metabolized aerobically by the TCA cycle. However, as the latter is more efficient in the generation of ATP, it produces about 25% of the ATP present in the lens, with 70% being produced by anaerobic glycolysis. The TCA cycle occurs more prominently in the lens epithelium.

SUMMARY

The important physiological processes necessary for the functioning of the eye relate to the blood-ocular barrier formation and circulation of intraocular fluid, maintenance of intraocular pressure and metabolism of the different ocular tissues.

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3

The Physiology of Vision

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The function of the eye is to form a clear image of a stimulus on the surface of the retina. The anterior surface of the cornea accounts for about two-thirds of the refractive power of the eye. The lens further refracts the rays of light entering the eye and is responsible for the ability to see objects at all distances. The ocular lens changes shape, more spherical for near objects and flatter for far ones, by a reflex contraction or relaxation of the ciliary muscles. The pupillary size is adjusted for varying light intensities by a reflex contraction and dilation of the sphincter and dilator pupillae.

There are approximately 1 million retinal ganglion cells in the human eye. In contrast, there are approximately 125 million photoreceptors. There is a one-to-one correspondence between photoreceptors and retinal ganglion cells at the fovea, but in the periphery there are more photoreceptors than ganglion cells leading to a progressive loss in resolution.

The eyes convert light energy in the wavelengths of 397-723 nm into electrical signals in the optic nerve. A single rod is able to detect a single photon of light with a peak sensitivity of 505 nm which is roughly green light, but the rods are low resolution detectors so the images are formed without much detail.

It follows that rays falling upon the optic disc give rise to no visual sensation and this is therefore called the *blind spot* (of Mariotte). Light falling upon the retina, however, causes two essential reactions, photochemical and electrical.

The *photochemical changes* concern pigments in the rods and cones. The most fully explored pigment is rhodopsin (visual purple), found in considerable quantity in the rods; several related pigments have been discovered in the rods of various types of animals, while it would seem that three different pigments are associated with the foveal cones. Rhodopsin is a chromoprotein, the molecule of which consists of a reactive part, a chromophore, responsible for the preferential absorption of light, attached to a protein which acts essentially as a support. The chromophore belongs to the family of carotenoids and when exposed to light it is broken down through several intermediaries to the colourless vitamin A, a reaction which is reversible. It is this photochemical reaction which initiates the visual process and gives rise to the changes in electrical potential which are transmitted through the bipolar cells to the ganglion cells and along the fibres of the optic nerve to the brain. The pigments in the cones have not yet been fully elucidated, but it is likely that each reacts preferentially to different bands of wavelength in the spectrum, which are perceived as red, green and blue.

RHODOPSIN CYCLE

Rhodopsin is the visual pigment in the outer segment of rods responsible for scotopic vision, or the ability to see in the dark. Rhodopsin has 11 *cis* retinal as its chromophore, which is embedded by three different chemical bonds inside a single peptide transmembrane protein called opsin. The role of rhodopsin in the signal transduction cascade of vision is to activate transducin,

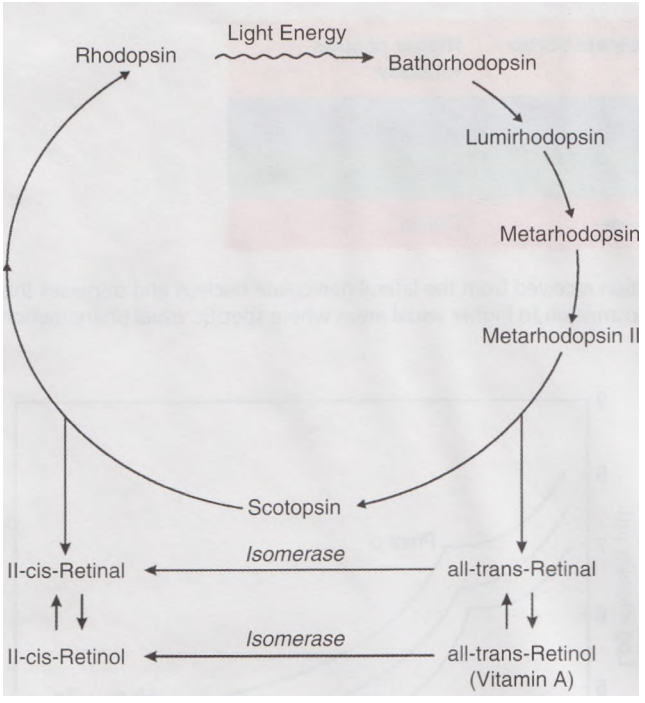


Fig. 3.1 Rhodopsin cycle.

a heterotrimeric G protein, upon absorption of light. Absorption of a photon of light by the chromophore leads to an initial photoreaction, and then conformational changes of protein that result in the activation of transducin. With this change, rhodopsin loses its colour leading to the term, 'bleaching'. The *cis-trans* isomerization of the chromophore occurs during the bleaching process of rhodopsin. A number of intermediate states are formed during this process (Fig. 3.1).

Formation of the electronically excited state of rhodopsin and photorhodopsin, as well as hypsorhodopsin, has been observed almost immediately. Bathorhodopsin is formed in picoseconds, lumirhodopsin in microseconds, metarhodopsin I in milliseconds, followed by metarhodopsin II, which activates transducin and produces all *trans* retinal and opsin. In the presence of darkness, these two products are brought together again within the retinal pigment epithelium to form 11 cis retinal.

A human rod cell can respond to a single photon absorption, demonstrating the efficiency of the photoisomerization.

MAGNOCELLULAR, PARVOCELLULAR AND KONIOCELLULAR PATHWAYS

The photoreceptors, when stimulated, transmit signals to the bipolar cells which connect with retinal ganglion cells. Retinal physiology at the level of neurotransmission and communication between cells is actually quite complex, with the cells connecting in specific patterns depending on the nature of the stimulus. For example, some domains are activated when a light is switched on and others when a light is turned off. In addition, the retinal ganglion cells themselves are of three types. In the human retina one class of ganglion cells is smaller, has thinner axons of smaller calibre, and is the predominant type in the macular region. These ganglion cells are colour sensitive, the physiological response is of the colour-opponent type with high spatial frequency resolution. These are known as the P cells and form part of the *parvocellular* or P *cell system.* P cell system responds transiently to constant stimulation with short latencies and are colour selective. The axons of the P cells, which constitute about 90% of the retinal ganglion cells, terminate in the parvocellular layers of the lateral geniculate nucleus (LGN). The remaining retinal ganglion cells are called M cells and are a part of the *magnocellular pathway.* These are larger cells, with thicker, larger axons which are fast-conducting and primarily transmit high temporal motion-related information of low spatial frequency unrelated to colour.

The lateral geniculate body regulates neural information from the retina to and from the cortex. It organizes incoming information to different layers based on the eye that the signals come from and also the originating retinal ganglion cells. The LGN is comprised of multiple layers with each receiving input from only one eye. There is ipsilateral input to layers 2, 3 and 5 and contralateral to layers 1, 4 and 6.

Retinal cells with a particular function project to similar LGN cells, e.g. those with red-on/green-off centre surround receptive fields.

M-cells synapse onto the magnocellular layers 1 and 2, P-cells synapse onto layers 3-6 of the LGN and these are called the parvocellular layers. Konio cells are present in the intralaminar area.

The cortical visual system is now thought to consist of two areas. The primary visual or striate cortex (VI) that transforms information received from the LGN and distributes it to separate domains in the secondary or extrastriate cortex (V2) for transmission to higher visual areas. It is likely that the visual attributes of colour, form and motion are not neatly segregated, instead, there are just two main streams composed of a mixture of magno, parvo and konio geniculate signals (Fig. 3.2).

The study of the *electrical* responses which follow has yielded results of great interest although all their implications are not yet clear. When the retina is stimulated, electrical variations (action potentials) occur in the optic nerve fibres, presumably initiated by the photochemical changes in the rods and cones.

These are of the same type as occur in all sensory nerves; they consist of biphasic variations always of the same amplitude (the all-or-none response) but varying in frequency with the intensity of the stimulation.

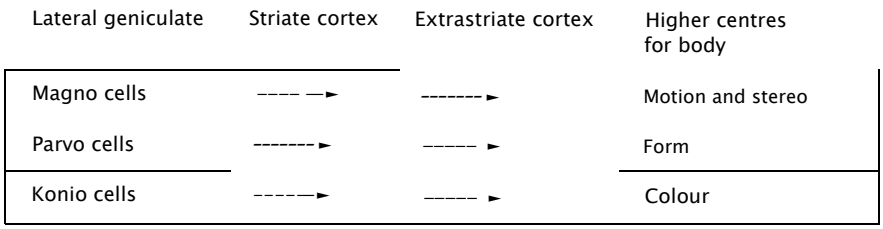


Fig. 3.2 The primary visual cortex, the striate cortex, transforms information received from the lateral geniculate nucleus and disperses this to appropriate areas in the extra striate or secondary visual cortex for transmission to higher visual areas where specific visual phenomenon is registered (as proposed by Livingstone and Hubei).

In vertebrate eyes some fibres show a burst of activity at the onset of stimulation (the 'on-effect'), others show activity while the stimulus lasts, and yet others show a burst of activity, presumably inhibitory in nature, when stimulation ceases (the 'off-effect'). A single nerve fibre reacts when a considerable area of the retina is stimulated; this (the receptive field) varies in extent from a diameter of 0.5-1.0 mm and indicates the synaptic link-up of each ganglion cell with a number of receptor cells. Moreover, differences in the reaction resulting from stimulation by isolated wavebands of light show that a neural mechanism exists that is capable of colour discrimination. Reaching the occipital cortex some 124 ms after retinal stimulation, these impulses modify the electrical activity of the brain as recorded by the electroencephalogram. A somewhat crude additive record of the electrical changes in the retina can be obtained clinically in the electroretinogram, a technique which can be of diagnostic value in retinal disease.

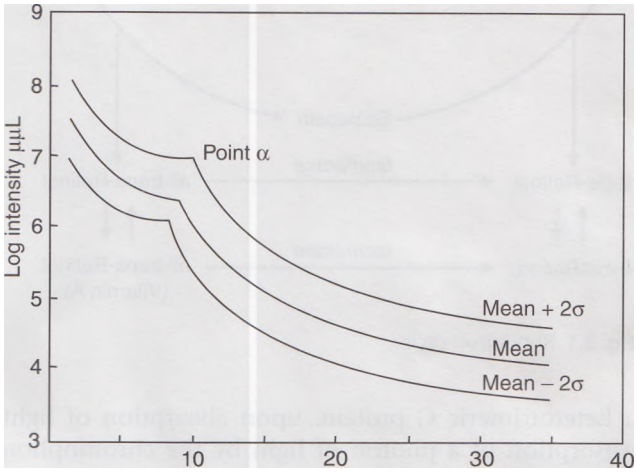


Fig. 3.3 Dark adaptation curve. The initial small symmetrical curve represents the adaptation of cones. It is broken at a sharp knee (a) and the remainder of the curve represents the adaptation of rods (after Sloan).

VISUAL PERCEPTIONS

Sensations which result from stimulation of the retina by light are of four kinds—the light sense, form sense, sense of contrast and colour sense.

Light sense

This is the faculty which permits us to perceive light, not only as such but also in all its gradations of intensity. If the light which is falling upon the retina is gradually reduced in intensity there comes a point when it is no longer perceived: this is called the *light minimum.* The eye functions in a wide range of lighting conditions, and adaptation to such changes is necessarily very rapid in daily life. This ability of the visual system to allow good visibility in different lighting situations is referred to as light and dark adaptation. We are all aware that if we go from bright sunshine into a dimly lit room we cannot perceive the objects in the room until some time has elapsed—the eyes have to become 'adapted' to the amount of illumination. Hence observations on the light minimum are only comparable when the eyes are in the same condition of dark adaptation as is obtained by excluding light from them for at least 20-30 minutes. The light minimum for the fovea is considerably higher than for the paracentral and peripheral parts of the retina, and retinal adaptation affects the macula relatively little (Fig. 3.3). It follows that in diseases which affect the rods particularly, much of the ability to adapt is lost and the patient is virtually night-blind.

The rods are much more sensitive to low illumination than the cones, so that in the dusk we see with our rods *{scotopic vision*); in bright illumination the cones come into play *(photopic vision).* Nocturnal animals, like the bat, have few or no cones; diurnal animals, like the squirrel have no rods; man has an ample supply of both.

Form sense

This sense, which is next in importance, is the faculty which enables us to perceive the shape of objects in the outer world. Here the cones play the predominant part, and the form sense is most acute at the fovea, where they are most closely set and most highly differentiated. It falls off very rapidly towards the periphery, as is shown in Fig. 3.4, and it is noticeable that the curve agrees fairly well with the diminution in the number of cones. Visual acuity is the capacity to see fine details of objects in

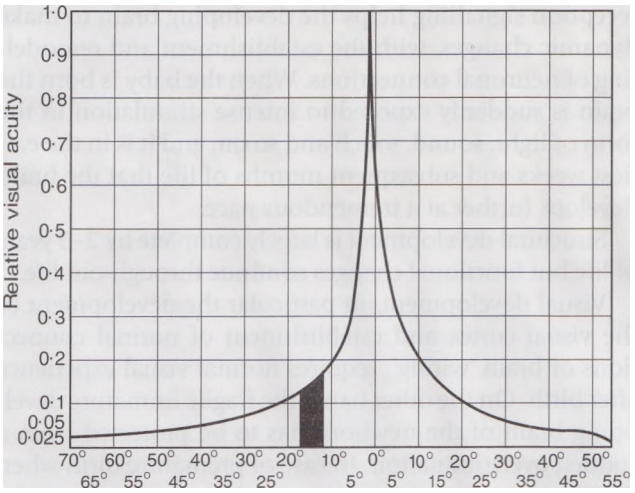
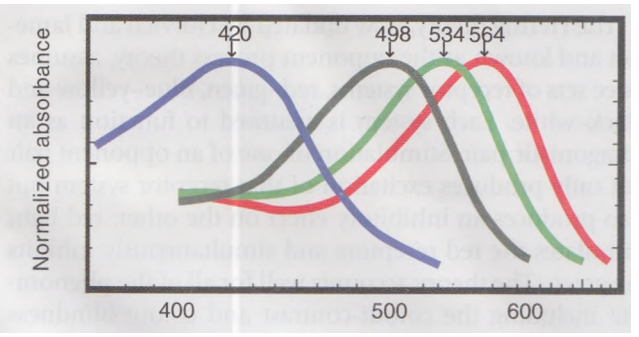


Fig. 3.4 Regional variations of visual acuity in the retina.



Fig, 3.5 Four classes of photopigments are found in human photoreceptors. The 420 curve is for short-wavelength cones, the 498 curve is for rods, and the 534 and 564 curves are for middle- and long-wavelength sensitive cones, respectively. (Bowmaker JK, Dartnall HJA. Visual pigments of rods and cones in a human retina. *J Physiol* 1980; 298:501–11)

the visual field. The acuity of vision, therefore, applies to central vision or the vision of objects, the images of which are formed at the fovea. The form sense is not a purely retinal function, for in the perception of composite forms—such as letters—it is largely psychological. Visual acuity is measured in a variety of ways, the most common being recognition (Snellen chart), resolution (acuity grating) and localization (Vernier acuity).

Sense of contrast

The ability to perceive slight changes in luminance between regions which are not separated by definite borders is just as important as the ability to perceive sharp outlines of relatively small objects. It is only the latter ability which is tested by means of the Snellen chart. In many diseases loss of contrast sensitivity is more important and disturbing to the patient than the loss of visual acuity *(see* p. 107).

Colour sense

This is the faculty that allows us to distinguish between different colours as excited by light of different wavelengths. The appreciation of colours is a function of the cones and therefore occurs only in photopic vision, that is, with lights of moderate or high intensity and with some degree of light adaptation of the retina. In very low intensities of illumination, the dark-adapted eye sees no colour and all objects are seen as grey, differing somewhat in brightness.

In different cones there are three pigments which absorb preferentially wavelengths of light in the spectrum corresponding to the colours red, green and blue (Fig. 3.5), and if these (or, indeed, any three colours sufficiently far apart in the spectrum) are chosen, all the other colours as well as white light can be formed by their combination in suitable proportions. Hence normal colour vision is called *trichromatic*. This is the basis of the Young-Helmholtz theory of colour vision. In its original form this theory does not adequately explain all the phenomena associated with the appreciation of colour by normal individuals and in the colour defective, but that there is a trichromatic stage in the visual process is undeniable.

Theories of colour vision

The two best-known theories are the Young-Helmholtz theory (also known as the trichromatic theory or trireceptor theory) and the Hering theory (or opponent process theory).

The Young-Helmholtz theory assumes three types of colour receptors. Although each receptor is assumed to respond to all wavelengths, they have different spectral sensitivities, so that one is more sensitive to long wavelengths (reds), one to medium wavelengths (greens) and one to short wavelengths (blues). All other colours are assumed to be perceived by combinations of these so that the perception of yellow, for example, is characterized as being due to the simultaneous stimulation of red and green receptors and their integration in the visual neural pathways and the visual cortex. The theory accounts well for the laws of colour mixing although it has some difficulty with the other basic phenomena. In particular, the theory cannot easily explain the fact that dichromats who confuse red with green see yellow. It also has difficulty explaining complementary colour after-images.

Hering hypothesized that trichromatic signals from the cones fed into subsequent neural stages and exhibited two major opponent classes of processing:

1. spectrally opponent processes, which were red versus green and yellow versus blue and
2. a spectrally non-opponent process, which was black versus white.

The Hering theory, now updated by Hurvich and Jameson and known as the opponent process theory, assumes three sets of receptor systems, red-green, blue-yellow and black-white. Each system is assumed to function as an antagonistic pair. Stimulation of one of an opponent pair not only produces excitation of that receptor system but also produces an inhibitory effect on the other; red light stimulates the red receptors and simultaneously inhibits the green. The theory accounts well for all of the phenomena including the colour-contrast and colour-blindness data which are bothersome to the trireceptor theory.

Edwin Land proposed another theoretical model of colour vision. He hypothesized three separate visual systems (retinexes), one responsive primarily to long-wavelength light, one to moderate, and the third to short-wavelength light. Each is represented as an analogue to a black-and-white picture taken through a particular filter, with each one producing maximum activity in response to red, green and blue light for the long-, moderate- and short-wavelength retinexes, respectively.

Both theories help to explain how our colour vision system works. The trichromatic theory operates at the receptor level and the signals are then recorded into the opponent process form by higher level neural systems of colour vision processing.

PHYSIOLOGY OF VISION AND THE DEVELOPING BRAIN

The brain is a dynamic organ which starts developing *in utero* and continues to change throughout life. The initial development of the visual pathway involves the correct 'wiring' of the system with the axons of the retinal ganglion cells reaching their correct destination in the lateral geniculate body. New cells arising from here then grow to reach their designated place in the visual cortex. The fibres develop further by establishing complex neuronal connections with association areas. This is genetically determined but environmental influences do play a role. Later on, there is a further rewiring and pruning of the various connections by which unwanted or underutilized connections simply get eliminated and the useful connections get selected and strengthened. The system has been compared to a giant telephone network where 'calls' are made from the retinal ganglion cells and appropriate wires connect to the right spot where the 'call' is registered. Initially the 'call' has the possibility of reaching several locations so that a particular spot in the brain can receive calls from different locations. However, as the machinery develops, the well-utilized pathways remain and the unused connections or unwanted paths get disconnected and disappear.

Even *in utero,* when the baby is completely in the dark, the retinal ganglia spontaneously send out signals and 'connect' to target cells in the brain. This stimulation and reception signalling helps the developing brain to make dynamic changes, with the establishment and remodelling of neuronal connections. When the baby is born the brain is suddenly exposed to intense stimulation in the form of light, sound, touch and so on, and it is in the earliest weeks and subsequent months of life that the brain develops further at a tremendous pace.

Structural development is largely complete by 2-3 years of life but functional changes continue through-out life.

Visual development, in particular the development of the visual cortex and establishment of normal connections or brain 'wiring', requires normal visual experience after birth. On the other hand, the fragile immature developing brain of the newborn has to be protected from a sudden overstimulation. In case of premature birth when the circuits are even more incomplete, the development is again modified as the normal intrauterine developing process has been interrupted and the brain is more sensitive to the environment which a full-term baby would not have been exposed to at the same stage of development.

The delicate balance between visual stimulation in the 'right amount' at the 'right time' and the development of the brain has been maintained by nature in ways which are partly understood and partly still remain a mystery.

What exactly a baby sees cannot be directly assessed in the same way as we estimate vision in adults.

According to infant vision research studies, the baby gets a blurred view of the world and it is the eye which naturally protects the immature brain from a level of stimulation which it cannot cope with initially. The newborn's eye is short, generally hypermetropic and the fovea is immature. The baby also sleeps most of the time so the eyes are closed during the greater part of the day. Apart from an inaccurate focusing and imaging system, the newborn's eyes are not binocularly coordinated so they do not have binocular stereoscopic vision and have a limited peripheral field of view. The visual cortex is also immature. Unlike the brain of an adult, the cells are intermixed and are not segregated by type or arranged as columns. Also, a majority of the cells have not yet acquired the fatty myelin sheath which is required for enhancing rapid communication between cells.

Starting from the moment of birth, the eye and the brain start developing together in consonance and any interruption or interference with the transmission of the light stimulus from the eyes to the brain disrupts the harmony and results in serious visual damage.

The work of Nobel laureates David Hubei and Torsten Wiesel with developing kittens and T. Lewis, Maurer and others in human children has helped provide insight into these physiological changes. The sensitive period is the time when the visual system is still plastic and if vision is obstructed, potentially permanent changes in the neural connections occur which are completely reversible by appropriate intervention only within this period.

The phrase 'use it or lose it' best describes the changes taking place in the selection or severing of connections which takes place if vision from one eye or both eyes is absent or remains unclear. In kittens, if one eye is kept closed for 8 weeks, the brain loses its ability to respond to stimulation from that eye but if initially closed and then reopened within the 8-week critical period the brain retains its ability to 'respond' to light stimulating that eye. In human children the sensitive period is up to 8 years but the first 3 years are the most crucial.

In the developing vision of an infant some milestones are worth remembering. Very soon after birth the baby can 'fix' or look at a light held a few inches away momentarily. By using black and white vertical stripes to estimate the limit of resolution of visual acuity, a week-old baby can only perceive stripes which are two-fifths of an inch wide at a distance of 4 feet, which is 30 times wider than the finest stripes an adult can visualize at the same distance. By 1 month the fixation of light becomes more steady and the baby develops a preference for looking at a face or a face-like stimulus over any other object nearby. By 3 months, binocular vision and eye coordination are established and the eyes will follow a torch held in front of the face or a person moving across the room. The baby smiles in response to a visible smile, stops crying when the mother enters the room or recognizes familiar faces and objects. By 4 months the infant displays a recognition pattern similar to adults if a face is presented upside down and recognizes a face presented in the left visual space more quickly than in the right, expressing a right-hemisphere dominance for recognizing faces.

By 6 months, EEG recordings confirm the infant's preference for looking at a human face, a clear preference for the mother as compared to a stranger and recognition of a familiar toy. At 6 months of age the ability to reach out, grasp and play with small objects and efforts to adjust position to see a toy develop. By 9 months most children 'look' for a toy if they see it being hidden. From 6 months onwards formal tests of vision can be attempted *(see* p. 101) but it is not until 6 years of age that the normal resolution visual acuity levels such as that of adults, i.e. 6/6, 20/20 are attained.

BINOCULAR VISION AND STEREOPSIS

The images of the two eyes are combined by the visual cortex and are seen as a single image. The eyes adjust their position by sensory and motor alignment based on visual input to the cortex and the visual association areas, which then project appropriate impulses to the centres controlling eye movements in the brain stem (see Chapter 25). This complex integrated network ensures that the image of the object being viewed falls on the foveae of the two eyes and all other objects are imaged on corresponding retinal points. This is easily understood by the concept of an imaginary line in space (horopter), which is the external projection of these corresponding retinal points (Fig. 3.6).

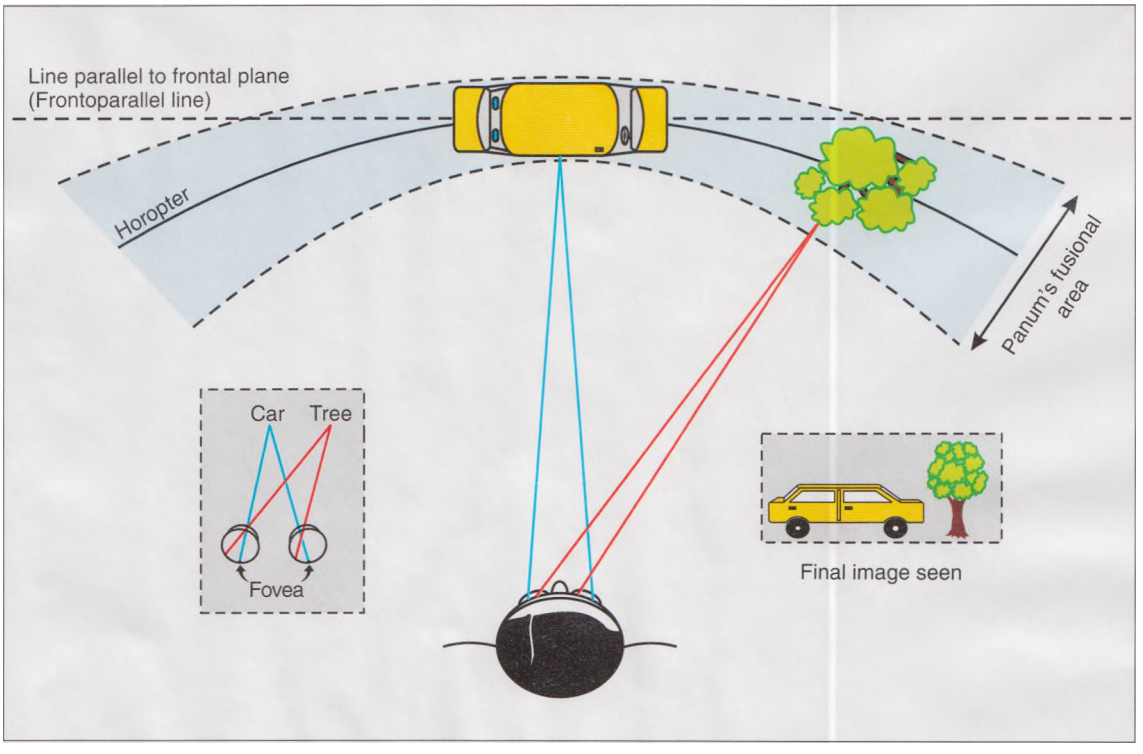


Fig. 3.6 Principles of binocular three-dimensional image formation.

In actual fact we get a three-dimensional view of the world created by the brain from two separate two-dimensional retinal images from the two eyes. This happens because there is an area in space (*Panum's fusional area)* on either side of the horopter which is still within the 'limits' of fusion such that objects spilling over into this space from the horopter are viewed as single. This gives both eyes a slightly different view of the object, as the eyes are separated in space, and this horizontal disparity gives the perception of depth or stereopsis. The location of the horopter and Panum's fusional area is determined by the distance at which the eyes are fixated. If the person is 'looking at' an object 1 m away, any object limited to the one meter horopter will be viewed as flat or two-dimensional, any object extending into Panum's area will be seen as three-dimensional and any object outside the region will actually be seen as double *(physiological diplopia).* The brain normally suppresses the images outside the fusion limits. Physiological diplopia can be demonstrated by 'looking' at an object at the far end of the room and holding up one's finger in front of one's nose. While still 'looking' at the distant object, if one consciously tries to simultaneously become aware of the image of one's finger, the finger appears double and *vice versa.*

Binocular vision has been graded into three levels—simultaneous macular perception, fusion and stereopsis. An object has to be simultaneously imaged by the foveae of the two eyes and the images perceived and fused by the brain, with the horizontal disparity leading to the perception of depth.

SUMMARY

The physiological apparatus responsible for eyesight consists of the focusing mechanism of the eye, the molecular pathways that are triggered by light falling on the neurosensory retina and the neural pathways that convey the information to the visual cortex of the brain. The visual cortex translates the signals into a visual image and also connects with the visual association areas for further neural processing of the sensory stimulus. The imagery of the two eyes is compiled by a complex motor and sensory apparatus which serves the purpose of providing perfect binocular vision and stereopsis.

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The Neurology of Vision

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THE VISUAL PATHWAY

The visual pathways have some unique features which are better understood if the afferent tracts of common sensation are compared with those of vision.

The sensory impulse of common sensation in a limb is carried by a nerve fibre along the sensory nerve and the dorsal spinal root to the cord: it travels up in the posterior columns of the cord to the nucleus gracilis or the nucleus cuneatus as the case may be. This entire course is along the processes of a single cell or neurone which is called the neurone of the first order (Fig. 4.1A). The impulse is taken up in the nucleus gracilis or cuneatus by a second cell and carried along the nucleothalamic tract or medial lemniscus to the opposite thalamus. The cells in the nuclei gracilis and cuneatus are the neurones of the second order *(see* II, Fig. 4.1A). A third cell situated in the thalamus, the neurone of the third order, carries on the nerve impulse to the cerebral cortex where it is transformed into a sensory perception.

Let us compare this pathway with the visual afferent tracts (Fig. 4.IB). The end organ is the neural epithelium

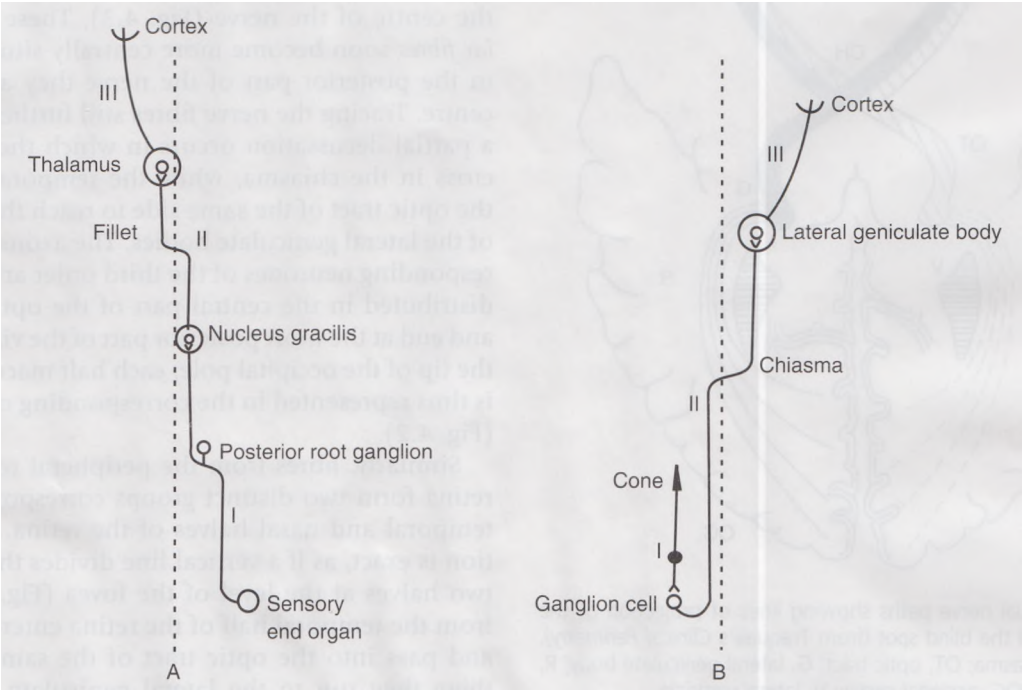


Fig. 4.1 (A) The path of somaesthetic sensation; (B) the visual pathway.

of the rods and cones. The first conducting nerve cell or neurone of the first order is the bipolar cell of the inner nuclear layer of the retina with its axon in the inner reticular layer. This microscopic cell corresponds morphologically to a dorsal root ganglion cell which, in some cases, has long processes stretching from the tip of the toe to the top of the spinal cord. The neurones of the second order are the ganglion cells in the retina, the processes of which pass into the nerve fibre layer and along the optic nerve to the lateral geniculate body. Here a new cell, the neurone of the third order, takes up the transmission of the impulse, travelling by way of the optic radiations to the cortex of the occipital lobe, which is the so-called *visual centre (see* Chapter 3).

The morphological identity of the two systems is apparent, despite the great anatomical differences which specialization has brought about. The peripheral 'optic nerve' proper corresponds to a bipolar cell in the inner nuclear and inner plexiform layers of the retina, while the structure we know as the optic nerve is a part of the central nervous system, homologous with the medial lemniscus in the medulla and pons.

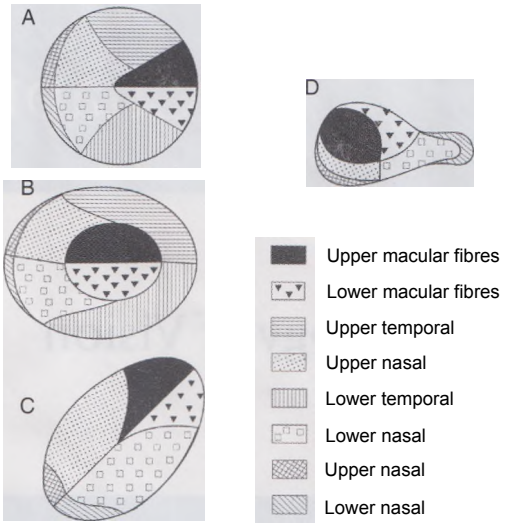


Fig. 4.3 The distribution of the fibres in the lower visual neurone of the right side. (A) Distal portion of the optic nerve; (B) proximal portion of the optic nerve; (C) optic tract; (D) lateral geniculate body. In each case the dorsal aspect is above, the medial to the left.

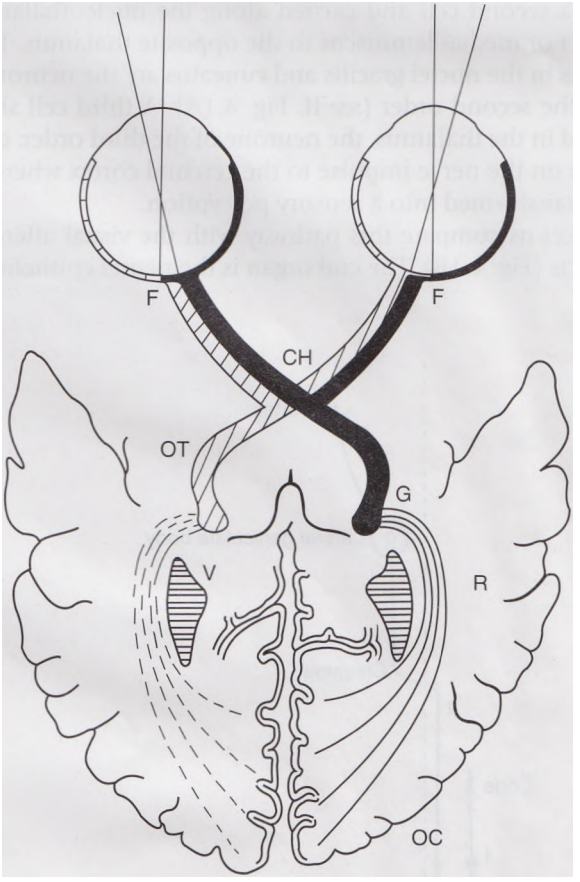


Fig. 4.2 The visual nerve paths showing lines of projection of the fixation area and the blind spot (from Traquair's *Clinical Perimetry).* F, fovea; CH, chiasma; OT, optic tract; G, lateral geniculate body; R, optic radiations; OC, occipital cortex; V, lateral ventricle.

The course of the fibres from the various parts of the retina is shown in Fig. 4.2. In general, it may be said that the fibres from peripheral parts enter the periphery of the optic nerve, while those from parts of the retina near the optic disc enter the central area of the nerve; they maintain this relative position as far back as the chiasma. Fibres from the macular region, however, behave differently. They enter the nerve on its outer aspect, where they are spread over an area which is triangular in section, with the apex towards the centre of the nerve (Fig. 4.3). These *papillomacular fibres* soon become more centrally situated, so that in the posterior part of the nerve they are all in the centre. Tracing the nerve fibres still further backwards, a partial decussation occurs in which the nasal fibres cross in the chiasma, while the temporal ones enter the optic tract of the same side to reach the dorsal part of the lateral geniculate bodies. The axons of their corresponding neurones of the third order are also widely distributed in the central part of the optic radiations and end at the most posterior part of the visual cortex at the tip of the occipital pole; each half macula (R and L) is thus represented in the corresponding occipital pole (Fig. 4.2).

Similarly, fibres from the peripheral regions of the retina form two distinct groups corresponding to the temporal and nasal halves of the retina. The distinction is exact, as if a vertical line divides the retina into two halves at the level of the fovea (Fig. 4.2). Fibres from the temporal half of the retina enter the chiasma and pass into the optic tract of the same side; from there they run to the lateral geniculate body where

all the visual fibres end. Fibres from the nasal half of each retina enter the chiasma, decussate and pass into the optic tract of the opposite side, the arrangement being such that the direct and crossed fibres pass to alternating laminae in the lateral geniculate body. The corresponding neurones of the third order originate in the lateral geniculate body and then pass by the optic radiations to the corresponding occipital lobes. It follows that a lesion of one occipital lobe or optic tract will cause blindness of the temporal half of the retina on the same side and of the nasal half of the retina on the opposite side. Projecting this outwards, such a lesion will cause loss of vision in the opposite half of the binocular field of vision, a condition which is known as *hemianopia.* The afferent pupilloconstrictor fibres have a similar semide cussation in the chiasma (Fig. 4.2).

The visual fibres in the optic radiations, like other sensory tracts, run behind the motor fibres in the internal capsule. Thereafter they separate considerably, the ventral fibres (projecting the lower quadrant of the retina or the upper quadrant of the visual field) running forwards into the temporal lobe before they turn backwards to the lower portion of the visual cortex, the dorsal fibres (projecting the upper retinal quadrant or lower field) running backwards in a more direct course to the upper part of the visual cortex (Fig. 4.2). They pass close to the posterior cornu of the lateral ventricle, so that when the ventricle is distended they may be subjected to pressure here.

The occipital cortex in and about the calcarine fissure differs from the cortex elsewhere in the possession of a white line, the line of Gennari, interpolated in the grey matter. This area, which is the primary visual or visuosensory area (Fig. 4.4A and B), is the cortical projection of the corresponding halves of both retinae. The same spatial arrangement is maintained in this projection—the parts above and below the calcarine fissure represent the upper and lower corresponding quadrants of both retinae, respectively, and the posterior part of the occipital lobe represents the macula.

NEUROLOGY OF THE BRAIN IN RELATION TO VISION

Unravelling the mysterious functioning of the 'living brain' has been a tantalizing but elusive quest for imaginative researchers over centuries. Meticulous recording of neurological examinations performed on people who had suffered brain injury or stroke and subsequently recovered, as also observations noted during surgery and autopsies, have provided rich details into the functions of a complex yet inaccessible organ. However, new options such as magnetic resonance imaging (MRI), 'functional' MRI, positron emission tomography (PET) scanning and the creation of computer algorithms, have provided further insight by actually 'seeing' the brain *in vivo.*

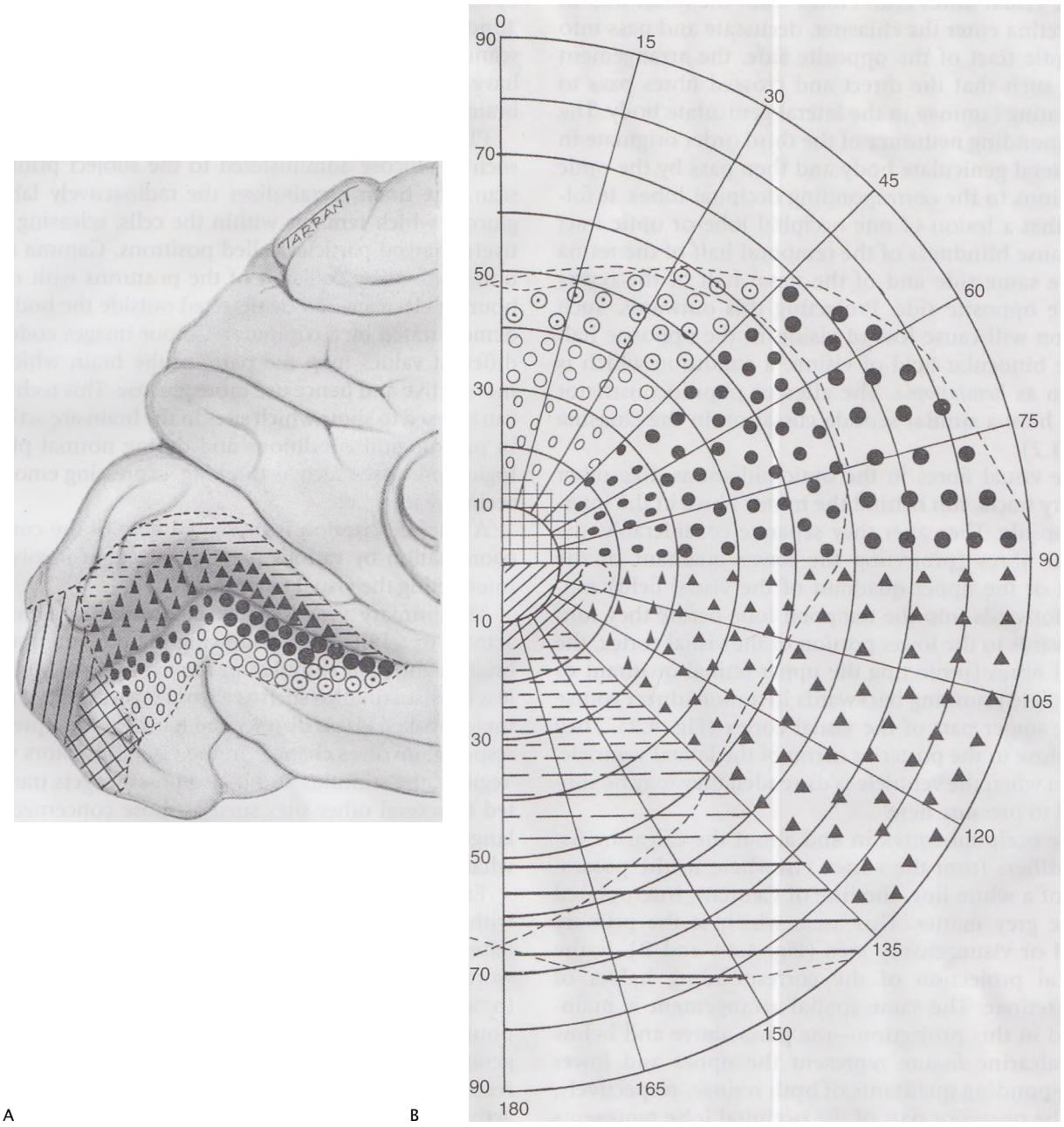
PET scanning uses radioactive labelling of substances such as glucose administered to the subject prior to a scan. The brain metabolizes the radioactively labelled glucose which remains within the cells, releasing positively charged particles called positrons. Gamma radiation released by collision of the positrons with neighbouring electrons can be detected outside the body and demonstrated by a computer. Colour images coded for different values map the parts of the brain which are more active and hence use more glucose. This technique can be used to show which sites in the brain are activated in pathological conditions and during normal physiological processes such as thinking, expressing emotions, seeing, reading, etc.

A brief description is presented here of the complex coordination by various parts of the brain involved in interpreting the visual environment.

The primary visual cortex demonstrates a peak of activity in a PET image following the presentation of a bright light flash stimulus to the eyes of a subject. If a less intense stimulus such as a word is presented, the PET image evoked is less distinct and harder to interpret. The response involves changes in the visual receptors which 'register' the stimulus and it also possibly gets transmitted to several other sites such as those concerned with language, memory, learning and emotion, depending on what word is presented.

English-speaking, literate subjects were presented with first an array of arbitrary symbols, then with real letters grouped in units which had the average length of words but were unpronounceable. Next, letters arranged to appear like normal words which could be pronounced but were not recognizable words and finally genuine English words were presented. The PET images recorded (Fig. 4.5) clearly showed a sharp increase in activity in the area known as the medial extrastriate cortex in the left hemisphere when the subjects applied the third and fourth level of the tasks. Subjects with brain injuries affecting this site have been known to have difficulty reading words, often despite having no problem with speaking or writing.

Similarly, utilization of the technique of functional MRI scan has shown that for engaging in what is considered as a simple task of reading, different parts of the brain (attention, vision and memory) must be activated in sequence and coordinated. To begin with, the brain must focus on the task of reading so that 'paying attention' involves the frontal cortex and thalamus. Next the words must be visualized, engaging the occipital visual cortex. Subsequently, to make sense of the seen words,



A B

Fig, 4,4 A diagram of the probable representation of the different portions of the visual fields in the calcarine cortex. (A) is a drawing of the medial surface of the left occipital lobe with the lips of the calcarine fissure separated so that its walls and floor are visible. The markings of the various portions of the visual cortex which is thus exposed correspond to those shown on the chart (B) of the right half of the field of vision. (By courtesy of Gordon Homes)

the visual information goes to an association area where the symbols or letters visualized are connected to a word's meaning.

This knowledge is of importance in the understanding of the physiological basis for dyslexia, and cortical atrophy or hypoxic damage in children who cannot 'see', though their distal afferent visual pathway may be intact. It also has implications for teaching and learning.

THE PUPILLARY PATHWAYS AND REACTIONS

The pupils are controlled by two muscles of ectoder-mal origin—the sphincter and dilator pupillae. The responses of these muscles to stimuli are very rapid and delicate, and are easily observed. The size of the pupil may be

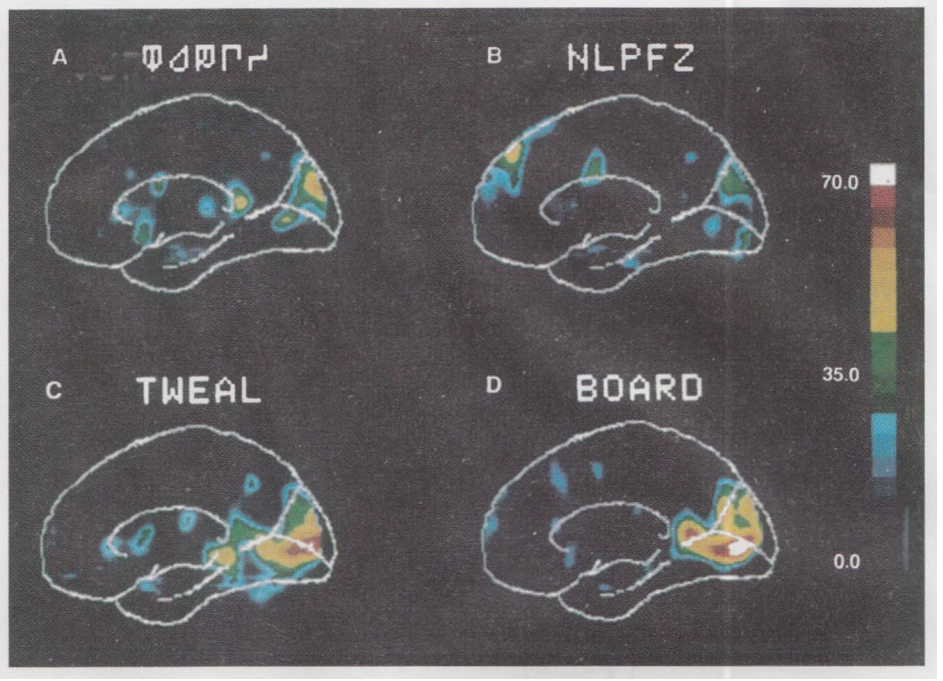


Fig. 4.5 Positron emission tomography images (single slices) showing areas of increased blood flow when subjects are presented with different sets of visual word-like stimuli. Each slice is taken from the same sagittal location 2cm left of the mid-sagittal plane. Anterior is at the left of each image and at the top of each section is a sample of the stimulus that produced this activation. For both the false font (A) and string of English letters (B) stimuli there are scattered foci of activation but little activation in the inferior and posterior parts of the image. Pronounceable non-word (C) and real word (D) stimulus presentation produces clear activation in the left medial extrastriate cortex. Reprinted with permission from Petersen SE, Fox PT, Snyder AZ, Raichle ME. Activation of extrastriate and frontal cortical areas by visual words and word-like stimuli. [Sc/'ence 1990; 249: 1041-4. Copyright (1990) American Association for the Advancement of Science.]

looked upon as essentially the result of their opposing forces. The innervation of these muscles is shown in Figs 4.6 and 4.7. The constrictor centre possesses 'tone' and is perpetually sending out impulses to the sphincter, which keep the pupil slightly contracted. Abnormal enlargement of the pupil is called *mydriasis,* abnormal contraction, *miosis.*

Nerve supply of the pupillary muscles

The sphincter is supplied by cholinergic nerves of the parasympathetic system through the third cranial nerve. The fibres start in the Edinger-Westphal nucleus near the third nerve nucleus in the floor of the aqueduct of Sylvius. This nucleus has connections with the dilator centre as well as with the frontal and occipital cortex. The fibres emerge from it and pass out of the mid-brain to run in the main trunk of the third nerve as far as the orbit. Here the fibres pass into the branch which supplies the inferior oblique muscle, leaving it by the short root of the ciliary ganglion. From the ciliary ganglion the fibres pass by the short ciliary nerves to the eye, piercing the sclera around the optic nerve accompanied by the

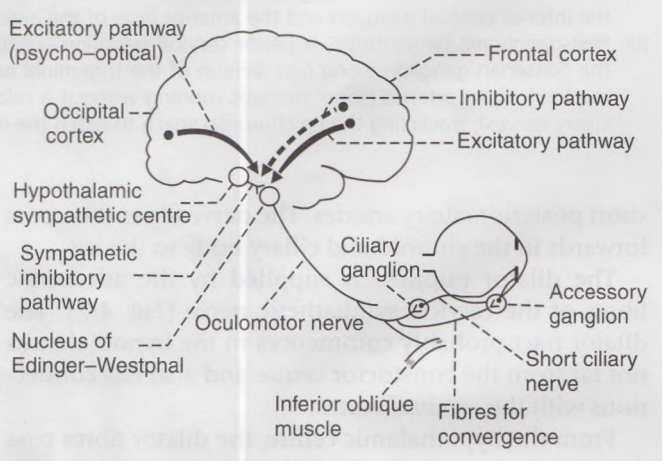


Fig. 4.6 The parasympathetic pupillary system. *Cortical control:* (a) excitatory pathways from the frontal and occipital (psycho-optical) cortex; (b) inhibitory pathway from the frontal cortex. *Sympathetic control* (inhibitory) from hypothalamic centre. *Parasympathetic pathway*—Edinger-Westphal nucleus-)third nerve —> inferior division -> branch to the inferior oblique muscle, (a) *Light reflex*—short root of ciliary ganglion ciliary ganglion-*short ciliary nerves->sphincter of iris, (b) *Near reflex*—leaving the third nerve at an unknown point -» (?) accessory ganglion -»sphincter of iris.

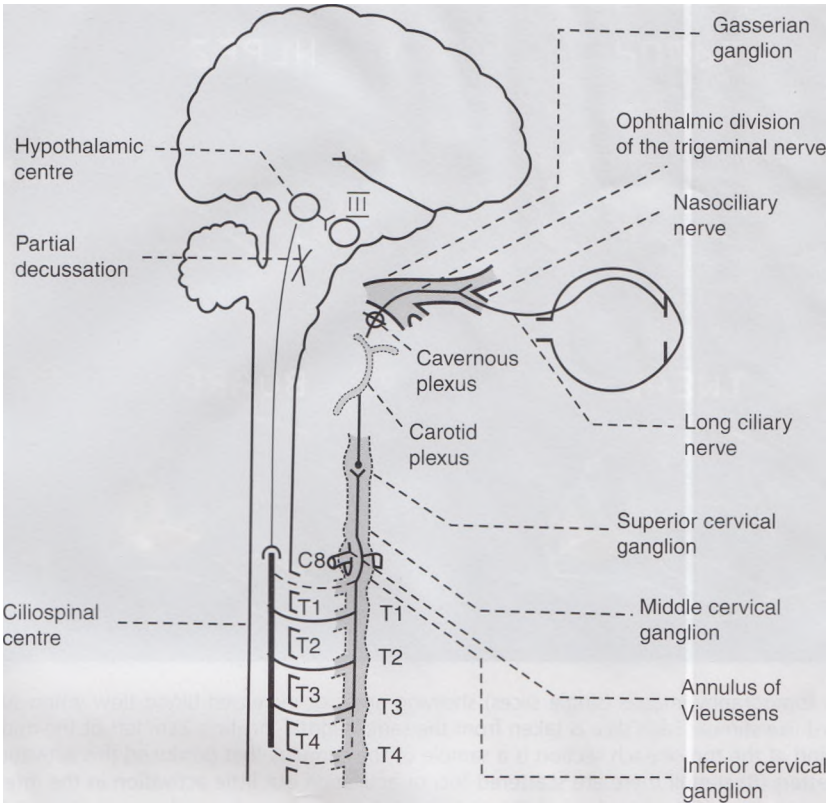


Fig. 4.7 Sympathetic pupillary system.

(I) Central. *Centre* in hypothalamic region—inhibitory pathway to the Edinger-Westphal group of the nucleus of the third nerve. *Tract* (hypothalamic-spinal) with a partial decussation in the mid-brain so that each hypothalamic centre supplies each ciliospinal centre but especially the contralateral: it traverses the reticular substance of the mid-brain and the lateral column of the cord.

(II) Pre-ganglionic sympathetic. Ciliospinal centre of Budge in the intermediolateral tract of the grey matter of the cord. Leaves by ventral roots of C8, Tl, T2 and T3 (largely Tl) via the white rami communicantes-* cervical sympathetic chain in which the fibres traverse the inferior cervical ganglion and the anterior loop of the ansa of Vieussens and terminate in the superior cervical ganglion.

(III) Post-ganglionic sympathetic. Superior cervical ganglion-center the skull with the carotid plexus-*cavernous plexus->travel over the Gasserian ganglion along first division of the trigeminal nerve—* nasociliary nerve-*long ciliary nerves, entering the globe with the long ciliary arteries (some perhaps running without a relay along the long and/or sympathetic root of ciliary ganglion-*short ciliary nerves), traversing the epichoroidal space to reach the iris and terminate in the dilator muscle.

short posterior ciliary arteries. The nerve fibres then pass forwards in the choroid and ciliary body to the iris.

The dilator pupillae is supplied by the adrenergic fibres of the cervical sympathetic nerve (Fig. 4.7). The dilator tract probably commences in the hypothalamus not far from the constrictor centre and also has connections with the cerebral cortex.

From the hypothalamic centre, the dilator fibres pass downwards through the medulla oblongata into the lateral columns of the cord. These fibres leave the cord by the ventral roots of the first three dorsal and probably the last two cervical nerves, enter the rami communicantes, and run to the first thoracic or stellate ganglion. From here they pass by the anterior limb of the ansa of Vieussens. In this nerve, they run up the neck to the superior cervical ganglion, from where they pass with the carotid plexus into the skull. They run over the anterior part of the Gasserian ganglion and pass into the first or ophthalmic division of the fifth nerve, following the nasal branch, which they finally leave to enter the long ciliary nerves, thus avoiding the ciliary ganglion. The long ciliary nerves enter the eye on each side of the optic nerve, accompanying the long ciliary arteries. Like them, the long ciliary nerves run forwards between the choroid and sclera, enter the ciliary body and thus reach the iris.

The balance of tone between these two antagonistic innervations maintains the pupil at its normal size, the essential factor being the superior tone of the sphincter. The pupils are normally equal on both sides; it is rare to meet with unequal pupils (*anisocoria*) in a normal person. Such cases do occur, but every pathological cause must be eliminated before concluding that the condition is an idiosyncrasy. On the other hand, the size of the pupils varies widely in different people under the same conditions of illumination. The pupils are smaller in older people than in the young, sometimes to so great

an extent that the pupils are almost 'pin-point'. They are often smaller in hypermetropes and larger in myopes than in emmetropes, and are commonly smaller in blue eyes than in brown.

The pupillary reflexes

The pupils participate in several reflexes, three of which are of clinical importance:

- The *light reflexes:* If light enters an eye, the pupil of that eye contracts (the *direct light reflex),* an activity shared equally by the pupil of the other eye (the *consensual light reflex).*
- The *near reflex:* A contraction occurs on looking at a near object, a reflex largely determined by the reaction to convergence but in which accommodation also plays a part.
- The *psychosensory reflex:* A *dilatation* of the pupil occurs on psychic and sensory stimuli.

The *light reflex* is initiated from the rods and cones throughout the retina. The fibres run up the optic nerve, partially decussate in the chiasma and enter the optic tracts with exactly the same distribution as the visual fibres (Fig. 4.8). Near the upper end of the tract, however, they part company with the visual fibres and, instead of running to the lateral geniculate body, they enter the

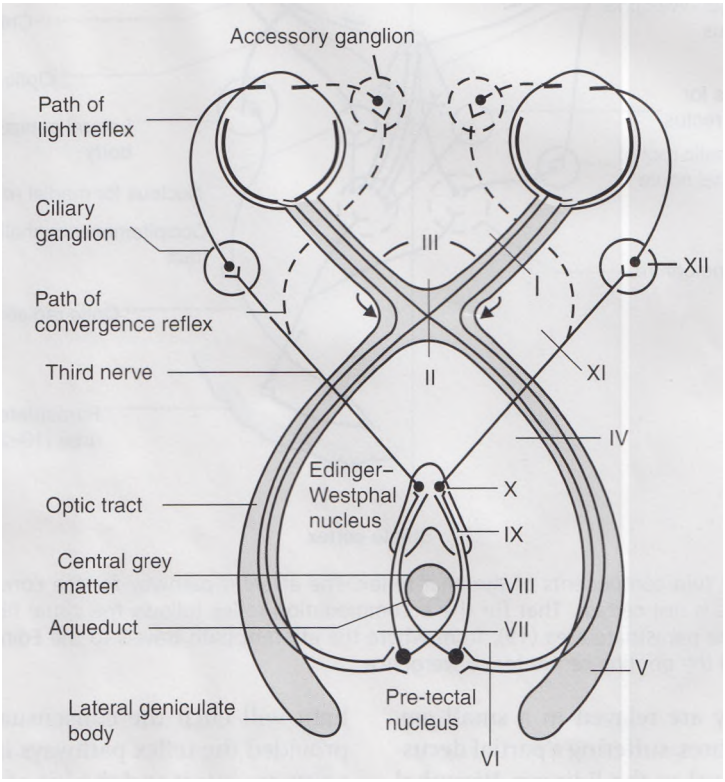


Fig. 4,8 The pupillary pathways for the light reflex. The numbers denote lesions accompanied by the following symptoms:

(I) Optic nerve: *unilateral amaurotic paralysis* (abolition of the direct reaction on the ipsilateral side and the consensual on the contralateral side: retention of the consensual on the ipsilateral side and the direct on the contralateral side). Retention of the near reflex and the lid reflex.

(II) Medial chiasma: *bitemporal hemianopic paralysis.*

(III) Lateral chiasma: *binasal hemianopic paralysis.*

(IV) Optic tract: *contralateral hemianopic paralysis* (Wernicke reaction).

(V) Lesion of the proximal part of optic tract: *normal* pupillary reactions.

(VI) Superficially in the region of the brachium and tectum: *contralateral hemianopic paralysis.*

(VII) Central decussation: *bilateral reflex paralysis*—inactivity to light (direct and consensual) with retention of the near reflex, the lid reflexes and the psychosensory reactions *(bilateral Argyll Robertson pupil)* (according to Behr).

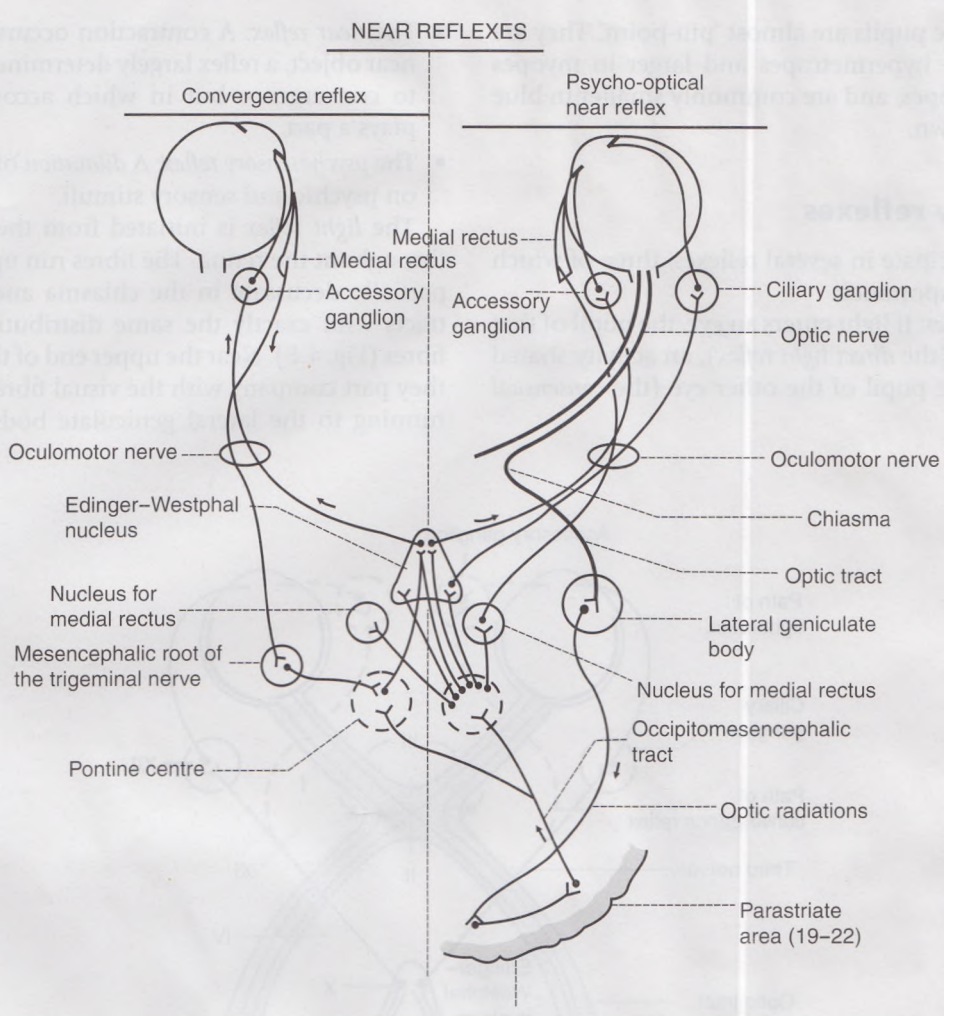
(VIII) Between the decussation and the constrictor centre: ipsilateral abolition of direct and consensual reactions with retention of both contralaterally—*unilateral Argyll Robertson pupil* (according to Behr).

(IX) A partial lesion corresponding to VIII: ipsilateral abolition of direct reaction with retention of consensual reaction; retention of both contralaterally.

(X) Nuclear or extensive supranuclear lesion: ipsilateral absolute pupillary paralysis.

(XI) Lesion of the third nerve: absolute pupillary paralysis.

(XII) Lesion of the ciliary ganglion: abolition of the light reflex with retention of the near reflex, sometimes with tonic contraction *(Adie pupil).*



Fig, 4.9 The nerve paths of the two components of the near reflex. The afferent pathway for the convergence reflex is indicated as running up the third nerve: this is not certain. That for the accommodation reflex follows the visual fibres to the striate area of the calcarine cortex, is relayed to the parastriate area (19), from where the efferent path travels to the Edinger–Westphal nucleus via the occipitomesencephalic tract and the pontine centre for convergence.

pre-tectal region. Here they are relayed in a small *pre-tectal nucleus,* and the new fibres, suffering a partial decussation in the mid-brain, travel to the Edinger-Westphal nucleus on each side. From these nuclei, the constrictor fibres travel to each iris as already described.

The decussation is important for it explains the mechanism of the consensual as well as the direct reaction to light and also accounts for several pathological reactions such as the Argyll Robertson pupil *(see* Chapter 31). It is obvious from a study of these paths that a lesion distal to the chiasma will abolish the direct reaction in the eye on the affected side and the consensual reaction on the other (Fig. 4.8). A lesion in the optic tract will produce a hemianopic reaction involving both eyes, while blindness due to a lesion affecting the visual pathways in or above the lateral geniculate body will leave the pupillary reactions unaltered. It is also obvious that if one eye sees and the other is blind, stimulation of the first by light will elicit the consensual reaction in the second, provided the reflex pathways in the mid-brain and third nerve are intact and the iris of this eye is functioning.

The *near reflex* is initiated mainly by fibres from the medial rectus muscles which contract on convergence (Fig. 4.9). From these muscles, afferent fibres run centrally, probably by the third nerve, to the mesencephalic nucleus of the fifth nerve, to a presumptive convergence centre in the tectal or pre-tectal region. From here the pathway is relayed to the Edinger-Westphal nucleus and along the third nerve to the sphincter muscle of the iris, so that the pupil contracts commensurately with convergence. At the same time, accommodation reinforces the reflex by visual impulses relayed from the cortex to the Edinger-Westphal nucleus.

The *sensory reflex,* which is initiated by the stimulation of any sensory nerve to the extent of causing pain or by emotional states and excitement, is more complicated

than the light reflex, for both the dilator and constrictor centres play a part in its production. Sensory stimulation causes first a rapid dilatation of the pupil due to augmentation of the dilator tone through the cervical sympathetic, and then a second dilatation, rapid in onset but slow in disappearance, due to inhibition of the constrictor tone.

Minute examination of the pupil when the intensity of the light entering the eye is altered shows that the pupil contracts and then oscillates rapidly, finally settling down into a condition of contraction which is slightly less than the summit of the first wave. In its sudden response, the pupil as it were oversteps the mark, oversteps it again in the opposite direction, and so on. Two different types of exaggeration of this oscillation are met with in abnormal conditions. One is the condition in which the oscillations are very large and easily seen, and are to a great extent independent of the light falling upon the eye. This is called *hippus*; it depends upon the rhythmic activity of the nervous centres, and is not a peripheral phenomenon. It is found in association with multiple sclerosis. More important is the lack of sustained contraction under the continued influence of light. Here the pupil contracts sluggishly when the intensity of the light is increased but slowly dilates, often with superimposed sluggish oscillations, while the light is kept constant. This is a pathological phenomenon dependent upon diminished conductivity in the afferent path of the light reflex, usually in the optic nerve, as in optic neuritis.

SUMMARY

The sensory apparatus of the eye connects to the brain via the visual pathways. The occipital cortex is the main visual centre and it also connects to visual association areas. Sensory information transmitted from the eye also traverses another path to the midbrain which is responsible for the pupillary light reflex. A thorough understanding of the pupillary pathways and pupillary reactions is of great clinical value in diagnosing different diseases based on their clinical presentations.

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II

Ophthalmic Optics and Refraction

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5

Elementary Optics

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This chapter aims to impart information about the nature and property of light to create a foundation of basic knowledge of optics as relevant to the routine practice of ophthalmology.

PROPERTIES OF LIGHT

Electromagnetic spectrum

The eye is sensitive to light which is a form of energy. *Optical radiation* is a part of the electro-magnetic spectrum and lies between X-rays and microwaves. The optical spectrum consists of non-ionizing radiation of wavelengths ranging from 200 nm (nanometer or 10^{-9}xm) to 10 000 nm. This is further subdivided into clusters or wavebands each consisting of radiations which elicit similar biological reactions. These sub-domains are *ultraviolet* (UV) (UV-C: 200-280 nm, UV-B: 280-315 nm and UV-A: 315-400 nm), *visible* (400-700nm), and *infrared* (IR-A: 700-1400nm, IR-B: 1400-3000nm and IR-C: 3000-10 OOOnm) radiations. The energy of the individual photons of optical radiation is inversely related to its wavelength.

By definition, *light* is visible radiation and it is incorrect to use terms such as ultraviolet light and infrared light. Visible light appears white to the human eye but it is actually composed of individual segments of coloured light corresponding to specific wavelengths. These colours are appreciated by the eye when viewed separately. White light, such as sunlight, can be split into its component colours by passing it through a suitable prism or diffraction grating. The effect produced is a spectrum of colours, consisting of rays differing from each other in wavelength. Of these, some colours are visible and appear to the majority of people as pure colours—red, orange, yellow, green, blue, indigo and violet, in the order named. The red has the longest and violet the shortest wavelength. The visible spectrum extends from about 397 nm at the violet end to 723 nm at the red end, or ranges roughly from 400 to 700 nm. Though part of the invisible UV component of optical radiation, wavelengths between 400 and 350 nm also stimulate the photoreceptors to a small extent. These are normally absorbed by the human crystalline lens, but in aphakic eyes or pseudophakic eyes with an intraocular lens without a UV-absorbing filter, such UV radiation is seen as a blue or violet colour. Few perceptive, newly aphakic patients have been observed to remark that 'everything looks bluer after the operation'.

Beyond the red end are IR rays of greater wavelength which, when absorbed, cause a rise in temperature and are commonly known as heat rays. Beyond the violet end are waves of smaller length, the UV rays, which are capable of causing chemical actions. The longer visible rays also cause a rise in temperature, and the visible rays are also actinic, though less so than the IR and UV, respectively. Absorption of these rays can cause pathological changes. The cornea absorbs almost all the optical radiation at shorter wavelengths of about 315nm (Fig. 5.1), i.e. UV-B and UV-C, the lens absorbs rays shorter than 350 nm, and the vitreous has an absorption band with its maximum at 270 nm. The cornea also absorbs long wavelengths in the IR region beyond 1400nm, i.e. IR-B and

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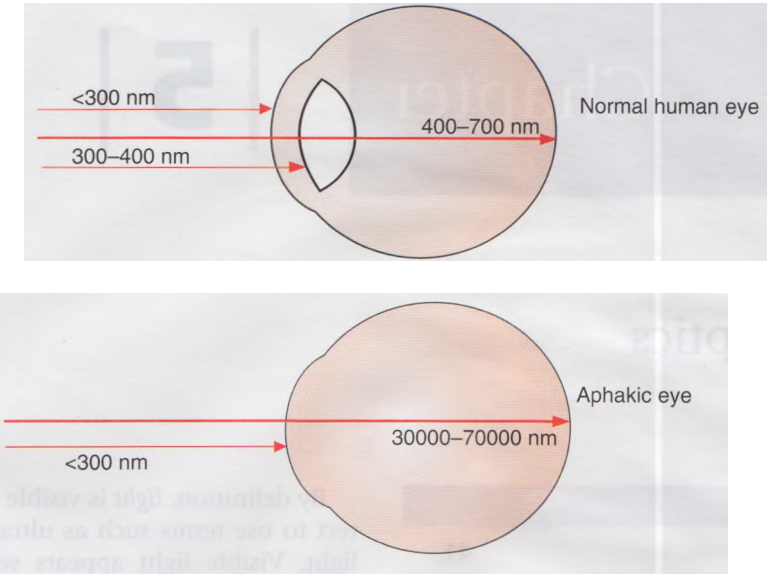


Fig. 5.1 Schematic diagram showing how different structures of the eye filter out different wavelengths of light. UV-C rays are of little concern as they are absorbed by the upper atmosphere and do not reach the earth's surface. UV-A rays are primarily absorbed within the lens of the human eye. UV-B rays are the ones that can affect the cornea by causing photokeratitis.

IR-C. Incident wavelengths of 400-700 nm pass through the ocular media in normal eyes to reach the retina. The pigment epithelium on the back of the iris absorbs radiation of all wave-lengths, and the same is true of the retinal pigmentary epithelium at the back of the eye.

In patients who do not have their crystalline lens, e.g. after cataract surgery, wavelengths in the UV-A region can reach the retina. Intraocular lens implants, made up of polymethylmethacrylate, absorb only UV rays <320 nm. Almost all modem intraocular lenses including polymethylmethacrylate, silicone and foldable acrylic are impregnated with UV-A absorbing substances called chromophores. Polymethylmethacrylate lenses with UV filtering chromophores absorb wavelengths <400 nm. In view of recent evidence that wavelengths of 350-441 nm are most likely to cause retinal damage in routine environmental conditions, there is the possibility that in future intraocular lenses will be produced with a pigment similar to that of the natural lens to block light of 400-441 nm.

Glass absorbs some of the heat (IR) rays and many of the UV rays, but prisms and lenses made of quartz allow most of the UV rays to pass unimpeded. Ordinary glass used for spectacles absorbs rays beyond 350 nm.

Sunlight at sea level is poor in UV rays, which are absorbed in the atmosphere. The exposure to UV radiation is more at high altitudes and in places where there is marked reflection of incident sunlight such as the open sea or on snow fields. Based on the principles highlighted above, special protective glasses designed to reduce the exposure of the eyes to harmful radiation are available. The most commonly used glass was Crookes B and C, but many other tints for glass and plastic lenses are now available. Sunglass standards advise that they must block at least 70% of UV-B and at least 60% of UV-A. The best quality sunglasses provide at least 98% protection from both UV-A and UV-B rays. Light reflected from surfaces such as snow, a flat road or smooth water is generally horizontally polarized. This horizontally polarized light can be blocked by vertically oriented polarizers in lenses. Polarized sunglasses reduce glare, and improve clarity, and are recommended in water sports, skiing, golfing, cycling and jogging. They are also recommended for driving and for light-sensitive patients.

Wave theory of light

Light travels through an optical medium in a straight line and is diagrammatically shown as a straight, arrowed line or a ray. Observations of the behaviour of light have shown that light in fact travels in waves and wavefronts similar to ripples created by throwing a stone in a pool of water.

As with all other forms of wave motion, wavelength is defined as the distance between two corresponding or symmetrical parts of the wave; one complete oscillation is a cycle. The amplitude is the maximum displacement of the wave from the baseline and any portion of the cycle is called a phase. When two waves of equal wavelength travel together in the same direction they are said to be in phase if they are perfectly aligned in their cycles, and out of phase if they are out of step.

Interference, diffraction and polarization

If two waves of equal wavelength are in phase and travelling together, they may be summated to result in a resultant wave of amplitude equal to the sum of the two and

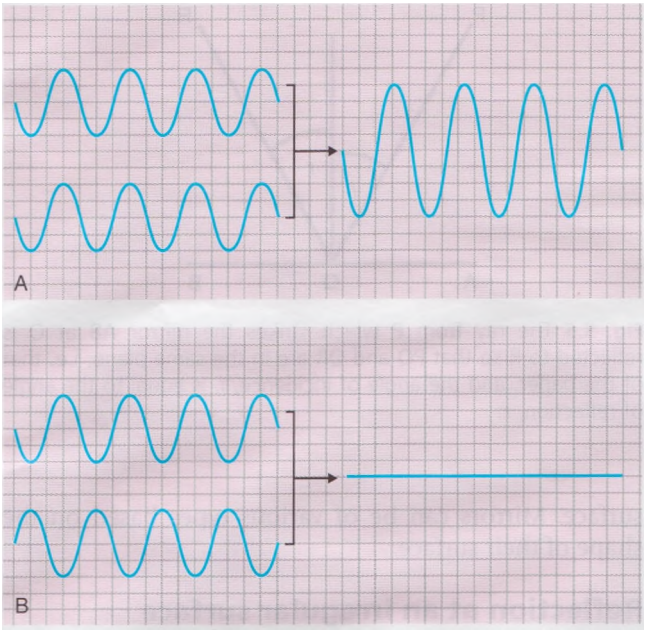


Fig. 5.2 (A) Constructive interference; (B) destructive interference.

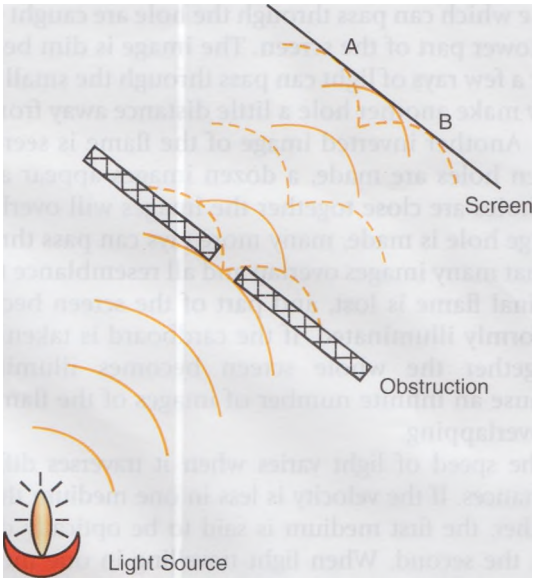


Fig. 5.3 Diffraction of light occurs after light waves pass through a narrow opening in an obstruction. After diffraction, the secondary waves are out of phase with the primary waves and lead to 'blurring' of the image produced on a screen.

this is known as *constructive interference* (Fig. 5.2A). This principle is used in lasers. If the two waves are out of phase by half a cycle and are of equal amplitude, the trough of one will correspond with the crest of the other and they will cancel each other out, resulting in a flat or no wave which is called *destructive inteiference* (Fig. 5.2B).

When the path of a wavefront is blocked by an obstruction which contains a narrow opening or an edge, the wave motion passes across and spreads out on the other side as if the obstruction behaves as a new source for producing secondary wavefronts. The secondary waves are out of phase with the primary waves. This phenomenon is known as *diffraction* (Fig. 5.3).

In normal circumstances, the three-dimensional plane of wave motion is random. In certain situations, the individual waves lie parallel to each other and move in the same plane; this is termed as *polarized light.* Polarizing substances are those which only transmit light rays vibrating in one particular plane and these materials can be used to produce polarized light from ordinary light. Light can also be polarized in ordinary circumstances under natural conditions if the incident light strikes the surface, such as water, at an angle equal to the polarizing angle of that substance. At other angles of incidence, the light will be partially polarized and consist of a mixture of polarized and non-polarized light. When polarization occurs in this fashion, the plane of polarization of the reflected light is parallel with the surface of the reflecting material. Polarization is utilized in the making of three-dimensional movies and the scanning laser polarimeter.

RAYS OF LIGHT AND IMAGES

A naked light emits rays in all directions. This is transmitted in straight lines, so that it may be imagined as coming from the source as an immense number of diverging straight lines, each of which is called a ray. Every point on such a ray represents, or is the image of, the point of light from which it arises. This is shown by a simple experiment carried out in a dark room. Make a pinhole in a piece of cardboard (A, Fig. 5.4) and hold the cardboard in front of a candle (C) at a little distance from it. Beyond the cardboard hold up a white screen (B) so that the cardboard is between the screen and the candle. A dim image (D) of the flame will be thrown upon the screen, and it will be noticed that it is upside down so that an inverted image of the flame is formed. This is due to the fact that the cardboard cuts off all the rays of light from the candle except those that can pass through the hole. The rays from the top of the

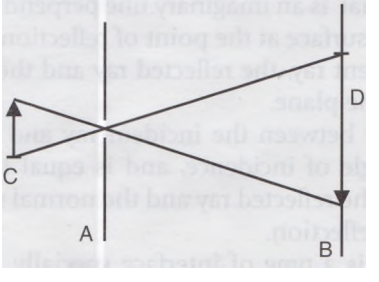


Fig. 5.4 Pinhole demonstration.

flame which can pass through the hole are caught upon the lower part of the screen. The image is dim because only a few rays of light can pass through the small hole. Now make another hole a little distance away from the first. Another inverted image of the flame is seen. If a dozen holes are made, a dozen images appear and if the holes are close together the images will overlap. If a large hole is made, many more rays can pass through so that many images overlap and all resemblance to the original flame is lost, and part of the screen becomes uniformly illuminated. If the cardboard is taken away altogether the whole screen becomes illuminated because an infinite number of images of the flame are all overlapping.

The speed of light varies when it traverses different substances. If the velocity is less in one medium than in another, the first medium is said to be optically denser than the second. When light travelling in one medium meets another medium, its behaviour at the interface depends on the nature of the two media involved. It may be absorbed by the second medium, may pass through it, may bounce back into the first medium, or may do all three in different proportions as happens when optical radiations fall on the cornea. If the second medium is opaque, none of the light is refracted and all the light is reflected back.

REFLECTION

When a ray of light travels from one medium to the other, it is reflected from the surface of the second medium. Before it meets the surface it is called an *incident ray,* after it is reflected from the surface it is called the *reflected ray.* This bouncing back or reflection of light takes place to a greater or lesser extent at all interfaces even if most of the light is transmitted or absorbed. This is how a window or door pane made of clear glass and a black curtain can be seen.

Laws of reflection

The following rules, illustrated in Fig. 5.5, govern reflection and are applicable to reflection of light at any interface:

- The 'normal' is an imaginary line perpendicular to the reflecting surface at the point of reflection.
- The incident ray, the reflected ray and the normal lie in the same plane.
- The angle between the incident ray and the normal is the angle of incidence, and is equal to the angle between the reflected ray and the normal which is the angle of reflection.

A mirror is a type of interface specially designed to maximize reflection by having a highly polished smooth surface. Mirrors can be of various types based on the shape of their surface.

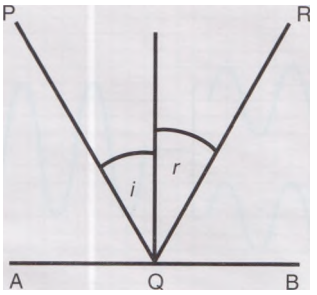


Fig. 5.5 The ray from P which strikes the mirror AB at Q is reflected to R so that PQ and QR are in the same plane, i.e. that of the paper, and the angle of incidence, /, is equal to the angle of reflection, *r*.

Reflection at an irregular surface

When parallel rays of light strike an irregular surface, they are reflected and scattered in many directions. This is called diffuse reflection. It is by this phenomenon that most non-self-luminous objects such as clothes, furniture, etc. are seen. A perfectly smooth reflecting surface, with no surface irregularities to cause diffuse reflection, is an ideal mirror which itself would be invisible and only the image formed in the mirror by light reflected from it would be visible.

Reflection at a smooth surface: plane, concave and convex mirrors

Plane mirrors

If P (Fig. 5.6) is a luminous point in front of the mirror AB, the ray PQ will be reflected towards R, and the ray PS towards T. The brain assumes that an object is present in the direction along which light enters the eye, thus the reflected rays QR and ST appear to come from p, a point as far behind the mirror as P is in front of it. As the rays QR and ST have to be produced backwards so that they may meet, no real image is formed, and such an image is called a virtual image. In other words, if the observer actually goes to the point p behind the mirror, there is no real image there and it cannot be captured on a screen. Note that rays reflected from a plane mirror are divergent. The same reasoning holds good for every point on the object PV, its image being pv, as far behind the mirror as the object is in front of it. Moreover, the size of the image is equal to that of the object. The image of an object formed by reflection at a plane surface is therefore characterized by the following:

- it is erect or upright;
- it is virtual;
- it is laterally inverted;

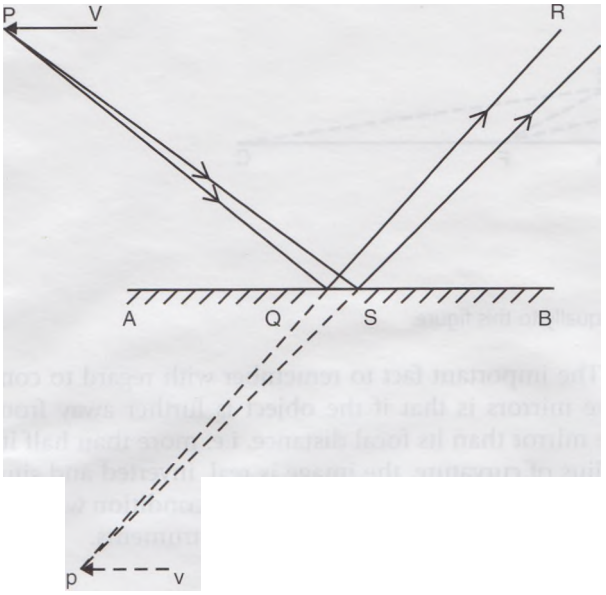


Fig. 5.6 Reflection of an object.

[1] it lies along a line joining the object and the surface which is perpendicular to the surface;

[1] its size equals that of the object and

◎ it is located as far behind the reflecting surface as the object is in front of it. Also, if a plane reflecting surface is rotated while incident light falls on its centre of rotation, the reflected ray rotates through an angle equal to twice the angle of rotation of the mirror.

Spherical mirrors

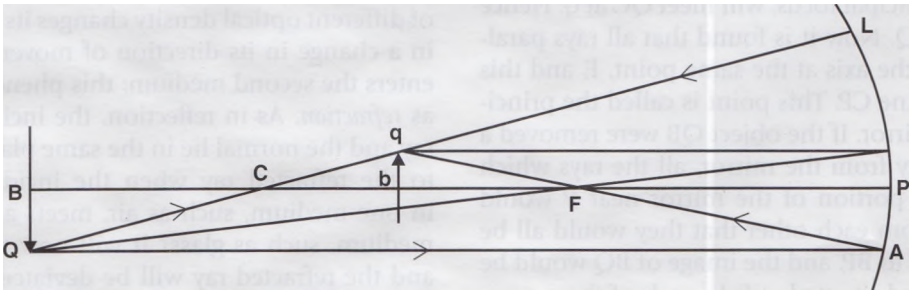
Concave or convex mirrors form part of a sphere. The geometric centre of the reflecting surface of the mirror is called the *pole* of the mirror, P. The *centre of curvature* C is the centre of the sphere of which the mirror is a part and the distance CP is the *radius of curvature, r.* Any line passing through the centre of curvature and striking the mirror is called an *axis* and that passing through the pole is known as *the principal axis.* Rays parallel to the principal axis (e.g. QA, Fig. 5.7) are reflected towards the principal focus in concave mirrors and away from the principal focus in convex mirrors.

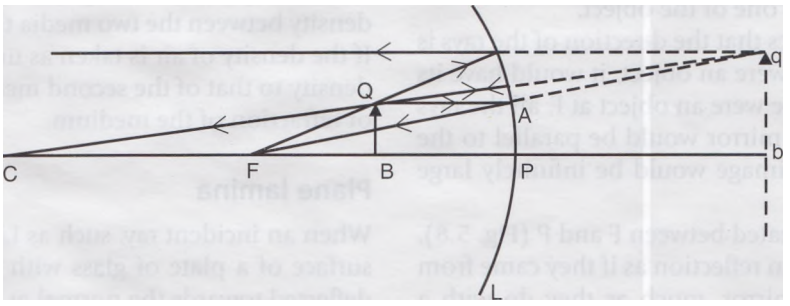
In simple diagrams an image is constructed using two rays:

1. A ray parallel to the principal axis which is reflected to or away from the principal focus.
2. A ray from the top of the object going through the centre of curvature which is reflected back along its path. Alternatively, a ray passing through the principal focus which is reflected back parallel to the principal axis. The image is formed at the point where these reflected rays meet or intersect.

For any object, the position of the image can be calculated by using the formula \/*v* — l/w=l//=2/r (^distance of the image from the mirror, *u* = object distance and r= radius of curvature).

Magnification or image size relative to object size can be calculated as $M = i/o = -v/u$. The sign convention for using these formulae must be followed, namely: (i) all distances are measured from the pole; (ii) distances in the same





Figs 5.7 (above) and 5.8 (below) Reflection of light by a concave mirror. The ray from Q parallel to the axis is reflected through F, the principal focus. The ray QC passes through the centre of curvature and is normal to the surface, and is therefore reflected on itself. The meeting point of any two of these rays will give the location of q, the image of Q.

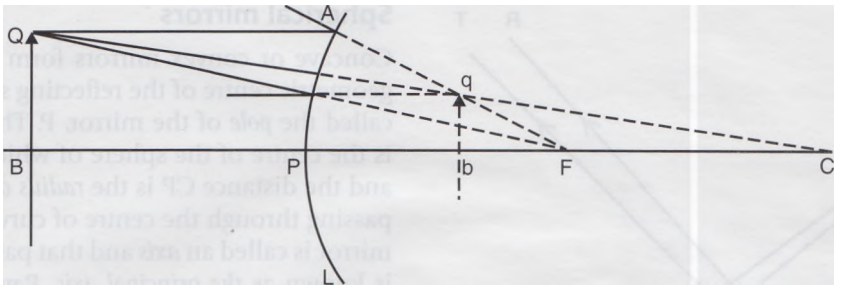


Fig. 5.9 Reflection by a convex mirror. The description of Fig. 5.8 applies equally to this figure.

direction as incident light are positive and in the opposite direction are negative; and (iii) the image size is positive for erect images and negative for inverted images.

Concave mirrors

A concave mirror is curved and forms part of a sphere with the reflecting surface lying along the inside of the curve. If AL (Fig. 5.7) is part of the section of a concave mirror and BQ is an object, C being the centre of the sphere, then the line PCB is called the principal axis, QCL a subsidiary axis and P the apex or pole of the mirror.

By convention, light-rays are shown travelling from left to right across the page in ray diagrams. Rays parallel to the principal axis (such as the ray QA in Fig. 5.7) are reflected towards the principal focus, F and the distance FP is the focal length of the mirror which is half of the radius of curvature.

The ray QC through the centre of the sphere will be reflected along itself, so that the image of Q must be on QC. The ray QA, parallel to the principal axis and reflected to the principal focus, will meet QC at q. Hence q is the image of Q. Now it is found that all rays parallel to the axis cut the axis at the same point, F, and this point bisects the line CP. This point is called the principal focus of the mirror. If the object QB were removed a great distance away from the mirror, all the rays which fell upon a small portion of the mirror near P would diverge so little from each other that they would all be practically parallel to BP, and the image of BQ would be extremely small and situated at F. In each of these cases the image is an inverted one of the object.

It is an axiom of optics that the direction of the rays is reversible. Hence, if qb were an object, it would have its image at QB, and if there were an object at F, all the rays from it reflected by the mirror would be parallel to the principal axis, and the image would be infinitely large and situated at infinity.

If the object were situated between F and P (Fig. 5.8), the rays would diverge on reflection as if they came from an object behind the mirror, much as they do with a plane mirror. The image would therefore be a virtual one, situated behind the mirror—it would be erect and larger than the object.

The important fact to remember with regard to concave mirrors is that if the object is further away from the mirror than its focal distance, i.e. more than half its radius of curvature, the image is real, inverted and situated in front of the mirror. This is the condition which is almost always used in ophthalmic instruments.

Convex mirrors

Convex mirrors are generally not used in ophthalmic instruments, but it is necessary to know their reflective properties, since the cornea acts as a convex mirror. As seen from Fig. 5.9, the image is always virtual, erect and smaller than the object. As with the concave mirror, if the object is a long way off, the image will be situated at the principal focus, i.e. at a distance equal to half the radius of curvature behind the mirror.

REFRACTION

Light passing from one transparent medium to another of different optical density changes its speed. This results in a change in its direction of movement as soon as it enters the second medium; this phenomenon is known as *refraction.* As in reflection, the incident ray, refracted ray and the normal lie in the same plane. What happens to the refracted ray when the incident ray, travelling in one medium, such as air, meets an optically denser medium, such as glass? It will now travel more slowly and the refracted ray will be deviated towards the normal to the surface. The greater the difference in optical density between the two media the greater the deviation. If the density of air is taken as unity, then the ratio of its density to that of the second medium is called the index of refraction of the medium.

Plane lamina

When an incident ray, such as LM (Fig. 5.10), meets the surface of a plate of glass with parallel sides it will be deflected towards the normal at M. When the ray passes out of the glass on the other side, it will be deflected away from the new normal at N just as much as LM was deflected towards it. Hence the emergent ray NO will

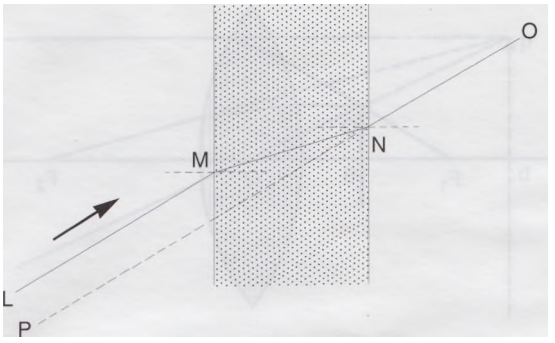


Fig. 5.10 Refraction by a plane lamina.

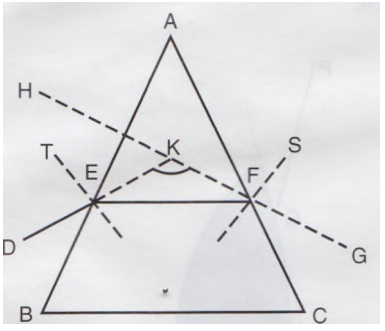


Fig. 5.11 Refraction by a prism.

be parallel to the incident ray LM but will be laterally displaced. If the plate of glass is very thin, NO will be practically continuous with LM.

Prisms

Imagine that the two sides of the plane lamina meet at a point A where a prism will be formed (Fig. 5.11). In this case, being similarly refracted with reference to the normals at these surfaces, the ray will be deflected along DEFG. The ray is thus deviated towards the base of the prism. When the angles of incidence and emergence are equal, the angle of deviation is least; this is called the angle of minimum deviation and the ray is said to pass symmetrically through the prism. In these circumstances, if the prism is made of crown glass, the angle of deviation of the ray (DKH) is approximately equal to half the refracting angle of the prism.

Objects are usually projected along the direction of the rays of light as they enter the eye, and in doing so the effect of refraction may be ignored. If a light D is observed through a prism as in Fig. 5.11, it will appear to come from H. Objects seen through a prism appear displaced towards the apex of the prism. Prisms may be categorized according to the apical angle or refracting angle, and the angle of apparent deviation, the centrad. Usually prisms are categorized according to prism dioptres (D), 1 D indicating the strength of the prism which produces a linear apparent displacement of 1 cm of an object situated 1 m away.

Lenses

Ordinary lenses are pieces of glass with spherical surfaces. The line passing through the centres of curvature of the surfaces is called the axis of the lens. Fig. 5.12 shows the chief varieties of lenses: (1) biconvex; (2) biconcave; (3) plano-convex; (4) plano-concave and (5) convexo-concave or meniscus. Lenses can also have one surface plane and the other curved at right angles to it or both surfaces curved but with different curvatures. Such lenses are termed cylindrical and toric, respectively (shown as 6 and 7 in Fig. 5.12).

The effect of a biconvex lens upon rays of light passing through it is very similar to what would occur if it were replaced by two prisms set base to base (Fig. 5.13).

If the incident rays are parallel to the axis they will be refracted in such a manner that they all cross the axis through a single point on the other side of the lens. This point is called the *principal focus* of the lens, and its distance from the lens is called the *focal distance* or length of the lens. When the lens has the same medium, such as air, on each side of it, the two principal foci, one on each side of the lens, are situated at equal distances from it if the

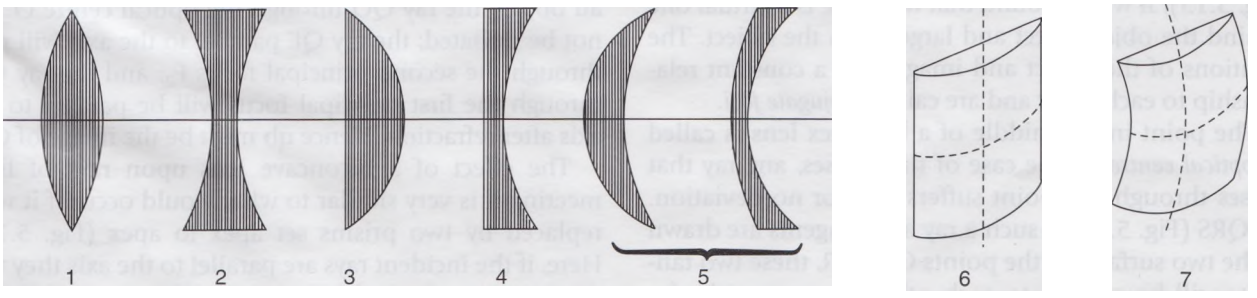


Fig. 5.12 Types of spherical lenses (1–5). Cylindrical (6) and toric (7) lenses.

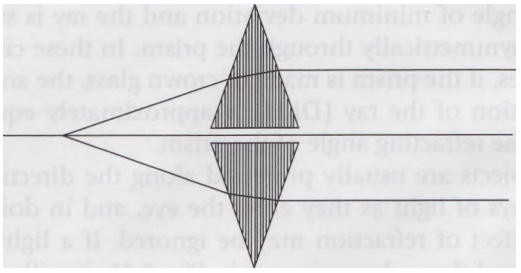


Fig. 5.13 Optical effect of two prisms base to base.

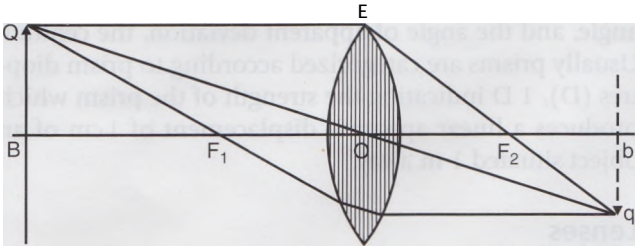


Fig. 5,14 The image formation of an object placed further to a convex lens than its principal focus is formed by refraction, and is located beyond the principal focus on the other side and is a real image. The ray QE, parallel to the axis, is refracted through the second principal focus F_2. The ray QF,, through the first principal focus, is refracted parallel to the axis. The ray QO, through the optical centre of the lens, is not deflected. The meeting point of any two of these rays gives the location of q, the image of Q.

two sides are of the same curvature. For thin glass lenses of low power the focal distance is equal to half the radius of curvature of the two surfaces when these are equally curved. If an object is placed at a large distance from the lens, the rays emitted are practically parallel when they reach the lens. Hence, in this case, an image of the object will be formed by the lens at its principal focus; it will be real, inverted and very small. If the object is gradually brought nearer and nearer to the lens (Fig. 5.14) the image will recede further and further from it; from being very small it will grow larger, until, when the object is at the principal focus, the image will have receded to infinity and it will be infinitely large. All the rays coming from an object at the principal focus are, therefore, parallel to the axis and to each other after refraction. If the object is brought closer to the lens than its focal distance (Fig. 5.15), it will be found that its image is a virtual one behind the object, erect and larger than the object. The positions of the object and image bear a constant relationship to each other and are called *conjugate foci.*

The point in the middle of a biconvex lens is called its *optical centre.* In the case of thin lenses, any ray that passes through this point suffers little or no deviation. If PQRS (Fig. 5.16) is such a ray and tangents are drawn to the two surfaces at the points Q and R, these two tangents will be parallel to each other. Consequently, for such a ray, the lens acts as if it were a plate with parallel

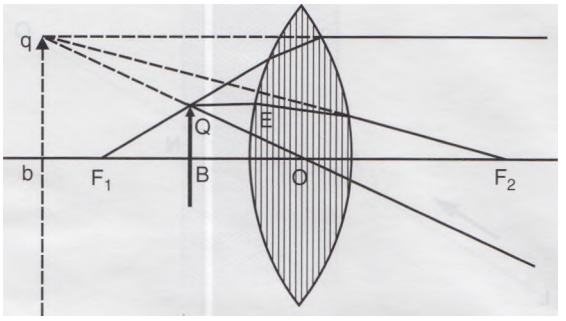


Fig. 5.15 The image formation of an object placed nearer to a convex lens than its principal focus is formed by refraction, and is located beyond the principal focus on the same side and is a virtual image. The description of image formation in Fig. 5.14 applies equally to this figure.

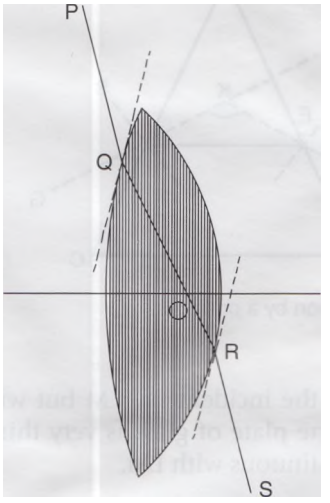


Fig. 5.16 Properties of the optical centre of a lens.

sides and, as already seen, in such a case the emergent ray is parallel to its original direction. If the lens is very thin the refracted ray will be practically continuous with the incident ray.

Rays that pass through the optical centre are not deviated, and rays passing through the principal focus are parallel to the axis after refraction. From the above-mentioned facts, the image of an object can be easily constructed in any given position. Thus, in Fig. 5.14, if QB is an object, the ray QO through the optical centre O will not be deviated; the ray QE parallel to the axis will pass through the second principal focus F_2; and the ray QF, through the first principal focus will be parallel to the axis after refraction. Hence qb must be the image of QB.

The effect of a biconcave lens upon rays of light meeting it is very similar to what would occur if it were replaced by two prisms set apex to apex (Fig. 5.17). Here, if the incident rays are parallel to the axis they will be divergent after refraction, and the amount of divergence of the individual rays will be such that if they

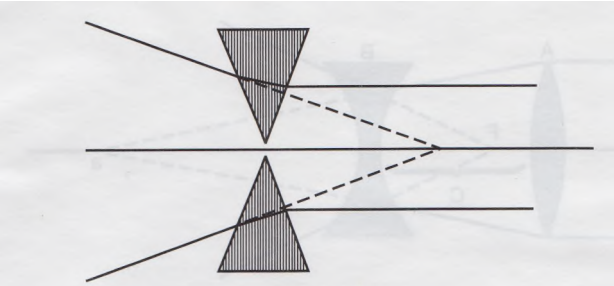


Fig. 5.17 Optical effect of two prisms apex to apex.

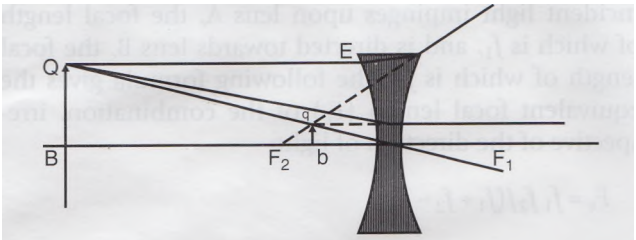


Fig. 5.18 The description of Fig. 5.14 applies equally to this figure

are produced backwards they will all cross the axis at a single point on the side of the lens from which they were emitted. This and the corresponding point on the other side of the lens are called the principal foci. The biconcave lens also has an optical centre, situated upon the axis within it and having the same properties as in the case of the convex lens. The image of any object formed by a concave lens can be constructed in exactly the same manner as for a convex lens (Fig. 5.18). It will be found that in every position of the object the image is always virtual, erect and smaller than the object.

Plano-convex and plano-concave lenses act like biconvex and biconcave lenses, respectively, but in them the optical centre is on the curved surface at the point where the axis cuts it. Menisci act as convex or concave lenses according to whether the convex or the concave surface has the greater curvature where the optical centre is outside the lens.

It has been observed that the refractive power of a lens varies inversely as the focal distance, i.e. a lens with a short focal distance will bend the rays more than one with a longer focal distance. Therefore, it is necessary to have some system of numbering lenses so as to indicate their refractive power. The most convenient system for ophthalmic purposes is the one which takes a lens with a focal distance of 1 m as the standard. Such a lens is said to have a refractive power of 1 dioptre (D).

A lens with a focal length of 0.5 m will be twice as strong as one with a focal length of 1 m: the refractive power of such a lens is therefore 2 dioptres (2 D). Similarly, a 3 D lens has a focal length of one-third of a metre, or 33 cm; a 4 D lens, 25 cm; and so on. The dioptric power is thus the reciprocal of the *focal length* (D = 1/F). It is important to remember that in this system the unit of measuring length is a metre, not a centimetre or a millimetre.

Convex lenses are indicated by a plus sign (+), and concave by a minus sign (-) before the number.

There are several ways of finding out whether a lens is convex or concave and what its refractive power is. The simplest way is to hold a convex lens up near the eye and look at distant objects through it; then move the lens a little from side-to-side: the distant object will seem to move in the opposite direction to that in which the lens is moved. When the process is repeated with a concave lens the objects will seem to move in the same direction as the lens. The reason is that a convex lens forms an inverted image, while a concave one forms an erect image. If two lenses of opposite signs but equal curvature are placed in contact with one another the combination will make a plate with parallel sides: such a plate causes practically no deflection of the rays of light. Hence, the strength of a lens can be determined by exactly neutralizing the movement of images with a lens of the opposite sign.

For example, to determine the strength of a particular lens, it is held up and if on moving it distant objects seem to move in the opposite direction to the lens, it confirms that it is a convex lens. A weak concave lens is then put in contact with it and the process repeated. If with a -2 D lens, objects still seem to move in the opposite direction, though not as much, with a -3 D lens there is only a trace of movement, and with a -3.5 D lens there is no movement at all, it leads to the conclusion that the original lens was +3.5 D. In performing this test it is important to have the two lenses and their optical centres as closely in contact as possible (Fig. 5.19). If the centre of one lens is higher than that of the other they will obviously not counteract each other exactly. If they are not in contact the result will be inaccurate.

Systems of lenses: The combination of using more than one lens forms an optical system. When all the component lenses are centred on a common optic axis the system is homocentric, in which event the principles already discussed are additionally applied.

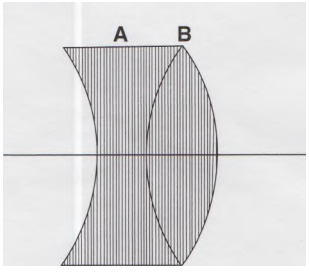
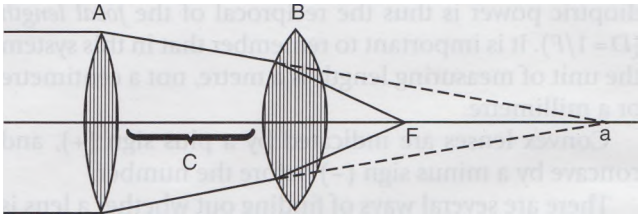


Fig. 5.19 Neutralizing lenses.



Fig, 5.20 Combination of two convex lenses.

When the lenses are in contact, the refractive power of the combination (D) is equal to the algebraic sum of the refractive powers of the two lenses *(d\, d_2):*

i.e. $D = d_x + d_2$ or 1/F = 1 $jf_x + l/f_2$

where *F*, $f_v f_2$, are the respective focal distances (Fig. 5.19).

However, if two convex lenses are separated by a distance *c* (Fig. 5.20), the lens A will make parallel rays converge towards *a,* but after a distance *c* they meet the lens B: hence the convergence of the rays by lens A is not expressed by $\backslash/f_l$ but by *l/(f* -c). Therefore, the combined effect of the lenses A and B, termed D, or 1/F, is now equal to

Power of lens A + Power of lens B
= D = *1/F = l/(f\-c)*+1//2

If the second lens (B) is concave (Fig. 5.21), its effect will be one of divergence, so that it must have a negative sign, and D will now be equal to

W1-O-1//2

It is to be noted that in the formula

1/F= l/(fi – c) + l/f_{2p}

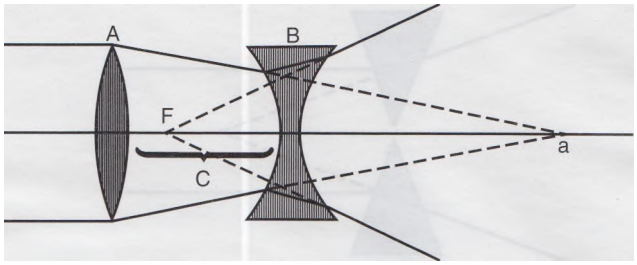


Fig. 5.21 Combination of a convex and a concave lens.

F is the posterior focal length of the combination. The incident light impinges upon lens A, the focal length of which is f_v and is directed towards lens B, the focal length of which is f_2. The following formula gives the equivalent focal length (F_e) of the combination, irrespective of the direction of light:

Fe = fi filifi + fi - c)

SUMMARY

The eye is a complex optical system which focuses light entering through the cornea and passing via the pupil to form an image on the retina. Basic principles of physics as applicable to the properties of light can be used to understand the various mechanisms involved in the optical process of vision.

SUGGESTED READING

1. Elkington AR, Frank H. *Clinical Optics.* Oxford: Blackwell Scientific, 1991.

6

Elementary Physiological Optics

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The study of the eye as an optical instrument is termed as physiological optics.

THE OPTICAL SYSTEM OF THE NORMAL EYE

The effect of a convex lens in bringing parallel rays of light to a focus is shown in Fig. 5.14. This model is accurate for thin lenses but is invalidated for thick lenses or a combination of lenses *(see* Fig. 5.20) because of the greater separation of the two surfaces by the refracting substance of the lens. The optical system of the eye, which can be considered as being equivalent to a thick lens system, can be deduced from this simple analogy. Instead of a simple convex lens with the same medium (air) on either side, the system of the eye comprises a curved optical plate (the cornea), the aqueous humour, the crystalline lens (which is itself optically complex), and the vitreous body. The aim of this complicated arrangement is to shorten the focal distance of the system, so that the eye may be smaller and more compact. Moreover, the medium in front of the cornea is air, while behind the lens is the vitreous which has a higher refractive index (Table 6.1).

The analysis of refraction by a thick lens such as the eye has been simplified by the concept of *principal points* and *principal planes* (Fig. 6.1). These are hypothetical points and planes, such that a ray falling at the first principal point or plane traverses the thick lens and leaves the second principal point or plane at the same vertical distance from the principal axis. The position of the principal point is calculated from the curvature of the lens surfaces, the refractive index of the lens and its thickness. Considering the eye as a refracting unit, the cornea has almost the same refractive index as the aqueous, which is also equal to that of the vitreous. The anterior surface of the cornea may be regarded as nearly spherical, the radius of curvature being 8 mm. The centres of curvature of the cornea and the two surfaces of the lens are all in the same straight line, which is called the *optic axis.* The major refracting interfaces in the eye are (i) air-cornea, (ii) aqueous-lens and (iii) lens-vitreous.

This optical system behaves like a combination of lenses or a thick lens system. To understand the focusing mechanism of the eye as an optical device, Listing in 1853 first introduced the concept of the reduced eye. In the reduced eye, the entire system can be regarded, with good degree of accuracy, as one lens with one optical centre (the nodal point, N) which lies in the posterior part of the crystalline lens (Fig. 6.2). Listing, Donder and Gullstrand calculated the equivalent elements of the system and the values were generally similar, with some differences. Basically the eye is imagined as a single, ideal spherical refracting surface whose radius of curvature is 5.73 mm, and power + 58.6 D, with a single principal point P, nodal point N, first focal point Fi and a second focal point F_2 (Table 6.2). The

Table 6.1 Refractive index of each component of the eye as an optical system

Refracting medium	Refractive index
Air	1.000
Cornea	1.376
Aqueous humour	1.336
Lens (cortex–core)	1.386–1.406
Vitreous humour	1.336

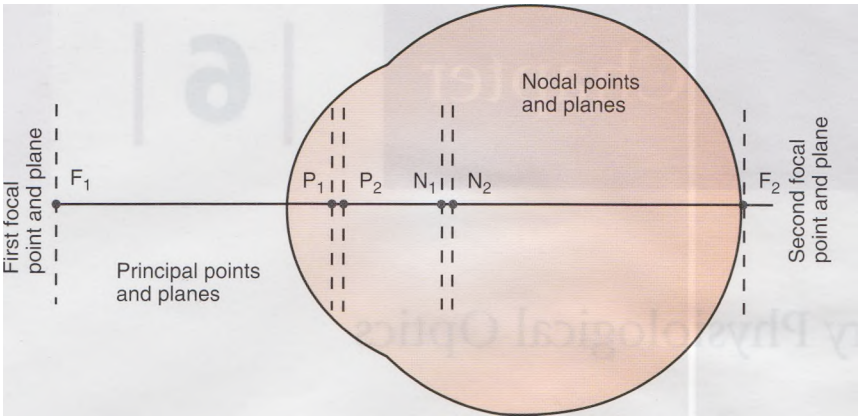


Fig. 6.1 The eye as an optical system based on Gullstrand's concept of a schematic eye.

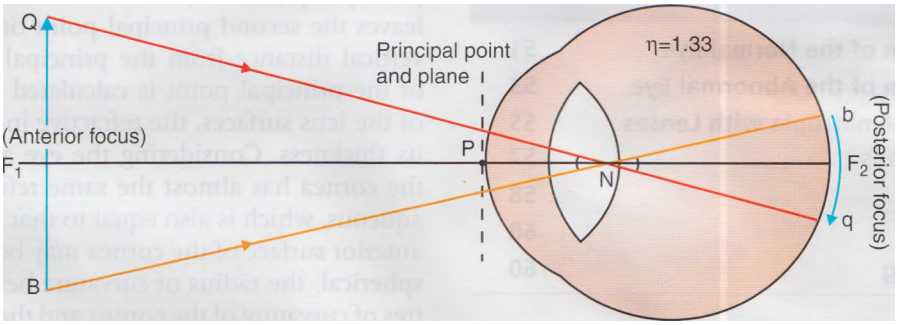


Fig. 6.2 The formation of retinal images in the reduced eye. The image qb of an object QB is formed by drawing lines Q and B through the nodal point (N). QNB or qNb represents the visual angle.

reduced eye is clinically useful in designing instruments and making calculations to derive a magnification effect, localizing a foreign body, deriving formulae for intraocular lens power, among others.

Since the rays enter and leave the refracting system through media of different optical density, the anterior and posterior focal distances are different. The anterior focal distance is about 15 mm in front of the cornea, and the posterior focal distance about 24 mm behind it, i.e. parallel rays falling upon the cornea will be brought to a focus 24 mm behind it. The small bundles of rays which enter the pupil may be considered parallel so that the image of distant objects formed by the normal eye will be on the retina. Hence, the normal eye in its condition of rest is so constituted that distant objects form their images upon the retina (Fig. 6.3).

The optic axis (a straight line passing through the centre of curvature of the front and back surfaces of a lens), produced backwards to meet the retina, cuts it almost exactly at the fovea centralis. Hence, any distant object on the prolongation forwards of the optic axis will have its image at the fovea, which is the spot for distinct vision. Here, just as with a convex lens, the image is inverted; and it is re-inverted psychologically in the brain.

Table 6.2 The distance (in mm) of each component of the reduced normal eye with overall refractive power of +58.6 D (calculations made by Gullstrand)

Optical reference	Distance from the anterior surface of the cornea (in mm)	Distance from the principal plane (in mm)
P: Principal point	1.35	
N: Nodal point	7.08	
First focal point (anterior focal distance)	−15.7	−17.05
F_2: Second focal point (posterior focal distance)	24.13	22.78

Note: By sign convention light is shown diagrammatically as travelling from left to right across the page and distances measured in the same direction are considered positive whereas distances measured in the opposite direction are taken as negative.

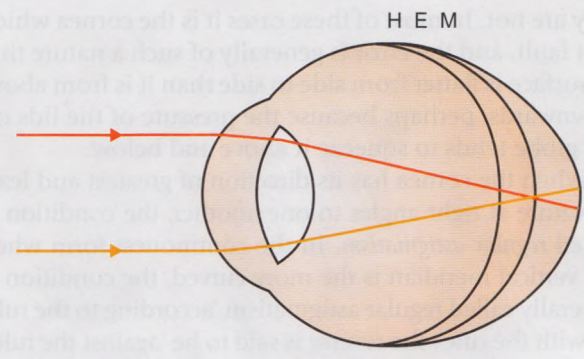


Fig. 6.3 Emmetropia, hypermetropia and myopia. In emmetropia (E), parallel rays of light are focused upon the retina. In hypermetropia (H), the eye is relatively too short; in myopia (M), it is too long.

It is easy to find the size of the retinal image which any external object will form, since the nodal point (N) corresponds to the optical centre of a convex lens. As in the case of lenses, any ray which passes through this point will not be appreciably deflected. If, therefore, there is an object QB (Fig. 6.2) in front of the eye, the size of its retinal image qb is found by joining the extremities of the object and the nodal point and extending these lines until they meet the retina. The lines will enclose an angle, QNB, which is called the *visual angle,* the angle subtended by the object at the nodal point. It is of course equal to the angle qNb, which is, subtended by the retinal image at the nodal point.

The schematic or reduced eye is based on certain assumptions and approximations. The normal living eye differs in the following ways: (i) its refractive surfaces are aspheric, with only the central area of each refractive surface, i.e. the cornea and lens being spherical and (ii) the refractive index of the lens is not uniform throughout, but increases towards its centre.

THE OPTICAL SYSTEM OF THE ABNORMAL EYE

In some eyes, the retina is not situated in exactly the right place for the images of distant objects to be clearly focused upon it. It may be too far forward, or too far back (Fig. 6.3); in the former case the eye is said to be *hypermetropic,* in the latter *myopic.* If the effect upon parallel rays is considered, it is seen that in the hypermetropic eye they have not yet come to a focus, whereas in the myopic eye they have not only come to a focus but have commenced to diverge. In each case a blurred image will be formed upon the retina, and vision will be impaired. Such conditions are called *errors of refraction* or *ametropia* (a, privative, ixexpov measure; not according to measure). In contradistinction to hypermetropia and myopia the normal condition is called *emmetropia.*

The condition of an eye, whether emmetropic, hypermetropic or myopic, is called its refraction, or more accurately its *static refraction,* since the term applies to the eye at rest. When, as commonly happens, the refractions of the two eyes are different, the condition is called *anisometropia.*

It has already been stated that in optics the direction of the rays is reversible. If a minute point on the emmetropic retina is imagined to be luminous, it will give out rays which will diverge in all directions. The rays which pass through the pupil and emerge out of the eye will undergo exactly the same optical deviations as the parallel rays falling upon the cornea when they pass into the eye and will therefore be parallel to each other when they leave the eye.

Suppose, however, that the eye is hypermetropic because it is too short (Fig. 6.3). The rays coming from a point on the retina will be relatively more divergent than the corresponding rays of the emmetropic eye before they fall upon the back of the lens (Compare the effect of placing an object closer to a convex lens than its principal focus, *see* Fig. 5.15). They will therefore still be divergent when they leave the eye, though of course not so divergent as when they were passing through the vitreous. In fact, their direction will be the same as if they came from a point behind the eye. The nearer the retina is to the lens, the more divergent they will be, and the nearer to the back of the eye will be the point from which they seem to come. This virtual point (R) behind the eye is called the *remote* or *far point* of the eye. The point on the retina and this point behind the eye are really *conjugate foci* (Fig. 6.4).

Suppose that the eye is myopic because it is too long (Fig. 6.3). The rays coming from a point on the retina will be relatively less divergent than the corresponding rays in the emmetropic eye before they fall on the back of the lens (Compare the effect of placing an object further away from a convex lens than its principal focus, *see* Fig. 5.14). The refractive media in front will therefore cause them to converge more than in the emmetropic eye. They will thus be convergent when they leave the eye, and will cross at a point (R) somewhere in front of the eye (Fig. 6.5). The further the retina is from the lens,

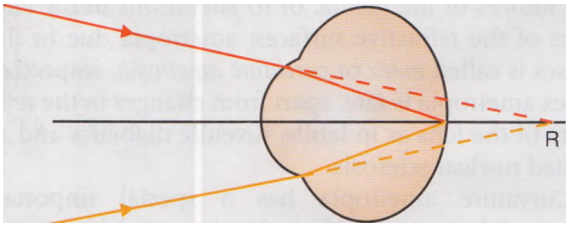


Fig. 6.4 Hypermetropic eye. Rays from a point on the retina are divergent when they emerge from the eye, as if they came from the point, R, behind the eye.

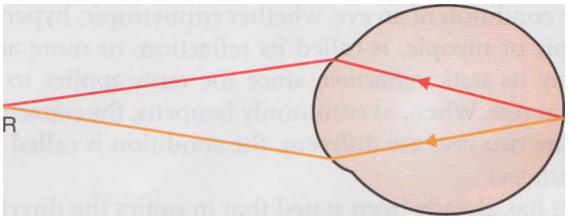


Fig. 6.5 Myopic eye. Rays from a point on the retina are convergent when they emerge from the eye, so that they cross at a real point, R, in front of the eye.

i.e. the higher the degree of myopia, the more convergent they will be, and the nearer to the front of the eye will be the point where they cross. This anterior point is again the conjugate focus to the point on the retina, but in this case it is a real point. It is also called the remote or far point of the eye.

In the emmetropic eye the emergent rays are parallel to each other. Since parallel rays meet at infinity, the far point of the emmetropic eye is at infinity.

In every case, the far point and a point on the retina are conjugate foci. Using the principle of the reversibility of rays, any object situated at the far point of any eye will have a sharp image upon the retina. Thus, emmetropes see only distant objects clearly with their eyes at rest, since the rays from such objects are nearly parallel; for practical purposes this applies to objects more'than 6 m away. On the other hand, patients with myopia can only see things which are near; they are 'shortsighted'. They can see things at a distance better if they screw up their eyes to make a narrow slit through which to look. This slit acts in the same way as the hole in the cardboard in the experiment illustrated in Fig. 5.4. The term myopia originated in this peculiarity (|xvetv to shut; COI|J the eye). Again, patients with hypermetropia can see neither distant nor near objects clearly with their eyes at rest, since the far point is virtual, and it is impossible to place an object at its situation. When young, hypermetropes are better off than myopes since they can alter their refractive power by accommodation.

Errors of refraction may also be due to causes other than axial shortening or lengthening of the eye (*axial ametropia).* They may be due to alterations in the refractive indices of the media, or to alterations in the curvatures of the refractive surfaces; ametropia due to these causes is called *index* or *curvature ametropia,* respectively. Index ametropia is rare, apart from changes in the refractivity of the lens as in labile, juvenile diabetics and age-related nuclear sclerosis.

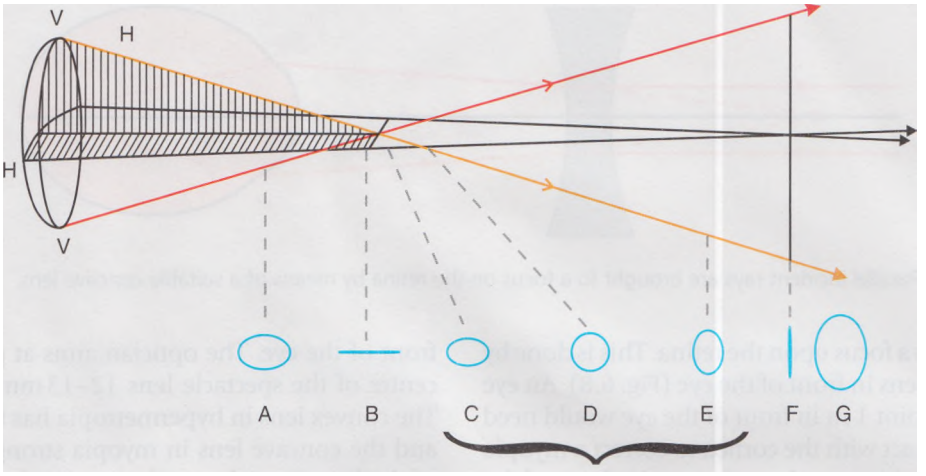
Curvature ametropia has a special importance because it is the cause of another very troublesome error of refraction called *astigmatism.* In most eyes the areas of the refractive surfaces uncovered by the pupil and used in vision are very nearly spherical. Sometimes, however, they are not. In most of these cases it is the cornea which is at fault, and the error is generally of such a nature that its surface is flatter from side to side than it is from above downwards, perhaps because the pressure of the lids on the globe tends to squeeze it above and below.

When the cornea has its direction of greatest and least curvature at right angles to one another, the condition is called *regular astigmatism.* In the commonest form when the vertical meridian is the more curved, the condition is generally called regular astigmatism 'according to the rule' or 'with the rule'; the reverse is said to be 'against the rule', but not infrequently the axes are oblique. Often, as after ulceration, the surface of the cornea is irregular so that the rays of light are refracted irregularly without any symmetry and different groups form foci in various positions. This is called *irregular astigmatism:* it cannot be corrected, and can only occasionally be improved by rigid contact lenses.

Although astigmatism is chiefly due to faulty curvature of the cornea, in some cases there is also lenticular astigmatism. This is not generally due to unequal curvature of the surfaces, but to slight tilting of the lens, so that the incident rays fall upon it obliquely. If printed matter is looked at through a tilted glass lens, the letters appear to be distorted and elongated in one direction, this is a form of astigmatism. The astigmatism of the crystalline lens is generally such that it tends to counteract corneal astigmatism although sometimes it may be additive. A situation of unequal lens curvature may also arise if there is selective damage to the zonules as in subluxated lenses and lens colobomas *(see* pp. 267-269).

A regularly astigmatic surface is said to have a *toric* curvature. The more curved meridian will have a greater refractive power than the less curved; hence if parallel rays fall upon a convex astigmatic surface the vertical rays will come to a focus sooner than the horizontal. The rays after refraction will be perfectly symmetrical when referred to the vertical and horizontal planes but they will have two foci. The entire bundle of rays is called *Sturm conoid,* and the distance between the two foci is called the *focal interval* of Sturm. It is difficult to represent this conoid on a plane surface (Fig. 6.6), but what sections of the bundle or pencil of rays would look like at different distances from the refractive surface (A-G, Fig. 6.6) can be seen quite clearly.

At A, the section will be a horizontal oval or oblate ellipse, because the vertical rays are converging more rapidly than the horizontal. At B, the vertical rays have come to a focus, while the horizontal are still converging: the section will be a horizontal straight line. At C, D and E the vertical rays are diverging and the horizontal are still converging. At one place in this focal interval there will be a spot (D) where the vertical rays have diverged from the axis exactly as much as the horizontal rays have converged towards it. Here the section is a circle, which is called the *circle of least diffusion.* At F the horizontal



Fig, 6.6 Sturm conoid: W, vertical meridian of refracting surface, more curved than HH, the horizontal meridian; A, I , C, D, E, F, G, sections of conoid; from B to F is the focal interval of Sturm; D shows the circle of least diffusion.

rays come to focus while the vertical are diverging: the section will be a vertical straight line. Beyond this point, as at G, both sets of rays are diverging, and the section will always be a vertical oval or prolate ellipse.

If the retina is situated at any of these points of the section, it is obvious that the retinal image will always be blurred. It is because the rays never come to a focus at a single point that the condition is called *astigmatism* (a privative; axt7(xa, a point). If the retina cuts the conoid at A, where none of the rays have come to" a focus, every meridian will have convergent rays though in differing degrees, as in the axial hypermetropic eye: this condition is therefore called *compound hypermetropic astigmatism.* If the retina is at B, the vertical meridian will be focused as in an emmetropic eye, while the horizontal will still be converging as in hypermetropia: this condition is called *simple hypermetropic astigmatism.* At C, D and E, the vertical meridian will be diverging as in myopia, and the horizontal still be converging as in a hypermetropic eye: this is called *mixed astigmatism.* At F, the vertical meridian is still myopic, while the horizontal is focused; this is *simple myopic astigmatism.* Beyond F, as at G, both meridians have diverging rays as in an axial myope, the rays having crossed in the vitreous; this is *compound myopic astigmatism* All these positions of the retina are met with in actual practice, although there is often a combination of axial and curvature defects.

Distant vision is often found to be surprisingly good with relatively high degrees of mixed astigmatism, probably because the circle of least diffusion falls on or near the neuroepithelium of the retina.

THE CORRECTION OF AMETROPIA WITH LENSES

In hypermetropia, the rays are given the requisite amount of convergence before they enter the eye by placing a convex lens in front of it, so that they are brought to a focus upon the retina (Fig. 6.7). This is done by means of spectacles. The refractive or convergent power of a convex lens is the reciprocal of its focal distance. Hence in hypermetropia of 1 D, a convex lens of 1 D or 1 m focal length placed in contact with the cornea, acting in combination with the refractive power of the eye, would bring the rays to a focus on the retina. However, lenses are only rarely worn in contact with the cornea. If the lens is placed 20 mm in front of the cornea its focal length will have to be 1020 mm instead of 1000 mm, but this small difference is negligible. Errors of refraction are measured by the strength of the lens which is required when it is placed in the ordinary position of a spectacle lens.

Similarly in myopia, the rays are given the requisite amount of divergence before they enter the eye so that

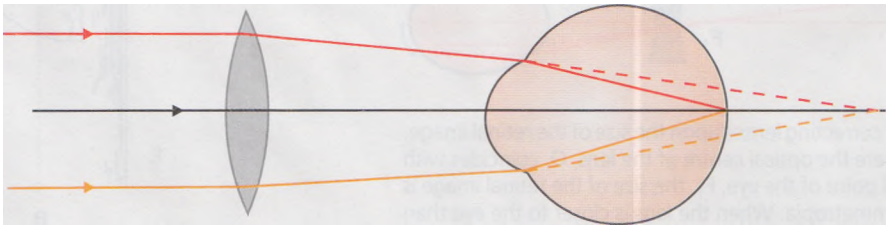


Fig. 6.7 Hypermetropic eye. Parallel incident rays are brought to a focus on the retina by means of a suitable convex lens.

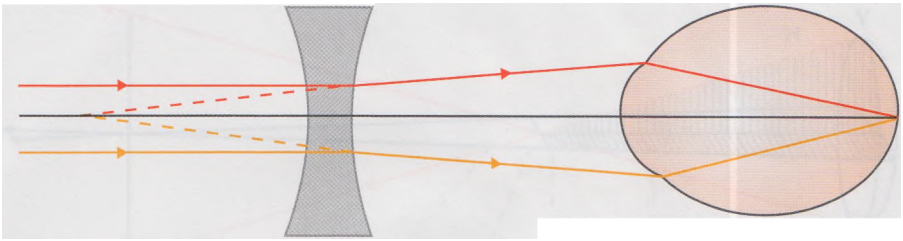


Fig. 6,8 Myopic eye. Parallel incident rays are brought to a focus on the retina by means of a suitable concave lens.

they are brought to a focus upon the retina. This is done by placing a concave lens in front of the eye (Fig. 6.8). An eye which has its far point 1 m in front of the eye would need a -1 D lens in contact with the cornea to correct a myopia of 1 D. If the glass is worn about 20 mm in front of the eye it will have to be somewhat stronger, i.e. it will have to have a focal length of 980mm instead of 1000 mm.

There is an advantage in having the correcting lenses in axial ametropia in the position of the anterior focus of the eye, because in these conditions the size of the retinal image is the same as if the eye were emmetropic (Fig. 6.9A and C). The anterior focus is about 15 mm in front of the eye. The optician aims at placing the optical centre of the spectacle lens 12-13 mm from the cornea. The convex lens in hypermetropia has to be made weaker and the concave lens in myopia stronger as the distance of the lens from the eye increases. There is also an effect on the size of the retinal image (Fig. 6.9B and D). If the lens is closer to the eye than the anterior focal distance, the size of the retinal image is diminished (convex lens, Fig. 6.9B) or enlarged (concave lens, Fig. 6.9D). If the lens is more than 15 mm from the cornea the retinal image in hypermetropia is larger, and in myopia smaller than the emmetropic image. The increase in size in hypermetropia is advantageous, but the diminution in myopia is a disadvantage, especially in very high myopes. Consequently, in myopes the spectacles ought to be made to fit as close to the eyes as possible.

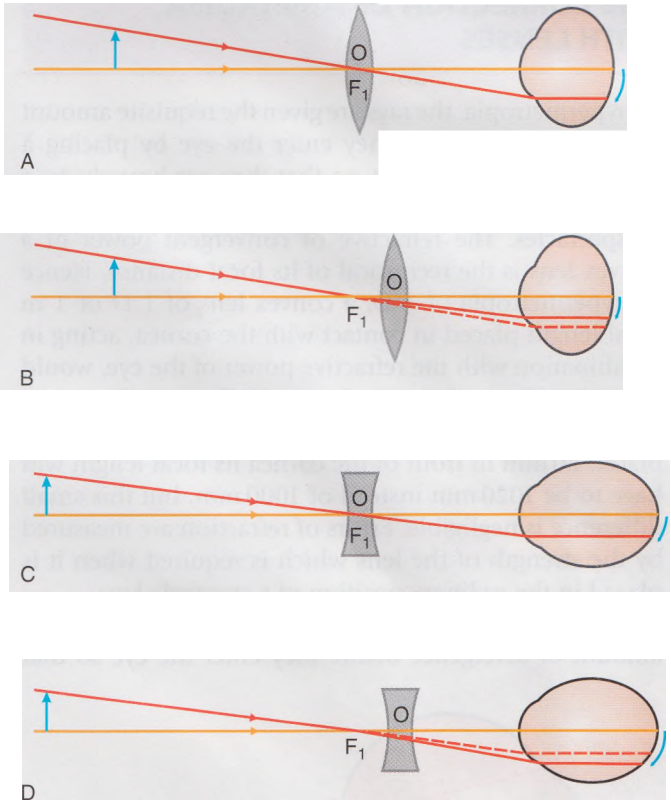


Fig. 6,9 Effect of correcting lenses upon the size of the retinal image. In (A) and (C) where the optical centre of the lens, 0, coincides with the anterior focal point of the eye, F,, the size of the retinal image is the same as in emmetropia. When the lens is closer to the eye than the anterior focal distance of the eye, the size of the retinal image is diminished (convex lens, B) or increased (concave lens, D).

In astigmatism some means of affecting one set of rays more than the other must be found. This is done by using cylindrical lenses. In a cylinder of glass CDEF (Fig. 6.10), AB is called the axis of the cylinder. If a slice is cut off the cylinder by a plane parallel to the axis, it would form a cylindrical lens. Figure 6.11 illustrates a convex and a concave cylinder. The direction ab is called the axis of the cylinder, since it is parallel

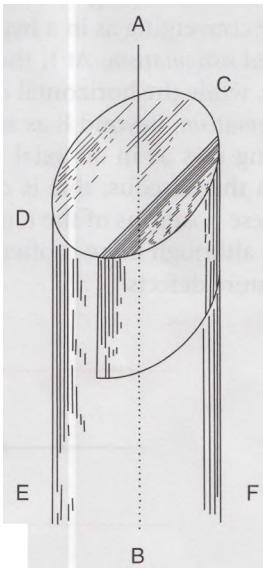


Fig. 6.10 Convex cylinder.

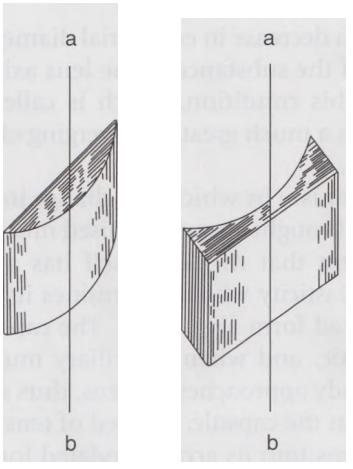


Fig. 6 .11 Convex and concave cylinder.

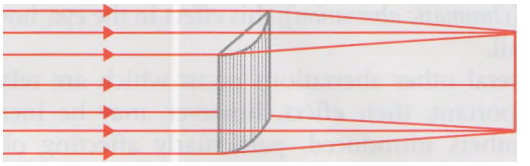


Fig. 6.12 Refrac on of parallel rays through a planoconvex cylinder.

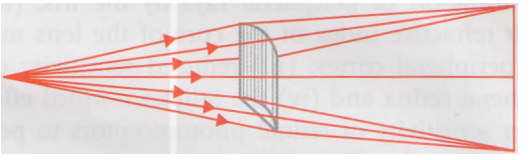


Fig. 6 .13 Refraction of divergent rays from a point of light through a planoconvex cylinder.

to the axis of the original cylinder from which the slice may be supposed to have been taken. It is important not to confuse the axis of a spherical lens and the axis of a cylindrical lens, as they are totally different. The axis of a cylinder has just been described; the axis of a spherical lens is the line joining the centres of curvature of the two surfaces.

Parallel rays falling upon a cylindrical lens will be affected in different ways. In the direction of its axis it is simply a plane lamina with parallel sides, so that it will have no effect upon the rays. In the direction at right angles to its axis it is spherical on one side and plane on the other. It will therefore act exactly like a planoconvex or a planoconcave lens, i.e. it will make the rays either converge or diverge (Figs 6.12 and 6.13). If a convex cylinder is held between a point of light and a screen, a position can be found for the screen such that a sharp bright line is thrown upon it (Figs 6.12 and 6.13); this is *the focal line* of the cylinder.

It is to be noted that the focal line is in the direction of the axis of the cylinder. If another convex cylinder of the same strength were held with its axis at right angles to the first, it would obviously form a focal line perpendicular to the first focal line. If the two cylinders are put in contact with their axes at right angles, all the rays after refraction must pass through both lines. The only place where they can go through both lines is where the lines intersect. Hence, two cylindrical lenses of equal strength, placed in contact with their axes at right angles, act exactly like a convex spherical lens of the same strength as either of the cylinders.

Optical aberrations

As in all optical systems in practical use, the eye is by no means optically perfect; the lapses from perfection are called *aberrations.* To a large extent, however, they affect the peripheral rays and are thus eliminated by the iris which acts like the diaphragm of any ordinary optical system, such as a photographic camera or a microscope. In the discussion on the effects of spherical mirrors in reflecting, and of spherical transparent surfaces in refracting rays of light, it was seen that in each case they were all brought to a focus at a single point. This is really only an approximation which is sufficiently accurate for rays close to the axis. In a convex spherical lens, for instance, only parallel rays near the axis meet at the principal focus; rays further away from the axis, however, are refracted too much, so that they cut the axis nearer the lens than the principal focus, thus causing a blurring of the edges of the image *(spherical aberration,* Fig. 6.14). A diaphragm cutting off these peripheral rays would prevent the blurring. In the eye the surfaces are not spherical, especially near the periphery, so that much more aberration is liable to occur, but the iris reduces the effects to a minimum.

In addition, there is another form of aberration due to imperfect refraction at spherical surfaces. White light is made up of all the colours of the spectrum. The component rays are refracted differently, the short, violet rays the most, the long, red rays the least. Hence there is a tendency for the white light to be split up into its components, in which case the image will have a coloured

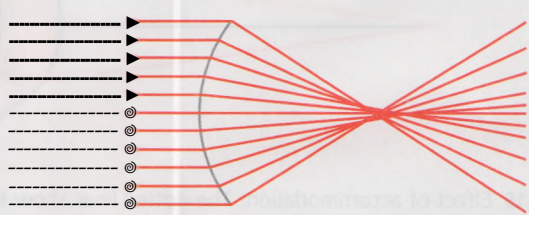


Fig. 6 .14 Spherical aberration.

edge (*chromatic aberration)-,* this effect in the eye, however, is small.

Several other aberrations occur which are relatively unimportant; their effect, however, may be increased and others introduced, particularly affecting oblique and peripheral rays, when the optical system is complicated by spectacles.

The natural mechanism of the eye to counteract the effect of or reduce the various aberrations include: (i) the cutting-off of peripheral rays by the iris; (ii) the higher refractive index of the core of the lens nucleus than peripheral cortex; (iii) reduced sensitivity of the peripheral retina and (iv) the Stiles Crawford effect or greater sensitivity of retinal photoreceptors to perpendicular rays rather than oblique rays.

ACCOMMODATION

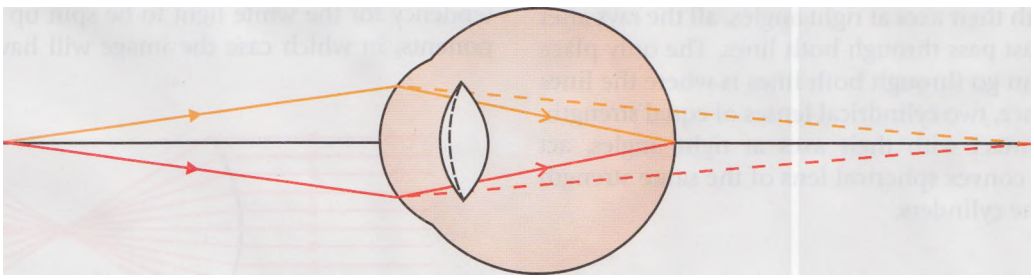
A person with normal sight can see not only distant objects, but also near ones. If an object is situated near the eye, as at ordinary reading distance (about 30 cm), the divergence of the rays emanating from the object (which it emits) cannot be neglected. Since the converging power of the refractive media of the emmetropic eye is only strong enough to make parallel rays come to a focus on the retina, it is obvious that divergent rays falling upon the cornea will not come to a focus at the same distance (Fig. 6.15). The necessary increase in their convergence power is accomplished by augmenting the refractive power of the crystalline lens by increasing the curvature of its surfaces by the phenomenon of *accommodation.*

The curvature of the surfaces of the lens at rest in the eye is approximately spherical; the radius of curvature of the anterior surface being 10 mm, and that of the posterior surface 6 mm. In accommodation, the curvature of the posterior surface remains almost the same, but the anterior surface changes so that in strong accommodation its radius of curvature becomes 6 mm. During accommodation, there is an increase in the thickness of the lens and a decrease in equatorial diameter with a displacement of the substance of the lens axially forwards. The eye in this condition, which is called its *dynamic refraction,* has a much greater converging effect upon the incident rays.

The mechanism by which this change in the curvature of the lens is brought about has raised much controversy. It would seem that the lens itself has a considerable amount of elasticity which determines its normal non-accommodated form (Fig. 6.16). The capsule, however, is more elastic, and when the ciliary muscle contracts the ciliary body approaches the lens, thus slackening the zonule so that the capsule, relieved of tension, is able to mould the lens into its accommodated form. The peculiar shape assumed by the lens thus deformed may be due to the peculiar configuration of the capsule which is thicker behind the iris than in the central area. The shape of the lens at any one time is thus the result of a balance between its own elasticity and that of its capsule.

Control over the ciliary muscle, though involuntary, is very delicate, so that all distances, even those quite close to the eye can be accurately focused. The nearest point at which small objects can be clearly distinguished is called the *near point* or *punctum proximum.* At this point accommodation is exerted to its maximum, the lens capsule is as slack as it is possible to make it, and an object closer to the eye can only be seen clearly by using a convex lens.

It has been shown that the *far point* or *punctum remotum* of the eye varies according to its static refraction, i.e. whether it is emmetropic, hypermetropic or myopic. The near point also varies with the static refraction as well as with the age of the patient, the reason being that the lens becomes less plastic as age advances. As stated, the lens is a mass of epithelium of which the central part is the oldest; as it gets older the central cells become sclerosed and more compressed, thus forming a relatively hard nucleus. The nucleus is less plastic than the younger cortex and, as age advances, more of the fibres become converted into the nucleus. Consequently, the lens tends to respond less to changes in tension of the capsule. Thus, a



Fig, 6.15 Effect of accommodation. The dotted lines show the curvature of the anterior surface of the lens and the course of rays with the eye at rest (static refraction). The solid lines show the curvature of the anterior surface of the lens and the course of rays with active accommodation (dynamic refraction).

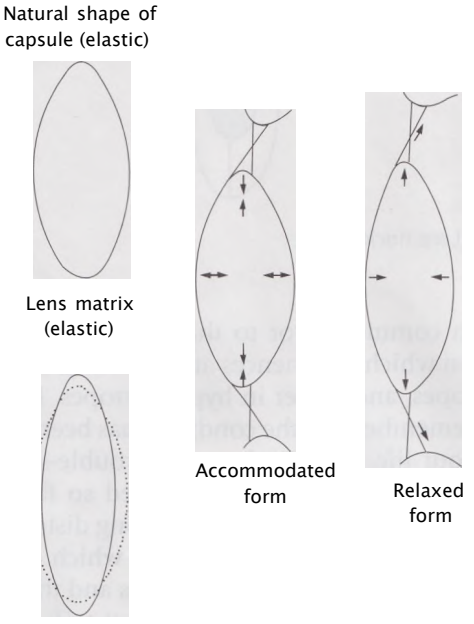


Fig. 6.16 The changes in the lens with accommodation. During accommodation the elastic capsule imposes its natural conoidal shape on the elastic lens substance which resists the former (after Weale).

child of 10 years is able to see a small object clearly when it is only 7 cm from the eye, while a person of 30 years of age may not see clearly at a distance less than 14 cm.

Normally the ciliary muscle has a considerable amount of tone which cannot be relaxed so that the full degree of hypermetropia is only apparent when this muscle is paralysed by a cycloplegic drug. This portion of the total hypermetropia which can only be revealed under complete cycloplegia is called the *latent h)>permetropia.* The remainder is called the *manifest hypermetropia.* The sum of the two gives the *total hypermetropia.* Of the manifest hypermetropia, that part which can be overcome by accommodation is termed *facultative;* that which cannot be thus compensated for is termed *absolute.* In extreme youth nearly all the hypermetropia is latent; the lens is so resilient that it is impossible to prevent its response to the slightest stimulus. As the lens becomes less plastic more of the hypermetropia becomes manifest, until finally, when accommodation disappears entirely, all the hypermetropia is manifest. The older the patient, the more nearly the manifest hypermetropia represents the total amount of hypermetropia.

The refractive power of a lens in dioptres is the reciprocal of its focal distance measured in metres and the same method is applied to measure the static refractive power of the eye. Applying the same method to the dynamic refractive power, the child of 10, whose near point is 7 cm from his eye, has a refractive power of 100/7 = 14 D, and a man of 30, whose near point is 14 cm from his eye, has a refractive power of 100/14 = 7 D.

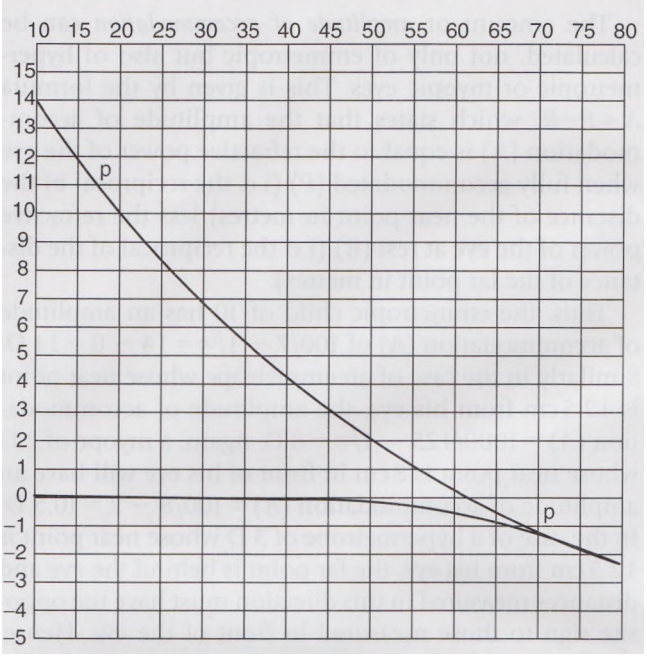
The amount or *amplitude of accommodation* can be calculated, not only of emmetropic but also of hypermetropic or myopic eyes. This is given by the formula $A = P—R$, which states that the amplitude of accommodation (A) is equal to the refractive power of the eye when fully accommodated (P) (i.e. the reciprocal of the distance of the near point in metres) less the refractive power of the eye at rest (R) (i.e. the reciprocal of the distance of the far point in metres).

Thus, the emmetropic child of 10 has an amplitude of accommodation (A) of 100/7 — 1/°°=14 — 0=14D. Similarly in the case of an emmetrope whose near point is 12.5 cm from his eye, the amplitude of accommodation (A) = 1000/125 — l/oo = 8 D. Again, a myope of 2 D whose near point is 8 cm in front of his eye will have an amplitude of accommodation (A) = 100/8 — 2= 10.5 D. In the case of a hypermetrope of 3 D whose near point is 12.5 cm from his eye, the far point is behind the eye and distances measured in this direction must have the opposite sign to those measured in front of the eye. Hence, A = 1000/125 - (-3) = 8 + 3 + 11 D.

The numbers given by these calculations for the amplitude of accommodation give the strength of the convex lens which would have to be placed in contact with the cornea so that the near point might be brought to the required distance without using the accommodation. Several interesting facts come to light from the calculations. Thus a hypermetrope of 3 D has to exert 11 D of accommodation to be able to see clearly at 12.5 cm, while an emmetrope has to exert only 8 D of accommodation to bring about the same result. The hypermetrope thus has to exert an amount of accommodation equivalent to the amount of the hypermetropia in order to focus parallel rays upon the retina and see distant objects clearly. Again, the myope of 2 D, whose far point is 0.5 m or 50 cm from the eye, can see clearly at that distance without accommodating, but has to exert 10.5 D of accommodation to see clearly at 8 cm from the eye. This patient, then, has to exert nearly as much accommodation to alter the points of clear vision from 50 to 8 cm, i.e. through 42 cm, as a hypermetrope of 3 D has to employ in order to move the point of distinct vision from infinity up to 12.5 cm. Therefore, the *range of accommodation,* i.e. the distance between the far point and the near point, is not always the same for a given amplitude.

The effect of age upon the static and dynamic refraction is given in Fig. 6.17, which is compiled from a large number of measurements. From this graph it can be seen that even the far point alters in advanced age. After about 50 years of age the eye tends to become hypermetropic, so that at the age of 80 it has about 2.5 D of hypermetropia; this is due to an alteration in the refractive index of the lens so that it has a weaker converging power.

The refractive indices of the successive layers of the lens increase from the periphery towards the nucleus.



Fig, 6.17 Chart of static (lower curve) and maximum dynamic (upper curve) refraction at various ages (Donders). Abscissa: age; ordinate: accommodation in dioptres.

The effect is two-fold; it tends to correct aberrations by increasing the convergence of the central rays, and the total refractive index of the whole lens is increased, becoming greater than the refractive index of the nucleus. The lens may be looked upon as a central biconvex lens encapsulated in two menisci (Fig. 6.18); these act as concave lenses because the curvature of the nucleus is greater than that of the periphery of the lens. Flence they tend to counteract the effect of the central lens, but not as much as if their refractive indices were the same. In old age the refractive index of the peripheral layers usually increases, so that the total refractive index of the lens becomes less, and the eye becomes hypermetropic. Index myopia occurs in individuals who develop a uniform sclerosis of the lens, as in brunescent cataracts.

The amplitude of accommodation gradually diminishes throughout life as seen by the curve of the near point in Fig. 6.17. Since one is accustomed to hold books for reading at about 25 cm from the eye, in order to see clearly, 100/25 or 4 D of accommodation must be exerted, which is all that an emmetrope has available at a little over 40 years of age; such a person will still be able to see clearly at 25 cm, but not closer. At about 46 years of age only 3 D of accommodation remains and a book will have to held further off, at 100/3 or 33 cm, a disability which will increase as age advances. This condition is called *presbyopia* (presbnz, old).

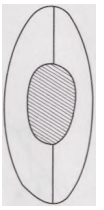


Fig. 6.18 Lens nucleus.

It is a common error to think that presbyopia is a condition which commences at about 45 years of age in emmetropes, and earlier in hypermetropes. It is important to remember that the condition has been increasing throughout life and first becomes trouble-some when the near point of the eye has receded so far that it is beyond comfortable reading or working distance.

There are two other phenomena which occur with accommodation, one affecting the iris and the other the direction of the eyes. For a near object to be seen with both eyes they must each turn inwards or *converge.* The amount of convergence, like the amount of accommodation, depends upon the distance of the object so that there is a close relationship between accommodation and convergence.

When accommodating for a near object the pupil becomes smaller, or constricts. This helps to diminish aberration by cutting out the peripheral parts of the lens, increases the depth of focus and compensates for the relative increase of light entering the eye from near objects. It may be noted that in accommodation the ciliary muscle contracts equally all round the circumference and simultaneously in the two eyes, so that this activity can correct neither astigmatism nor anisometropia.

SUMMARY

The eye behaves like a biological optical device. Normal variations in its properties result in differences in functional effects which manifest as ametropia or refractive errors.

The phenomenon of accommodation enables the eye to have flexibility of focus allowing for the ability to see both distant and near objects clearly within a physiological range.

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7

Refraction

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In determining the refraction of the eye the routine is to first estimate the condition objectively, and then to verify and adjust these values by subjective tests. The commonly employed objective methods are retinoscopy and the use of the refractometer. Corneal astigmatism is objectively measured by the keratometer.

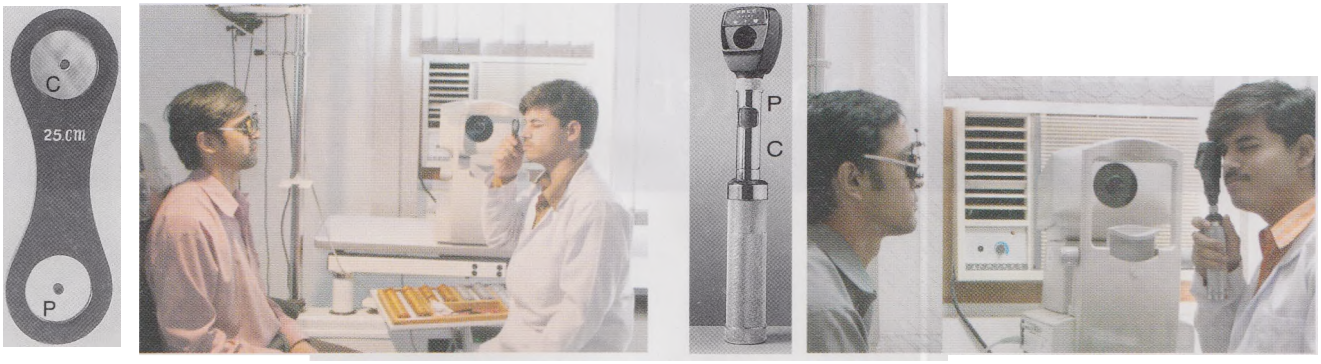
RETINOSCOPY

The theory of retinoscopy

Retinoscopy or, more correctly, *skiascopy* or the *shadow test* is the most practical method of estimating the condition of the refraction objectively. It is based on the principles outlined in Chapters 5 and 6. The process begins with directing light into the patient's eye illuminating the retina. Rays of light from the patient's retina emerge from the patient's pupil, forming an image of the patient's retina at the far point of the patient's eye. The location of this image depends on the refractive status of the eye and is estimated by moving the illuminated spot or slit across the fundus and observing the behaviour of the luminous reflex seen by the observer in the patient's pupillary area. The light seen in the pupil is the blurred image of the illuminated area of the fundus as seen by the observer when accommodating for the observed pupil; it is bordered by a shadow representing the edge of the image of the illuminated area.

The source of light for retinoscopy could be either external or internal. An external source of light is directed into the patient's eye with the help of a mirror retinoscope. Alternatively, an internal bulb situated inside a self-illuminated retinoscope can be used. A mirror retinoscope such as the Priestley-Smith retinoscope (Fig. 7.1) has a plane mirror at one end and a concave mirror at the other. The mirrors project a circle of light into the patient's eye through the pupil. Both the plane and the concave mirrors have a central hole 2.5 mm wide anteriorly and 4.0 mm posteriorly fitted with a low polar convex lens for viewing the reflex thus created. Either of the two mirrors can be used for retinoscopy. A self-illuminated streak retinoscope performs the same function but projects a streak rather than a circle of light. The retinoscope illuminates an area of the retina. An image of this portion of the retina is then formed at the patient's far point. The observer does not exactly see this image but views rays of light emanating from the illuminated retina which are seen in the patient's pupillary area from a convenient working distance. Depending on the behaviour of this luminous reflex the observer knows whether the emerging rays are convergent, divergent or parallel. Lenses from a trial set are used to neutralize this movement. The point of reversal or neutral point of retinoscopy is reached when the subject's far point coincides with the observer's nodal point and the examiner sees a diffuse bright red reflex in the patient's pupil and no movement of the reflex is discernible.

If light is thrown into a myopic eye (with more than 1 D of myopia) from a plane mirror at a distance of 1 m and the mirror is tilted in any direction the light, or what is easier to observe—the shadow at the edge of the light—moves across the pupil in the opposite direction. If a concave mirror is used, the other conditions remaining the same, the shadow will be seen to move in the same direction as the movement of the mirror. If the eye is hypermetropic,



Fig, 7.1 (A) Left: Mirror retinoscope: C, concave mirror; P, plane mirror. Retinoscopy being performed with a mirror retinoscope. Right: Streak retinoscope. Retinoscopy being performed at 1 m distance with a self-illuminating streak retinoscope which functions similar to a concave mirror with the lens adjustment sleeve in position C and plane mirror in position P.

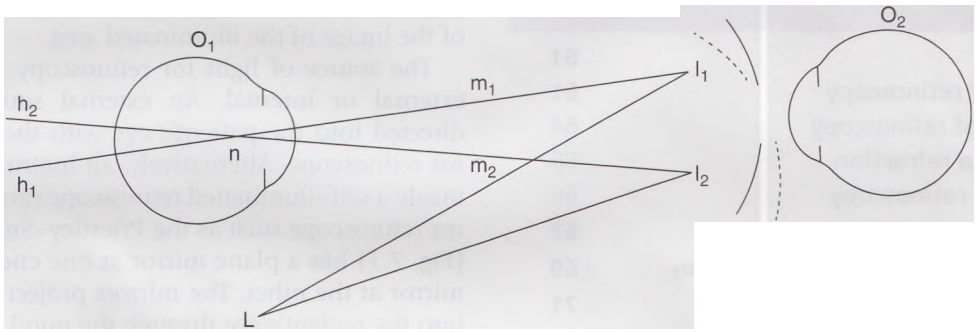


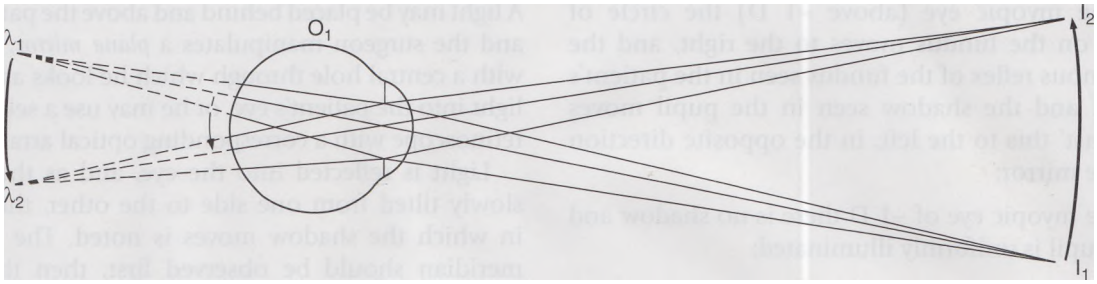
Fig. 7.1 (B) Retinoscopy with a concave mirror. 0,, the observed eye; 0_2, the observer's eye. The image of the source of light (L) is formed at I–| (the immediate source of light) by the mirror. If 0, is hypermetropic a virtual image of I–i is formed on the line I,n, passing through the nodal point n as at h,. If 0–, is myopic a real inverted image is formed as at m,. If the mirror is tilted downwards, as shown by the dotted line, I, moves to I_2, h_1–h_2 and m_1–m_2. This shows that the shadow seen by the observer moves in the opposite direction in hypermetropia and in the same direction in myopia.

the direction in which the shadow moves is the opposite to that with the myopic eye. *If the eye has 1 D of myopia* and retinoscopy is performed at a distance of 1 m, no shadow will be visible; the pupil will be either completely illuminated or completely dark. The method, therefore, consists of placing lenses in front of the eye until no shadow is seen. If the surgeon is 1 m away from the patient, the combination of the optical system of the patient's eye and the lenses is equal to 1 D of myopia. Hence the patient's refractive state will be 1 D less than the lenses used to neutralize the movement.

A simple optical explanation is as follows. Rays from a point of light in front of the eye illuminate a circular area of the fundus or a streak in the case of a self-illuminated streak retinoscope, varying in size according to the refraction of the eye. If the source of light moves upwards (which happens when the concave mirror is rotated upwards or the plane mirror is rotated downwards) the light on the retina will move downwards.

In the hypermetropic eye the rays reflected from the illuminated area and emerging from the patient's eye will be divergent, as if they came from a point behind the eye. This far point, corresponding to the illuminated area, will move in the same direction as the light falling on the retina, i.e. downwards. If an observer, placed in front of the eye, looks towards a point of light situated at the position of the far point, but accommodates for the position of the observed pupil, a circle of light with a blurred margin will be seen, not a point, because accommodation is not accurate for the far point. When the illumination on the retina moves down, the circle of light which the observer sees will also appear to move 'with' it, downwards (Fig. 7.2).

In a myopic eye, the rays of light reflected from the illuminated area on the fundus will be convergent and cross at a real point in front of the eye. This far point, corresponding to the illuminated area, will move upwards when the illuminated area moves downwards. If an observer placed in front of the eye and further from it than the far point looks towards the far point but accommodates for the observed pupil, a circle of light with a blurred margin will be seen. When the illumination on the retina moves down, the circle of light which the observer sees will move up, i.e. in the opposite direction to the movement seen in the case of the hypermetropic eye (Fig. 7.3).



Fig, 7.2 The course of incident rays and field of illumination of the fundus in hypermetropia: I,, the source of light illuminates the superior retina and forms a virtual image at the light source moves to I_2, the inferior retina is illuminated and the virtual image appears to move inferiorly to X_2, i–e– 'with' the illumination of the retina. The field of illumination is determined by the pupil of O,.

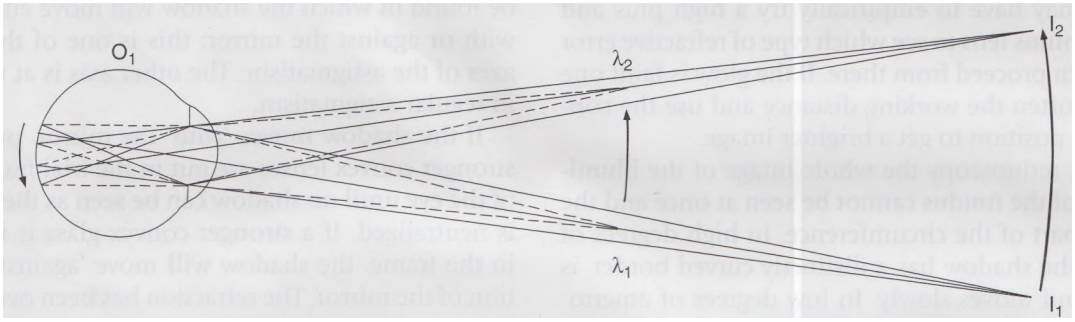


Fig. 7.3 The course of incident rays in myopia more than 1 D.

If the observer's eye is 1 m in front of the observed eye, and the latter has 1 D of myopia, the far point of the observed eye will be at the situation of the observer's eye (Fig. 7.4). In this case a very slight movement of the light on the observed fundus will throw the image at the far point off the observer's eye altogether; in other words, the observed pupil will appear to be completely bright or completely dark.

If, again, the observed eye is emmetropic, its far point will be at infinity; it may be regarded as being infinitely far behind the observed eye. Here, again, there will be scarcely any shadow, although in reality there is a very faint shadow moving in the same direction as for the hypermetropic eye.

The type of mirror used is a subsidiary matter; it merely determines the direction of movement of the immediate source of light, i.e. the point of light in front of the eye which "has "been considered above. The Image' of a real light behind the patient's head, formed by a concave mirror, is situated in front of the mirror. If the mirror is tilted up, the 'image' moves up. The 'image' of a real light behind the patient's head, formed by a plane mirror, is situated as far behind the mirror as the light is in front of it. When the mirror is tilted up, the 'image' moves down. It is this 'image' formed by the retinoscopic mirror which forms the source for the 'point' of light diverted into the patient's eye.

Hence under the actual conditions of *retinoscopy at 1 m distance* with a *plane mirror,* wᵀhen the mirror is tilted towards the right side, the immediate source of light moves to the left, and

1. in the hypermetropic eye, the circle of light on the fundus moves to the right and the shadow seen in the pupil moves 'with' it to the right in the same direction as the mirror;

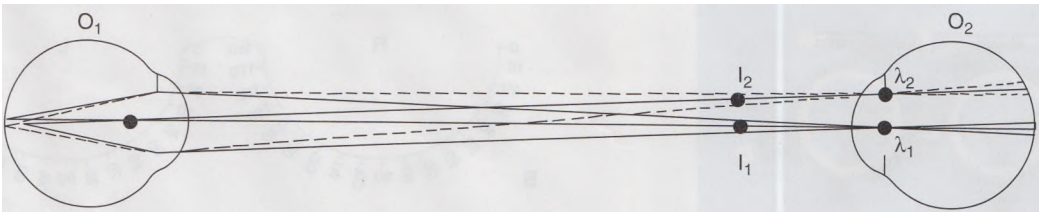


Fig. 7.4 The course of the emergent rays in myopia of 1 D and at the point of reversal. So long as the light source I, is in the pupillary area of 0_2, the pupil of O, appears uniformly illuminated, and there is no shadow. Directly I, passes to I_2 the light is completely cut off, so that the pupil of Oj becomes completely dark.

2. in the myopic eye (above -1 D) the circle of light on the fundus moves to the right, and the luminous reflex of the fundus seen in the patient's pupil and the shadow seen in the pupil moves 'against' this to the left; in the opposite direction to the mirror;
3. in the myopic eye of -1 D there is no shadow and the pupil is uniformly illuminated;
4. in emmetropia and myopia of less than - ID there is a very faint shadow moving to the right.

With high refractive errors the initial glow may be so faint that the direction of movement is difficult to ascertain. One may have to empirically try a high plus and then high minus lens to see which type of refractive error it is and then proceed from there. If the glow is faint one can also shorten the working distance and use the concave mirror position to get a brighter image.

In actual retinoscopy the whole image of the illuminated area of the fundus cannot be seen at once and the shadow is part of the circumference. In high degrees of ametropia the shadow has a distinctly curved border, is very dark and moves slowly. In low degrees of ametropia the border of the shadow looks straight, is faint and moves rapidly.

The movement of the shadow, being a purely optical phenomenon, is, of course, independent of the cause of the ametropia. Consequently, in astigmatism, if one axis is hypermetropic and the other myopic (mixed astigmatism) the shadow moves in opposite directions in the two meridians. Often the periphery of the cornea is flatter than the centre; correction of the refraction of the central part, which is the more important, will then differ from that of the peripheral part. These variations produce very puzzling shadows in many cases.

The practice of retinoscopy

Retinoscopy is conducted in a dark room. The surgeon sits 1 m from the patient or at a convenient working distance which is often an arm's length (about two-thirds of a metre). The patient wears a trial frame (Fig. 7.5) and fixes his gaze at a spot of light at the far end of the room.

A light may be placed behind and above the patient's head and the surgeon manipulates a *plane mirror,* perforated with a central hole through which he looks as he reflects light into the patient's eye, or he may use a self-luminous retinoscope with a corresponding optical arrangement.

Light is reflected into the eye, and as the mirror is slowly tilted from one side to the other, the direction in which the shadow moves is noted. The horizontal meridian should be observed first, then the vertical. If the shadow appears to swirl around, not moving in the same meridian as the mirror, the eye is astigmatic, and the mirror is not moving in a direction which corresponds to either axis. A direction of movement can be found in which the shadow will move either directly with or against the mirror; this is one of the principal axes of the astigmatism. The other axis is at right angles in regular astigmatism.

If the shadow moves 'with' the mirror, progressively stronger convex lenses are put in the trial frame in front of the eye until no shadow can be seen as the movement is neutralized. If a stronger convex glass is now placed in the frame, the shadow will move 'against' the direction of the mirror. The refraction has been overcorrected. The point at which there is absolutely no shadow—*the point of reversal*—is somewhere between the last two lenses, and at that point the refractive error (*R*) of the eye, together with the neutralizing lens (L) in place, is equivalent to 1 D of myopia. The refractive error of the eye, or spectacle power required, would be the power of the neutralizing lens (L) minus 1 D.

R + L = -1D or *R - L - I D*

If, for example, the shadow can still be seen to move with the mirror with *a* + 4 D lens in the frame, and moves against it with +4.5 D, we shall not be far wrong in considering that the point of reversal is +4.25 D (Table 7.1). A lens of +4.25 D would therefore make the eye 1 D myopic. The actual refractive error is therefore +3.25 D.

Similarly, for spherical myopia, if -4 D eliminates the shadow against the mirror and -4.5 D gives a distinct shadow with the mirror, we know that -4.25 D will still leave the eye with -ID. Ilence the refractive error is-5.25 D.

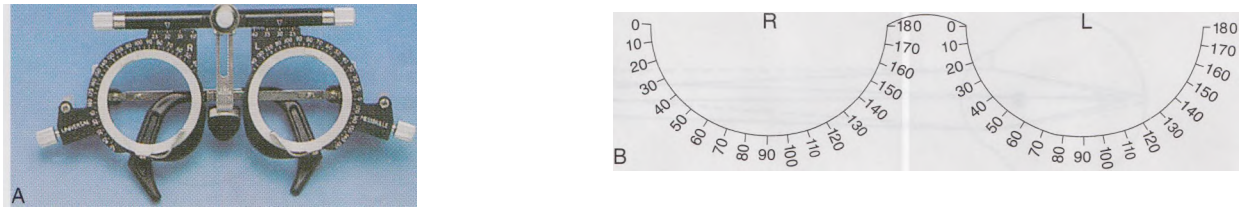


Fig. 7.5 (A) Trial frames (By courtesy of Keeler). (B) The standard notation of axes of cylinders. To avoid ambiguity in ordering glasses, the axes of cylinders should be uniformly numbered according to the method recommended by the International Council of Ophthalmology.

Table 7.1 Retinoscopy findings in different refractive states

Refractive status	Direction of movement: Circle of light on the fundus	Direction of movement: Luminous reflex of the fundus
Hypermetropia	Right*	Right; shadow in the pupil
Myopia (>1 D)	Right*	Left; shadow in the pupil
Myopia (=1 D)	Right*	No shadow, no movement
Emmetropia and myopia (<1 D)	Right*	Right; faint shadow, very slight movement

*Moves to the right if a plane mirror is tilted to the right or a concave mirror is tilted to the left.

In astigmatism each principal meridian is corrected separately in the same way. When one meridian is approximately corrected the shadow assumes the shape of a band, the edge of the band being parallel to the axis of the corrected meridian. Even if the light is not moved in a direction accurately at right angles to this meridian, the shadow still seems to move in the same direction. This is due to an optical illusion. If, in Fig. 7.6, a straight edge, AB, is placed obliquely behind a circular hole in a card and is then moved horizontally in the direction of the arrow C, it will appear to be moving in the direction of the arrow D at right angles to its own edge. The shadow is most sharply defined if the mirror is moved at right angles to its edge, i.e. at right angles to the corrected meridian.

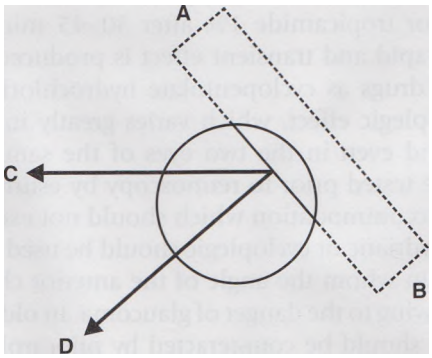


Fig. 7.6 Optical illusion in astigmatism.

The strength and direction of the axis of the cylinder are then verified by placing the appropriate sphere and cylinder in the trial frame and again studying the shadow effects. If there is any shadow in any direction the appropriate correction should be made. Further accuracy is achieved by the surgeon leaning towards and then away from the patient, repeating his observations on each occasion. In the first case a shadow should move in the same direction as the tilt of the plane mirror, in the second in the opposite direction. If the expected change does not occur in both directions symmetrically, the neutralizing lenses are wrong.

In streak retinoscopy instead of a circular source of light as is obtained by an ordinary plane mirror, a streak of light is used; this has some advantages. The streak effect is obtained by using a piano-cylindrical lens. The appearances are more dramatic (Fig. 7.7A-C), as the band of light in the pupillary aperture moves 'with' or 'against' the band of light outside the pupil, the axis of astigmatism is more easily determined, and on neutralization the streak disappears and the pupil appears completely light or completely dark.

Most streak retinoscopes consist of an optical head, a sleeve and a battery handle. The optical head projects a slit beam called a 'streak' which can be observed through a peephole on the other side. The sleeve assembly allows the streak of light to be converged or diverged, changing the width and focus of the slit, by moving the sleeve

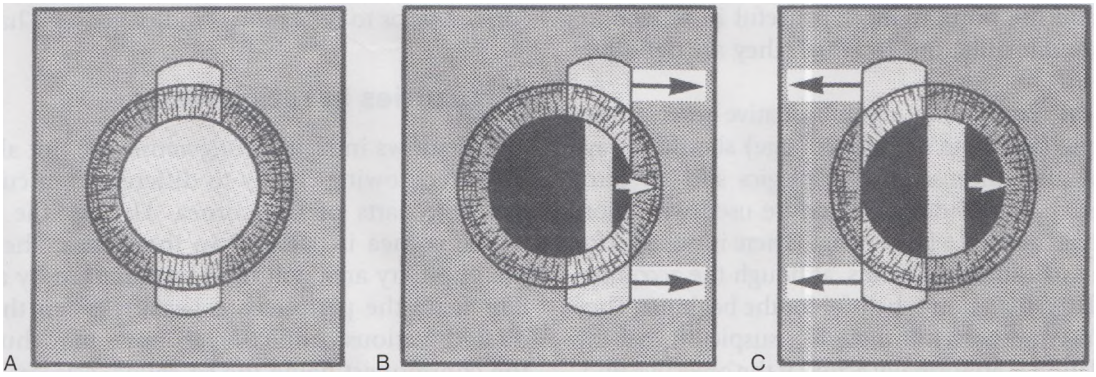


Fig. 7.7 Streak retinoscopy. (A) shows the reflex at the point of neutralization, (B) the reflex and streak in a 'with movement in hypermetropia' plane mirror and (C) the reflex and streak in an 'against movement in myopia' plane mirror.

up or down. The sleeve also allows rotation of the slit through 360°.

The streak is used with its slit beam maximally wide and out of focus. The retinoscope is held in one hand and the thumb or index finger of the same hand is used to hold the sleeve in the right position and also orient the slit in different directions. The patient is seated in a darkened room and asked to view a non-accommodative distant target. The trial frame or phoropter is placed on the patient's face and the interpupillary distance adjusted for each eye. The observer sits as far back as possible to increase the accuracy of measurements.

The streak is passed across the pupil of the eye with the streak in a perpendicular orientation to the direction of the movement. When examining the patient's right eye, the retinoscope is held with the observer's right hand and viewed by the observer's right eye, *vice versa* for the left. As *the streak is moved across the pupil the light reflex may move 'with', 'against', be 'neutral' or indeterminate.* The width of the slit and its apparent speed as it moves across the pupil give an indication of the degree of refractive error.

The aim of retinoscopy is to convert 'with' or 'against' movement of the slit to a neutral reflex. This is accomplished by adding a lens of the required power manually or with the phoropter. The width of the slit reflected and its apparent speed as it moves across the pupil give an indication of how far one is from neutrality. A very wide, slow-moving reflex that almost fills the pupil denotes a high refractive error and needs the addition of high power lenses to reach neutrality. The streak tends to narrow and speed up as lenses of appropriate power are added to reach neutrality. Close to or at the point of neutralization, the slit widens again, but now moves extremely fast, resulting in visualization of a fully illuminated pupil at one point and a dark pupil the next moment.

Cycloplegics in refraction

The use of cycloplegics, whereby the ciliary muscle is paralysed and the pupil dilated, is useful in refraction. There are certain situations in which they are definitely indicated.

Because of their strong accommodative reserve, very young people (less than 16 years of age) should always be refracted after the use of cycloplegics such as atropine but less powerful drugs should be used with most hypermetropes above 16 years of age. There is no need for cycloplegia as a routine in adults, although the accompanying pupillary dilatation is helpful for the beginner. They should be used, however, if there is a suspicion that the accommodation is abnormally active, if the objective findings by retinoscopy do not agree with the patient's subjective requirements, if definite symptoms of accommodative asthenopia are present which do not seem to be explicable by the error found without a cycloplegic, and if the pupil is small and refraction presents technical difficulties.

A cycloplegic-mydriatic may also be indicated for ophthalmoscopic purposes to view the macula or the periphery of the fundus. It is to be remembered, however, that refraction under cycloplegia is not final because the shape of the lens has been altered, and after the lens has assumed its normal shape, minute errors cannot reasonably be transposed to the dioptric system in the ordinary conditions of use. Moreover, with a mydriatic the refraction of the peripheral part of the lens is often estimated, not the central part which, in practice, is used for vision. A post-cycloplegic test is therefore advisable. When the refraction is estimated under cycloplegia a correction must be made to compensate for the normal tone of the ciliary muscle. On average, 1 D is deducted when using atropine, 0.5 D with other cycloplegics, somewhat more in young hypermetropes and somewhat less in myopes.

Atropine is the most powerful cycloplegic and for young children should be instilled as 1% ointment, not drops, as systemic toxicity occurs due to absorption of atropine from the conjunctival and nasal mucosae. The ointment should be instilled two or three times a day for 3 days before examination. In older children, a drop of 2% homatropine or 1% cyclopentolate is effective after an hour or tropicamide 1% after 30-45 minutes. For adults a rapid and transient effect is produced by such synthetic drugs as cyclopentolate hydrochloride (1%). The cycloplegic effect, which varies greatly in different people and even in the two eyes of the same person, should be tested prior to retinoscopy by estimating the residual accommodation which should not exceed 1 D.

Any mydriatic or cycloplegic should be used with care in adults in whom the angle of the anterior chamber is narrow, owing to the danger of glaucoma. In older people mydriasis should be counteracted by pilocarpine (1%), and if suspicion of a tendency to angle-closure glaucoma exists and dilatation of the pupil is necessary, a gonioscopy and prophylactic laser iridotomy should be performed prior to dilatation if indicated (*see* Chapter 19).

Difficulties in retinoscopy

The shadows in *regular astigmatism* are not always easy to correct, owing chiefly to differences in curvature of different parts of the cornea. Usually the periphery of the cornea is flatter than the centre. The centre of the pupillary area will then be corrected by a different lens from the periphery, especially when the pupil is dilated. Various conflicting shadows may thus be seen, the commonest being the so-called 'scissors' shadows, where two shadows appear to meet each other and cross as the light is moved in a given direction. These

difficulties are diminished with the undilated pupil. In *irregular astigmatism,* the shadow moves in various directions in different parts of the pupillary area and an accurate correction cannot be made by spherical or cylindrical lenses. In a *conical cornea,* a triangular shadow with its apex at the apex of the cone appears to swirl round its apex as the mirror is moved.

In conclusion, a word of caution must be added. The correction of a given refraction by retinoscopy may be easy or difficult. A large number of refractions should have been carefully corrected and confirmed by subjective tests before the beginner should consider himself justified in ordering spectacles without supervision.

REFRACTOMETRY AND KERATOMETRY

Refractometry is the estimation of refractive error with a machine and utilizes the principle of indirect ophthalmoscopy in which a condensing lens brings rays emergent from the retina of the patient to a focus at a convenient distance. The rays from a test-object are collimated to enter the pupil as a parallel beam and, consequently, if the eye is emmetropic, are focused on the retina; emerging from the eye as a parallel beam, they are focused again by the objective lens at the position of the test-object. If the eye is myopic, the emergent rays will be convergent and the image will be formed at a nearer point; if hypermetropic, the emergent rays will be divergent and the image will be formed further away by an amount depending on the degree of ametropia. Ametropia is estimated by the direct observation of this image, the end-point being the maximum sharpness of focus. A more accurate method is to employ the principle of displacement by parallax which was elaborated by Henker in the *parallax refractometer.* By displacing the line of view to one side, the optical system is arranged such that if, as in emmetropia, the distances of the object and the image from the objective lens are equal, the image will be superimposed on the object and will not be seen. If in myopia the image is nearer the lens than the test-object, it will be displaced to the side next to the illuminating tube. If in hypermetropia it is further away, it will be displaced to the other side. When the two do not coincide the te.si-object is moved until coincidence is attained, and the refractive error can be read from a scale.

An alternative principle has been utilized by Fincham and Hartinger in their *coincidence optometers.* In these instruments, when the target is not in a position which is conjugate to the subject's retina, the retinal image is displaced from the axis. The image is viewed through a system of prisms which divides the field into two and reverses one-half, so that when the image is out of alignment the halves of the line-image move in opposite directions. The setting is correct only when an unbroken line is formed.

Automated refractometers (autorefractors) are designed to objectively determine the refractive error using infrared light and are based on one of three principles: (i) retinoscopic principle; (ii) *Scheiner disc* principle and (iii) *grating-focus* method. In (i) a retinoscopic reflex is generated and the direction of its movement registered by light sensors and the lenses required for neutralization, i.e. refractive data displayed numerically. In instruments using the Scheiner disc, an opaque disc with two pinholes is used to direct light into the patient's eye. A photoelectric sensing device records the end-point by capturing the light rays coming back from the retina. Correcting lenses are used to focus the image (Fig. 7.8) and determine the refractive status. In the grating-focus method, a luminous grating serves as a target and its image is projected on the retina. An image of the illuminated grating thus formed is scanned, the device compares the view with a sharp standard image, appropriate lenses are used to yield a sharply focused picture and the refractive data calculated and displayed.

A *keratometer (ophthalmometer*) measures the curvature of the anterior surface of the cornea at two points about 1.25 mm on either side of its centre. Since considerable lenticular astigmatism may co-exist, the technique is untrustworthy in estimating the full astigmatism except in aphakia. In pseudophakia and operated corneal grafts it is helpful in assessing the corneal component of astigmatism. The method is based on the fact that the surface of the cornea acts as a convex mirror so that the size of the image reflected by it varies with the curvature. The greater the curvature of the mirror, the smaller the image. To measure the size of the image a device is employed, originally adopted by Thomas Young, of doubling the images by a double refracting prism. The object consists of two illuminated 'mires' AB (Fig. 7.9A) disposed on a rotatable circular arc, and the curvature of any diameter of the cornea can be measured by observation through a telescope (T). The mires are seen as in ab (Fig. 7.9B) and are considered as the ends of a luminous object which appears in the cornea in duplicate as ab and a'b'. A and B are adjusted on the arc so that the two images a' just touch each other as in Fig. 7.9B. The arc is now rotated through 90° and a similar reading made. If a' and b still touch there is no astigmatism. If the *curvature in this* meridian is greater, the image is smaller and the mires will overlap as in Fig. 7.9C. If the curvature is less, the opposite effect will be observed. The mire a' is so constructed that each step corresponds to a dioptre of refractive power, the number of dioptres of astigmatism being thus read off directly.

The Bausch and Lomb keratometer uses mires of a fixed original size and the variable image size is measured to record the corneal curvature. It has the advantage that both horizontal and vertical meridians can be measured simultaneously (Fig. 7.10).

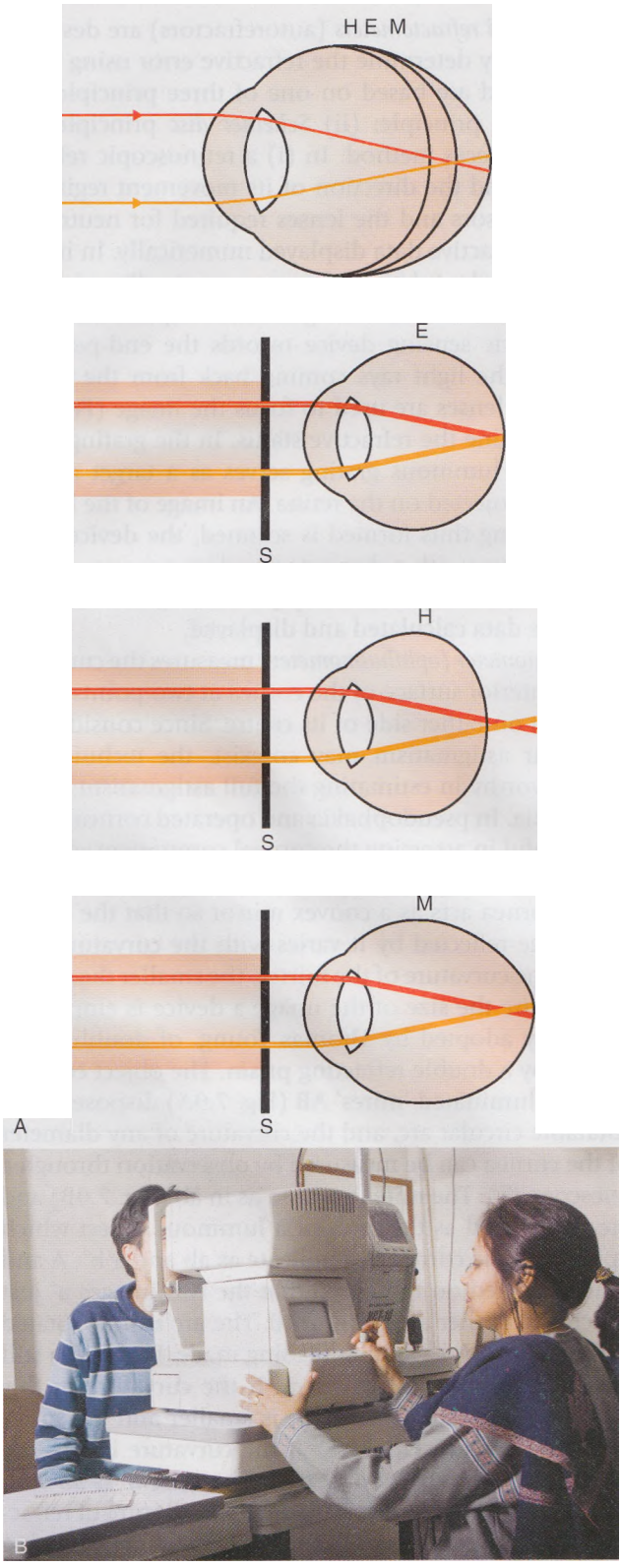


Fig. 7.8 (A) The Scheiner disc principle is used in automated refractometers (autorefractors). The Scheiner disc (S) has two pinholes through which light enters and produces two images on the retina. A photoelectric device senses the focused beam and estimates the refractive error. H: hypermetropia; E: emmetropia; M: myopia (By courtesy of S Majumdar). (B) Autorefractor.

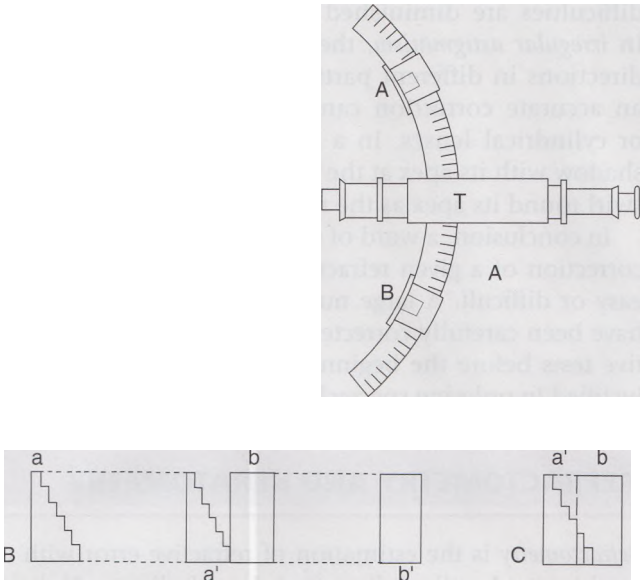


Fig. 7.9 (A–C) The principle of the keratometer of Javal and Schiotz.

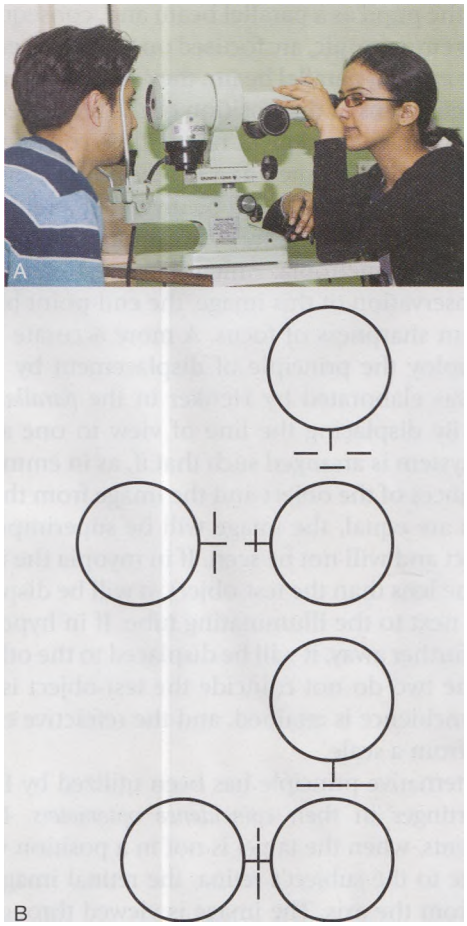


Fig. 7.10 (A) Bausch and Lomb keratometer (By courtesy of S Majumdar). (B) Bausch and Lomb keratometry mires. The upper figure shows non-aligned mires and the lower figure shows the end-point for alignment.

THE SUBJECTIVE VERIFICATION OF REFRACTION

After the refraction has been estimated objectively it should always be verified subjectively by testing the patient's visual acuity with corrective lenses in place, and if a cycloplegic has been used, the process should be repeated in a *post-cycloplegic test* The final refraction is tested with appropriate lenses, as measured by the objective test, inserted in the trial frame (Fig. 7.5). Each eye is tested separately while an opaque disc is placed in the other compartment of the frame, and then the two are finally tested together.

The patient is asked to read the test-types, and slight modifications in the power of the lenses are tried in each eye separately; any small change which gives a marked improvement in visual acuity is incorporated in the final prescription.

These manoeuvres are greatly facilitated by the use of a *cross-cylinder,* a' mixed cylindrical combination of various strengths in which the spherical component is one half the power of the cylindrical and of opposite sign with the axes at right angles (Fig. 7.11). The cross-cylinder is identified by the strength of its cylindrical component. The handle of the cross-cylinder is at an angle of 45° to both axes. The most convenient form is a combination of a -0.5 D sphere with a +1.0 D cylinder which has an effective strength of +0.5 D cylinder in one meridian and -0.5 D cylinder in the meridian perpendicular to the first. The cross-cylinder is first used to verify the axis and then applied to finalize the strength or power of the cylindrical correction. To check the axis of the cylinder the principles of obliquely crossed cylinders are applied. A moderately strong cross-cylinder (±0.5 or+1.0) is held before the eye with its handle aligned with the axis of the cylindrical trial lens and then flipped over so that each side of the cross-cylinder lies alternately 45° to either side of the axis of the trial cylinder. The patient is asked to look at the line of test-types two lines above the smallest visible to him, because the cross-cylinder blurs vision and larger letters are needed to help the patient differentiate clarity in different positions. If visual improvement is attained by one or the other alternative, the correcting cylinder is rotated slightly towards the axis of the cylinder having the same sign in the cross-cylinder. The test is then repeated several times until the position of the trial cylindrical lens is such that flipping of the cross-cylinder gives no alteration in clarity in either position.

To check the power of the cylinder, the 0.5 D cross-cylinder is used for patients with good vision and the 1 D cross-cylinder in those with poor vision. One of the two cylindrical axes of the cross-cylinder is first placed in the same direction as the axis of the cylinder in the trial frame and then perpendicular to it by flipping it over. In the first position the cylindrical correction in the trial frame in front of the patient's eye is enhanced by 0.25 D (or 0.5 D), in the second it is diminished by the same amount. If the visual acuity is unimproved in either of these positions, the cylinder in the trial frame is of correct power. If the visual acuity is improved, a corresponding change should be made in the correction

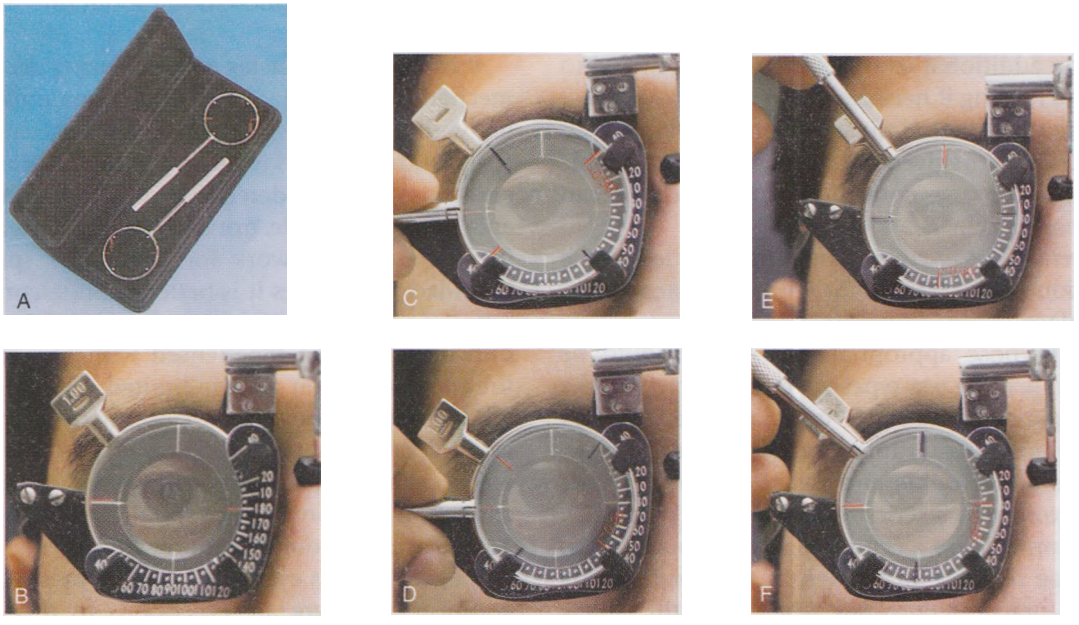


Fig. 7.11 (A) is a set of cross-cylinders (By courtesy of Keeler). (B-F) Photographs showing the clinical use of cross-cylinders: (B) showing cylindrical correction in place; (C and D) finalizing the axis and (E and F) finalizing the power of the cylindrical lens of the right eye (By courtesy of S Majumdar).

unless it is especially contraindicated, and the new combination verified by running through the cycle again.

The cross-cylinder is also useful to confirm the absence of a cylindrical refractive error. The plus axis is held at 45, 90, 135 and 180° in front of the patient's spherical correction. If the patient prefers any option then proceed to determine the axis and power as outlined above.

It is not always easy for the patient to give definite answers with the use of the test-types alone, especially in cases of small degrees of astigmatism. In these, the results may be confirmed by the use of an *astigmatic fan* (Fig. 7.12). On looking at such a figure, if any of the lines are seen more clearly than the others, astigmatism must be present; if the vertical lines are clear, the diffusion ellipses on the retina must be vertical, that is, the horizontal meridian must be more nearly emmetropic than the vertical and *vice versa.* A cylinder placed in front of the eye with its axis horizontal will therefore correct the vertical meridian, and when the correct glass is found, all the lines appear equally distinct.

The cylinder which thus renders the outline of the whole fan equally clear is a measure of the amount of astigmatism, and the axis of the cylinder is at right angles to the line which was initially the most clearly defined.

As a clinical routine the test should be carried out with the patient's vision slightly fogged by an amount sufficient to overcorrect every meridian by +0.5 D, and the patient is asked to observe if any of the lines stand out more clearly than the others. If astigmatism is present the patient will see one or a neighbouring group of lines more sharply defined by a degree depending on the amount of astigmatism; concave cylinders are now added, their axes lying at right angles to this until all the lines—including those at right angles to the first—are equally clear, additional convex spheres being added to maintain the fogging if necessary.

The entire examination must be done slowly and leisurely and the patient given the strongest hypermetropic or the weakest myopic correction with which he can attain normal vision.

The *correction of near vision* should be preceded by the determination of the near point with the distance correction in place.

For this purpose appropriate test-types should be used. Snellen reading test-types were constructed on the same principle as his distance types and are therefore theoretically accurate. Ordinary types in common use, however, are more legible and easily obtained. Jaeger, therefore, introduced a series of test-types in print such as was in common use a century ago corresponding so closely in size to those of Snellen as to be sufficiently accurate for practical purposes. These are still widely used and the sizes of print are numbered J1, J2, etc. A similar card of types has been standardized by the Faculty of Ophthalmologists, London and numbered from

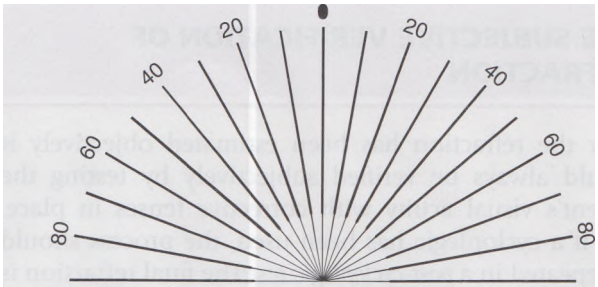


Fig. 7.12 Astigmatic fan.

N5 to N48, corresponding to the modern Times Roman type in various sizes from 5 point to 48 point.

The patient is given the reading test-types and asked to hold them at the distance at which he is accustomed to work or read. When they are not distinctly seen, appropriate convex lenses should be added to the distance correction so that the near point is brought within the working distance, and the types are easily and comfortably read. The position of the *near point* should now be determined. This is most accurately done by approximating to the eye a card on which is drawn a fine line 0.2 mm in breadth or width, until the line appears blurred (not doubled). For practical purposes it is sufficient to use the smallest test-type and move it towards the eye until it can no longer be easily read. The last position at which it can be read gives the near point. The distance of the near point from the eye is then measured in millimetre. The range of accommodation is deduced from the formula $A - P - R$. The correction given should be such that some amplitude of accommodation (about one-third) is kept in reserve.

Presbyopic spectacles should never be prescribed mechanically by ordering an approximate addition varying with the age of the patient. Each patient should be tested individually, for the individual variation is large, and those lenses ordered, which give the most serviceable and comfortable, not necessarily the clearest, vision for the particular work for which the spectacles are intended. In all cases it is better to undercorrect than to overcorrect since, if the spectacles tend to be too strong, difficulties will be experienced with convergence, and the range of vision will be limited. In any case, lenses which bring the near point closer than 28 cm are rarely well tolerated (that is, a total power of 3.5 D), and if for any reason the demands of fine work require a higher correction, the convergence should be aided with prisms as well as the accommodation with spheres.

Generally both eyes require equal presbyopic or near addition but there are exceptions to this rule which include unilateral aphakia, unilateral pseudophakia or unilateral Adie pupil with paralysis of accommodation in the affected eye.

SUMMARY

Refraction is the process of determination of the focusing power of the optical system of the eye. This is achieved by the procedure known as retinoscopy It can also be determined with the help of automated equipment known as autorefractometers or autorefractors. The refractive power of the cornea is based on its curvature and refractive index, and can be measured using a keratometer.

Refraction when estimated in the normal physiological state is known as dry refraction and when performed under the effect of topical cycloplegic agents used to relax accommodation is termed as cycloplegic refraction. Objective testing is followed by subjective verification of the refraction before final prescription of glasses.

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8

Refractive Errors of the Eye

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EMMETROPIA

Emmetropia is the condition in which there is considered to be an absence of any refractive error because parallel beams of light come to focus on the retina, with the eye at rest. At birth the average axial length is 18 mm, the cornea is more curved and anterior chamber slightly shallow. Overall the eye of the newborn is hypermetropic. The degree of hypermetropia varies but the slightly steep cornea compensates to some extent for the short axial length. The infant eye undergoes rapid growth in the first few years of life to reach an axial of length of about 23 mm by the age of 3 years, the cornea becomes slightly flatter, the anterior chamber deepens and the degree of hypermetropia reduces gradually.

From 3 to 14 years of age, the axial length increases further by 1 mm and the power of the crystalline lens changes to achieve and maintain emmetropia. This entire process from birth onwards is known as emmetropization.

AMETROPIA

The condition in which incident parallel rays of light do not come to a focus upon the light-sensitive layer of the retina may be due to one or more of the following conditions:

1. *Axial ametropia*: Abnormal length of the globe—too long in myopia, too short in hypermetropia. A 1 mm elongation produces approximately 3 D of myopia and 1 mm shortening 3 D of hypermetropia.
2. *Curvature ametropia:* Abnormal curvature of the refracting surfaces of the cornea or lens—too strong a curvature in myopia, too weak in hypermetropia. A 1 mm change in the radius of curvature of the cornea produces a 6 D refractive change. Steeper (more curved) corneas produce myopia and flatter corneas hypermetropia.
3. *Index ametropia:* Abnormal refractive indices of the media. In index myopia the refractive index, either of the cornea, the aqueous or of the lens (produced by a high index in the nucleus or a low index in the cortex or both) is too high, and that of the vitreous maybe too low as in a vitrectomized eye with silicone oil in the vitreous cavity. In index hypermetropia the opposite conditions are operative, and the error

is high when the lens is absent as in aphakia or absence of the lens from the pupillary plane.

4. *Abnormal position of the lens:* Displacement forwards causes myopia, displacement backwards hypermetropia.

Of all these factors the axial length of the globe is perhaps the most important.

Emmetropic eyes may differ in length by as much as 1-2 mm, and the radius of curvature of the cornea may vary from 7 to 8 mm. Emmetropia therefore results from the integration of all the variables mentioned above and a deviation in one factor is often compensated by the opposite tendency in another. Statistically, its incidence is expected to resemble the Gaussian frequency curve, but since the full development of emmetropia is never present normally at birth the curve will have a certain 'skew deviation'. Most infants are born hypermetropic; almost inevitably some cases will fail to reach emmetropia and remain hypermetropic, while others will proceed too far and become myopic. Of these the former are by far the more numerous. Most cases of low ametropia (including myopia) are merely biological variants around a mean and cannot be regarded as pathological (Fig. 8.1).

Myopia

Myopia, also known as 'short sight', is that dioptric condition of the eye in which, with the accommodation at rest, incident parallel rays come to a focus anterior to the light-sensitive layer of the retina. The majority of cases merely result as variants in the frequency curve of axial length and curvature, the former being the more important, although curvature myopia occurs commonly as a factor in astigmatism. Such cases of *simple myopia* are in no sense pathological, there are no degenerative changes in the fundus although peripheral retinal degeneration often becomes evident in later life, and they do not progress after adolescence when a degree of 5 or 6 D may be attained. In severe illness, however, or states of debility, the sclera may stretch and the myopia increase.

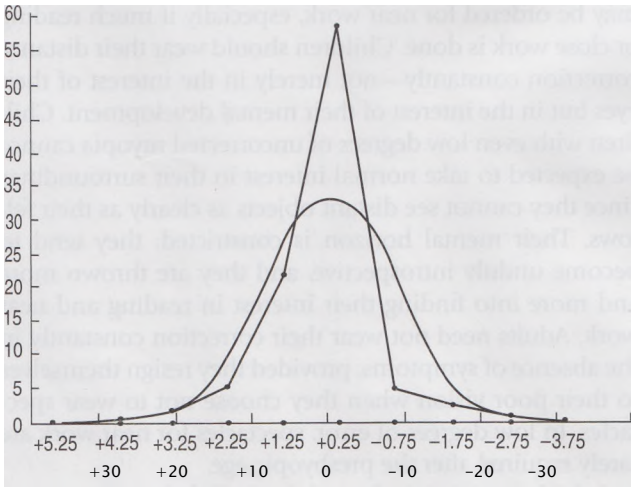


Fig. 8.1 The relative incidence of refractive errors. The refraction curves of Scheerer and Betsch (the higher curve) as compared with the theoretically derived binomial variation curve (the lower curve and lower figures). The abscissae are refractions measured without cycloplegia.

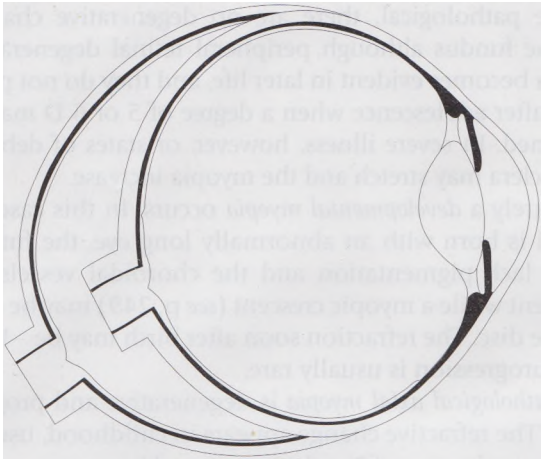
Rarely a *developmental myopia* occurs. In this case the child is born with an abnormally long eye, the fundus may lack pigmentation and the choroidal vessels are evident while a myopic crescent (*see* p. 249) may be seen at the disc. The refraction soon after birth may be -10 D, but progression is usually rare.

Pathological axial myopia is degenerative and progressive. The refractive change appears in childhood, usually between the ages of 5 and 10 years, and increases steadily up to 25 years or beyond, finally amounting to -15 or -25 D or more. The degenerative changes in the fundus, on the other hand, do not appear until later in life, becoming marked at about the fifth decade. The condition is strongly hereditary, being commoner in women than in men. It has a racial predilection, being common, for example, among Jews and Japanese and most cases are of genetic origin. Many other aetiological theories have been advanced—excessive accommodation and convergence in near work, vascular congestion due to a dependent position of the head, and so on—but they have little to recommend them.

The condition is essentially a disturbance of growth on which are imposed the degenerative phenomena; these will be considered at a later stage *(see* Chapter 17). Endocrine or nutritional disturbances, debility or illness, probably act as incidental factors which may increase the general tendency; but, despite popular belief which still lingers, environmental conditions such as excessive near work probably have little influence upon the condition which is genetically pre-determined, except in so far as they inhibit normal healthy development.

Pathological curvature myopia is seen typically in keratoconus. *Index myopia* accounts for myopia as a premonitory symptom of senile cataract, when it is due to the increased refractive index of the nucleus of the lens; it also accounts for myopia in some cases of diabetes, with or without cataractous changes in the lens.

In degenerative axial myopia the increase in length of the eye affects the posterior pole and the surrounding area; the part of the eye anterior to the equator may be normal (Fig. 8.2). The elongation is probably not due to stretching but to a primary degeneration of the coats of the eye including the posterior half of the sclera. In high degrees of myopia, the sclera may bulge out at the posterior pole to form a *posterior staphyloma,* distinguishable clinically by the optical condition and the associated changes in the fundus. The edge of the bulge may be actually visible by the indirect method of ophthalmoscopy owing to the presence of a crescentic shadow two or three disc



Fig, 8.2 The two eyes of the same individual superimposed: the one emmetropic, the other with −15 D of myopia.

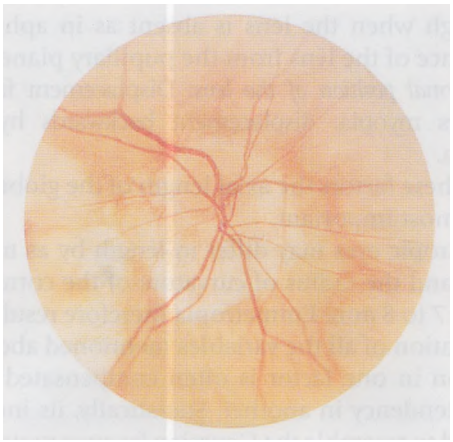


Fig. 8,3 Myopia with extensive retinal degeneration.

diameters to the temporal side of the disc and concentric with it and to the change in course of the retinal vessels.

The only symptom in low myopia may be indistinct distant vision. In other cases and in high myopia there is often, in addition, discomfort after near work, due largely to disproportion between the efforts of accommodation and convergence often leading to exophoria. The eyes may be sensitive to light. Black spots may be seen floating before them, and sometimes flashes of light are noticed; the latter may occur irrespective of any tendency to detachment of the retina.

In very high myopia the eyes are prominent, the pupils are large, and the anterior chamber appears deeper than normal, probably only owing to the dilatation of the pupil. There may be an apparent convergent squint *(see* Chapter 26). Vision may be very poor, even with optical correction; scotomata may be present, both central and peripheral.

Two typical ophthalmoscopic appearances are seen in high myopia—changes at the disc typified in the development of a myopic crescent, and changes in the central area of the fundus described as chorioretinal myopic degeneration (Fig. 8.3). Degenerative changes also occur at the periphery of the retina which may lead to a retinal detachment, and degenerative changes in the vitreous are common, giving rise to dust-like vitreous opacities or large floaters composed of elements of the vitreous framework. These 'floaters' are seen more plainly by myopic than by other eyes because the entoptic image is larger. These degenerative changes may have serious visual consequences; in fact, they are among the more common causes of severe visual disability.

As regards *prognosis,* low or moderate degrees of simple myopia (up to 5 or 6 D), unless occurring in young children, have a good prognosis. They are not likely to progress. The same condition in a child before the age of 6 or 7 should give rise to anxiety if it is not of the congenital type, since at this stage the degenerative condition is clinically indistinguishable from the simple. The former is of grave prognosis, because it is almost certain to progress so that eventually there may be 10 or 15 D of myopia or more, accompanied by serious degenerative changes in the fundus and defects of vision. The likelihood of these developments must be judged by the acuity of vision after correction, the condition of the fundus and the evidence of heredity.

Treatment

Each case must be considered on its merits. Attention must be paid to the use of suitable correcting spectacles.

Myopia must never be overcorrected with spectacles; however, opinions differ as to details. In low myopia of up to 5 or 6 D, no harm is done by ordering the full distance correction for constant use, and if this is done the patient must be warned not to hold near work closer than ordinary reading distance. If any discomfort is experienced, weaker lenses may be ordered for near work, especially if much reading or close work is done. Children should wear their distance correction constantly—not merely in the interest of their eyes but in the interest of their mental development. Children with even low degrees of uncorrected myopia cannot be expected to take normal interest in their surroundings since they cannot see distant objects as clearly as their fellows. Their mental horizon is constricted, they tend to become unduly introspective, and they are thrown more and more into finding their interest in reading and near work. Adults need not wear their correction constantly in the absence of symptoms, provided they resign themselves to their poor vision when they choose not to wear spectacles. In low degrees of error, spectacles for near work are rarely required after the presbyopic age.

In high myopia it is always wise to slightly under-correct even for distance, and the same or still weaker lenses may be ordered for near work. In the highest grades, patients often see best with lenses which are decidedly weaker than the full correction; they should be allowed to choose those

they prefer. One reason is that strong minus lenses considerably diminish the size of the retinal images and make them very bright and clear. The retinal images are diminished because the lenses have to be worn further from the eye than the anterior focal plane. Spectacles for high myopia should therefore be made to fit as closely to the eyes as possible. The very bright, clear images are uncomfortable because the retina has become accustomed to large and indistinct images. Moreover, much artificial astigmatism and therefore distortion of the image is produced by looking obliquely through strong lenses. Very shortsighted people thus get into the habit of turning the head rather than the eyes to avoid looking obliquely through the lenses. Indeed, some high myopes can find their way about better without any spectacles. Contact lenses may be of great value in cases of this type.

If spectacles are not constantly worn in very high myopia, the requisite amount of convergence for near work may be impossible. The effort to converge is thus abandoned so that reading and other near work become uniocular and the disused eye becomes divergent.

In myopia, especially in the young, near work should be held in the proper position and undertaken in good light. It need not be restricted if the general health and physical development of the child are satisfactory. Special educational methods should be adopted if the visual acuity of the child makes it difficult for him to keep pace with his fellows at school. These include oral teaching and limiting visual instruction to specially printed large types. Maintenance of the child's general health is the most important factor.

The prognosis of degenerative high myopia in later life can be grave. For economic reasons, high myopes with degenerative changes in the fundus or a positive family history should avoid an occupation in which close work is necessary. Consideration should also be given to the hereditary propagation of the disease; two high myopes with pronounced degenerative changes in the fundi should seek genetic counselling before deciding to have children. They should also be counselled on the warning signs of retinal breaks or early signs of retinal detachment so that they can seek medical attention early *(see* p. 322). In addition, contact sports, or any activity involving danger of blunt injury to the eye should be specifically avoided.

Contact lenses may be worn instead of spectacles to correct myopia. They have the advantage of providing a wider field and larger image size compared to glasses in patients with high myopia.

Surgical treatment for myopia: For patients who do not wish to use spectacles and those who are intolerant to

Table 8.1 Types of surgery used to correct myopia

Surgery	Range of myopia	Possible complications
Methods to induce flattening of the central cornea		
Radial keratotomy*	1 to 6 D	Perforation, infection, surgically induced astigmatism, corneal scarring, late rupture with trivial trauma
Intracorneal rings or segments (ICR or INTACS)+	1 to 6 D	Unpredictable results, keratitis
Excimer laser photorefractive keratotomy (PRK)*	1 to 4 D	Delayed visual recovery, faint corneal haze, glare and loss of contrast sensitivity
Excimer laser-assisted *in situ* keratomileusis (LASIK)§	2 to 12 D	Dry eye, infection, diffuse lamellar keratitis, interface debris and epithelial ingrowth, flap displacement, surgically induced astigmatism or aberrations, regression, iatrogenic thinning and ectasia, glare, difficulty with night driving and retinal detachment
Laser assisted epithelial keratomileusis (LASEK)™	1 to 6 D	Same as LASIK except there are no microkeratome-related complications
Femtosecond laser-assisted LASIK**	2 to 12 D	Diffuse lamellar keratitis, incomplete flap and interstitial corneal stromal haze are still potential problems
Methods to reduce the overall refractive power of the eye		
Clear lens extraction	> 15 D	Retinal detachment, endophthalmitis
Phakic intraocular lensll	5 to 22 D	Endophthalmitis, cataract

'Radial keratotomy: Linear radial incisions (80% depth) are made peripherally in the cornea sparing a central optic zone. The incisions are allowed to heal spontaneously leading to paracentral relative ectasia and resultant flattening of the central cornea.

fIntracomeal rings (ICR) or ring segments (INTACS) are inserted in a paracentral stromal pocket lead to paracentral bulging and central flattening.

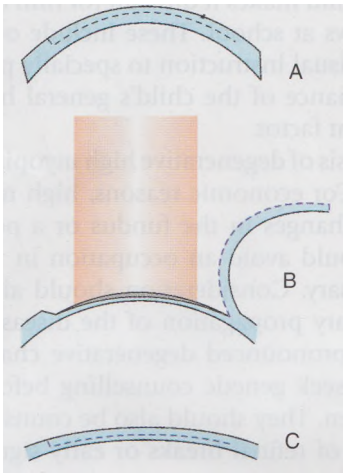
◆Photorefractive keratotomy (PRK): Excimer laser ablation of the superficial layer of the cornea, after removing the epithelium.

SLASIK: Excimer laser beam reshapes the cornea by ablating the superficial stroma to a predetermined extent after lifting a flap of the cornea with a sharp microkeratome.

ttLASEK: Resembles excimer laser PRK with an epithelial flap. As compared to LASIK, no microkeratome is used.

"Femtosecond laser in used to cut the anterior corneal flap, eliminating microkeratome-related complications.

llPhakic intraocular lens: Concave intraocular lenses of appropriate power are fitted in the anterior chamber or posterior chamber anterior to the natural crystalline lens.



Fig, 8,4 LASIK. (A) Microkeratome cut; (B) laser photoablation with flap lifted; (C) flap reposited. Thinner, flatter cornea.

the use of contact lens, refractive surgery to correct the myopia is an option (Table 8.1).

Laser-assisted in situ keratomileusis or LASIK (Fig. 8.4) with the excimer laser is the most popular and widely accepted treatment modality among all the choices available at present. Surgical correction is only undertaken in individuals 21 years of age and above who have a stable refractive error, who have had unsatisfactory results with non-surgical treatment, and in whom corneal thinning disorders that lead to curvature myopia such as keratoconus have been ruled out.

Surgical procedures have been described on page 82 and are outlined in Table 8.1.

Clear lens extraction: If an eye has axial myopia of 21 D, its length will be about 31 mm. If the crystalline lens of such an eye is removed, parallel rays will be focused upon the retina without the intervention of any correcting lens, and the retinal images of distant objects will be larger than those of the emmetropic eye. Hence, extraction of the lens has been advocated in high myopia, often with immediately satisfactory results. The operation is, however, attended with considerable danger because such eyes withstand operative measures badly. In such cases, the vitreous is likely to be fluid and there is an increased tendency of retinal detachment due to the degenerated state of the retina and choroid. Minus-powered concave intraocular lenses (IOLs) designed to be implanted in phakic eyes, i.e phakic IOLs, are therefore becoming more popular. Phakic IOLs are implanted either in the posterior chamber fixated in the ciliary sulcus anterior to the natural crystalline lens or in the anterior chamber fixated to the iris or supported by the anterior chamber angle. They can correct myopia from -5 to -22 D, but are generally reserved for patients not suitable for LASIK.

Hypermetropia (hyperopia)

Hypermetropia is also known as 'far sight'. In this dioptric condition of the eye, with the accommodation at rest, incident parallel rays come to a focus posterior to the light-sensitive layer of the retina.

As in myopia, the chief factor in clinical hyper-metropia is *axial*—an abnormal shortness in the length of the eye. It must be remembered that a small eye, although too short, is not necessarily hypermetropic since there may be uniform diminution of all the parts. This is, perhaps, most easily understood if a diagram such as Fig. 6.2 is considered; if such a diagram is uniformly diminished, as by photography, the parallel rays will still come to a focus on the retina. As a matter of fact, highly hypermetropic eyes are almost invariably also smaller than normal.

Curvature hypermetropia occurs commonly as a factor in astigmatism; it is almost unknown as a cause of spherical hypermetropia (the only example is cornea plana). *Index hypermetropia* accounts for the hypermetropia of old age *(see* p. 54), and is attributable to the increased refractive index of the cortex of the lens relative to the nucleus so that the overall refractive power of the crystalline lens decreases.

Hypermetropia rarely exceeds 6-7 D, which is equivalent to a 2 mm shortening of the optic axis. Individual cases of much higher degrees—up to 24 D—without any other anomaly have been recorded.

In the young, the condition may cause no symptoms. When symptoms are present or arise, they are chiefly referable to the abnormal amount of accommodation to which these eyes are subjected, and to the lack of balance between accommodation and convergence. A healthy youth has an ample reserve of accommodation, and if hypermetropic, can accommodate for distant and near objects without being conscious of the act. If the youth is in poor health or does much near work the perpetual overaction of the ciliary muscle is likely to produce symptoms; the condition is often called *accommodative asthenopia* or 'eye strain'.

The symptoms are noticed chiefly after close work, especially in the evening by artificial light. The eyes ache and burn; they may feel dry, so that blinking movements are more frequent than usual, or there may be lacrimation. The conjunctiva and edges of the lids become hyperaemic and if near work is persisted in, headaches, usually frontal, develop. Children with refractive errors may present with a history of recurrent styes, chalazia or blepharitis possibly due to increased eye rubbing with dirty fingers.

In young children, hypermetropia is a pre-disposing cause of convergent strabismus. Latent convergent squint (esophoria) is often found in hypermetropes, although other forms of heterophoria may occur *(see* Chapter 26). The presence of heterophoria increases the tendency to headache and other symptoms of eye strain.

In older patients, no symptoms may be caused until the power of accommodation has diminished to the extent that the near point is beyond the range of comfortable reading distance and work has to be held further off than usual in order to be seen clearly. The greater the degree of hypermetropia the sooner will this symptom arise; in other words, apparent presbyopia commences at an earlier age than usual.

The fundus may appear normal on ophthalmoscopy. A bright reflex, suggesting the appearance of watered silk, is commoner in hypermetropic than in emmetropic or myopic eyes; and in some cases optic neuritis is nearly simulated—a condition known as pseudopapillitis *(see* Chapter 22).

Anatomically, the smallness of the eye is not confined to the post-equatorial segment as in myopia, nor are abnormalities found in the retina or choroid. The diameter of the cornea is often reduced and regular astigmatism is common. The anterior chamber is shallower than usual, owing partly to the normal size of the lens, a configuration which pre-disposes to angleclosure glaucoma.

Newborns are almost invariably hypermetropic (average 2.5 D). In the first decades of life the incidence of hypermetropia falls rapidly, remaining at about 50% after the 20th year. There is no predilection for either sex. It is interesting that primitive races and the higher mammals, especially the carnivora, are generally hypermetropic.

Treatment

Correcting lenses should be prescribed. Unless there are definite symptoms or a tendency to develop a convergent squint, there is no reason for insisting upon the use of spectacles in young patients with low hypermetropia. In elderly people the hypermetropia must be corrected for near work. The ordinary presbyopic addition as appropriate for the needs and age of the patient must be added to the hypermetropic correction, but care should be taken that these cases are rather under than overcorrected.

Other options include contact lenses, non-contact Holmium:YAG laser thermo keratoplasty, hyperopic LASIK and phakic IOLs. Hyperopic LASIK is used to correct mild-to-moderate hypermetropia (+1 D to +4 D) and phakic IOLs for higher degrees of hypermetropia (+4 D to +10 D). Phakic IOLs for hypermetropia are specially designed, foldable, convex, thin lenses implanted in the posterior chamber behind the iris and in front of the normal crystalline lens. Non-contact Holmium:YAG laser or conductive thermokeratoplasty is suitable for lower hyperopia of + 1 D to +2.5 D where multiple radially distributed spots in the paracentral cornea lead to shrinkage of the collagen in the mid-peripheral stroma and consequent steepening of the central cornea. Older patients with hyperopia who want greater spectacle independence are suitable candidates for refractive lens exchange *(see* p. 84).

Astigmatism

In this condition of refraction a point of light cannot be made to produce a punctate image upon the retina by any spherical correcting lens. The varieties of regular astigmatism have already been outlined *(see* p. 54).

Regular astigmatism, the only form susceptible to optical correction by spectacle lenses, invariably produces some defect in visual acuity. It is particularly liable to cause the worst forms of asthenopia or eye strain; the asthenopia in these cases is only in part accommodative. It is often worse in the lower degrees of astigmatism than in the higher because of endeavours to accommodate so as to produce a circle of least diffusion upon the retina. Aching of the eyes and headache are common symptoms; the eyes quickly become fatigued with reading and the letters are described as 'running together'.

Regular astigmatism is usually a congenital defect, due in most part to differences in the curvature of the cornea in different meridians. It must be remembered that frequently it is not the cornea alone which is at fault, for corneal astigmatism may be increased or partially corrected by lenticular astigmatism. Regular astigmatism may be traumatic following a wound, frequently surgical such as in the corneoscleral margin following cataract surgery, since contraction of the scar after extracapsular cataract extraction causes flattening of the cornea in the meridian at right angles to the wound. Tight sutures further accentuate this effect by causing corneal steepening in the same axis as the tight suture. Astigmatism due to this cause continues to alter for some weeks after the injury; therefore, final spectacles should not be ordered for at least 6 weeks thereafter. Following sutureless surgery by phacoemulsification there is usually some flattening of the cornea in the axis of the wound.

Higher degrees of astigmatism cause a lowering of visual acuity; this is usually least in mixed astigmatism, probably because the circle of least diffusion falls upon or near the retina.

Treatment

If the astigmatic error is small (less than 0.5 D) and not associated with symptoms, spectacles are unnecessary unless the highest visual acuity is desired. However, in all cases in which astigmatism causes asthenopic symptoms, full optical correction should be ordered for constant use, that is, both for distant and near vision. Other measures are rigid contact lenses, toric contact lenses, astigmatic LASIK (1.5-5 D), arcuate keratotomy and toric phakic IOLs.

Aphakia

When the crystalline lens has been removed the eye is said to be aphakic. If the eye was earlier emmetropic or

had only a low grade of ametropia before removal of the lens, it becomes extremely hypermetropic and all accommodation is lost. The hypermetropia, as estimated by the correcting lens required when worn in the usual position is about 10 or 11 D if the eye were previously emmetropic.

The optical condition of the aphakic eye is very simple. It consists of a curved surface—the cornea—separating two media of different refractive indices, air and aqueous plus vitreous. Knowing the radius of curvature (8 mm) and the refractive indices (1 and 1.33), it is easy to calculate the focal distances; the anterior focal distance is 23 and the posterior 31 mm, as compared with 15 and 24 mm, respectively, for the normal eye. If the aphakic eye was 31 mm long, parallel rays falling on the cornea would be brought to a focus on the retina and no correcting glass would be required for distant vision. The axial myopia of a phakic eye which is 31 mm long equals -21 D.

The retinal image of the aphakic eye wearing spectacles is about a quarter (25%) larger than the emmetropic retinal image. Hence vision of 6/6 with a correcting lens after extraction is not quite as good as it seems. Owing to the disparity of the images, any attempt to correct unilateral aphakia with spectacles when there is good vision in the other eye leads to an intolerable diplopia. With contact lenses, comfortable binocular vision may be attained. However, IOLs are by far the best method for optical correction of aphakia.

In addition to the hypermetropia, there is always some astigmatism in those cases in which a corneal or corneoscleral section has been made. If the sutureless, phacoemulsification incision is in the upper part of the cornea, the astigmatism is 'against the rule' since the cornea is flattened in the vertical meridian. The astigmatism usually amounts to 0.5-1 D. If an extracapsular cataract surgery is performed with sutures, and the section is in the upper part of the cornea, 'with the rule' astigmatism, generally from 1 D to 3 D, is common. This reduces after suture removal and gradually diminishes thereafter.

Treatment

The refractive error is determined by retinoscopy, autorefraction and by subjective tests; the keratometer is helpful in determining astigmatism. The optical condition of aphakia with a strong correcting spectacle lens and with no accommodation is difficult and great patience is often necessary for the patient to adapt to the situation. Sometimes these difficulties can be much improved by a contact lens provided the patient can manipulate and tolerate it.

The *difficulties of aphakia and its correction by spectacles* include the following:

- an image magnification of about 25-30%;
- spherical aberrations producing a 'pin cushion effect';
- lack of physical coordination;
- a 'jack-in-the-box' ring scotoma from prismatic effects at the edge of the lens;
- prismatic errors resulting from displaced optical centres of the lenses;
- reduced visual fields and poor eccentric acuity;
- inaccurate correction because of erroneous vertex distances and
- physical inconvenience and cosmetic deficiency of heavy spectacle lenses.

In an attempt to overcome these difficulties, aphakic spectacles may be had in various forms, namely *spherical,* lenticular and full field. In *aspheric* lenses, the front lens surface has a progressive peripheral flattening starting 12 mm from the centre with the power ground on the posterior surface. The smaller *lenticular* lens (40 mm diameter) has a bull's-eye effect with a -3.5 D rear curve, moderate asphericity (1.5 D power drop), a small peripheral field, a smaller more central scotoma, less distortion, greater central magnification and better eccentric acuity. The reduced distortion makes it more suitable for a first aphakic lens. The *full-feld* lenses have a flat rear curve, more asphericity (2-5 D power drop peripherally), variable but usually larger diameter, larger peripheral field, larger but more peripheral scotoma, somewhat more distortion, less central magnification and poorer eccentric acuity. These full-field lenses have increased field, more secure mobility and improvement in eye-hand coordination and spatial orientation.

General problems in the use of *contact lenses* in aphakic persons include lack of dexterity in older patients and intolerance owing to a foreign body sensation or 'lens awareness'.

IOL implantation has the following advantages:

- minimal after-care of patient;
- minimum aniseikonia (difference in image size seen by the eyes);
- rapid return of binocularity and
- normal peripheral vision.

The operation is now a routine part of cataract surgery and carries very few added risks to routine cataract extraction. Some complications which may arise are incorrect calculation of IOL power with a 'refractive surprise' after surgery, implant dislocation, posterior capsule opacification and cystoid maculopathy.

IOLs are made of monomer-free acrylic or clinical quality Perspex, i.e. polymethyl-methacrylate (PMMA). The lenses are 4-6 mm in diameter and biconvex or plano-convex. The standard power lens of 19.5 D in aqueous is approximately equivalent to an 11 D sphere spectacle lens. Lens power measurements for primary implantation necessitate axial length measurement with

ultrasonography, keratometry and the use of standard calculation tables. In children a stronger lens is required.

Lens loops were initially made from nylon or prolene, but now both these materials are not in use and have been replaced by flexible methylmethacrylate. Foldable IOLs made of silicone or various polymers of acrylic, some of which are hydrophobic and others hydrophilic, are also available for insertion through a small incision following cataract surgery by phacoemulsification.

Ametropia in pseudophakia

Pseudophakic eyes may also have a residual refractive error which needs some spectacle correction. This includes near addition (because of loss of accommodation), correction of residual spherical error (due to under- or overcorrection of the IOL power, either intentional or accidental, because of inaccurate calculation) and correction of surgically induced astigmatism.

ANISOMETROPIA

This is the condition in which the refractive state of the two eyes shows a considerable difference. A slight difference is very common but all varieties and degrees of anisometropia occur. The condition may cause asthenopic symptoms. In the lower grades there is usually binocular vision, although it is imperfect and the effort of fusion may produce symptoms of eye strain. In the higher grades exceeding 2.5 D, this is impossible and vision is then uniocular. In such cases there is some danger of the eye which is not used becoming amblyopic in young children and divergent.

Treatment

The correction of anisometropia is often difficult. It has already been mentioned that if correcting lenses are placed at the anterior focal plane of the eye *(see* Fig. 6.9), the retinal images in axial ametropia are of the same size as the emmetropic retinal image. In practice, the lenses are nearer to the eyes so that with concave lenses the retinal image is diminished; with convex, enlarged. In high grades of anisometropia (such as unilateral aphakia), therefore, there will be a considerable difference in the size of the retinal images of the two eyes (*aniseikonia*). Patients find it difficult or impossible to fuse these sharp but diverse images. Moreover, on looking obliquely through the lenses the prismatic effect and distortion are different in the two eyes, enhancing the discomfort. The use of ordinary spectacle lenses thus presents difficulties, and if a full correction cannot be tolerated a compromise may be adopted wherein each eye is under-corrected. *Iseikonic* or *size-lenses,* which correct such a difference in their optical construction, require specialized methods of manufacture and their clinical results are often disappointing. *Contact lenses* diminish these optical defects and may be ordered in suitable cases. Alternatively, uniocular vision or monovision may be resorted to, one eye being used at a time—a habit which grows more comfortable with practice as is seen in the use of a uniocular microscope or monocle. It is particularly fortunate when one eye is nearly emmetropic and the other myopic because the former can be used for distance, and the latter for near vision without the aid of spectacles.

ANOMALIES OF ACCOMMODATION

In this condition the accommodative power is below the lower limit of what might be accepted as normal for the patient's age; in a sense presbyopia *(see* p. 60) is a physiological failure of accommodation due to hardening of the lens. Such an insufficiency is usually due to weakness of the ciliary muscle, the aetiology embracing all the causes of muscular fatigue (general debility, anaemia, toxaemia, etc.) accompanied by excessive use of the eyes particularly for close work. A rapid failure of accommodation also occurs in the prodromal stages of glaucoma, due probably to impairment of the effectivity of the ciliary muscle by the increased pressure.

The symptoms are those of eye strain with particular difficulty associated with near work. The treatment should be directed essentially to the causal condition, but if close work is difficult, reading spectacles may be prescribed; the same procedure being adopted as that recommended for presbyopia. In general the weakest convex lenses which will allow adequate vision should be ordered so that the accommodation may continue to be exercised and stimulated rather than completely relieved.

Paralysis of accommodation or cycloplegia

This occurs in disease as well as from the direct action of cycloplegic drugs. Unilateral cycloplegia is generally due to drugs, contusion, Adie tonic pupil or paralysis of the third nerve. Bilateral paresis, less commonly paralysis, occurs typically after diphtheria, but may appear after debilitating illness, or with syphilis, diabetes, alcoholism and cerebral or meningeal diseases.

In diphtheritic cases the paralysis of accommodation follows the primary attack after an interval of several weeks, and is often associated with paralysis of the palate, loss of knee jerks, etc. The sore throat may have been very slight and its diphtheritic character unrecognized.

In complete paralysis the sphincter pupillae is also generally paralysed so that the pupil is widely dilated. In paresis the pupil may be mildly affected, especially after diphtheria, and in fact in this disease the reverse of the Argyll Robertson pupil may be met, with loss of reaction to accommodation and retained reaction to light. The symptoms depend upon the condition of the refraction. If the patient is myopic, the defect may pass unnoticed; if he is emmetropic, near vision alone will be affected; if he is hypermetropic, both distant and near vision will be affected, but particularly the latter. In paresis it may be possible to diagnose the condition only by carefully measuring the range of accommodation. The prognosis is good in cases due to drugs or diphtheria. In traumatic cases the condition may be permanent.

Treatment is that of the cause. Whenever the condition is bilateral, near work can be carried on by using suitable convex lenses, as in the correction of presbyopia. Miotics are sometimes used.

Spasm of accommodation

It has already been mentioned that the ciliary muscle has physiological tone which is abolished by atropine, and is equivalent to about 1 D. In spasm of the ciliary muscle, it is found that atropine produces a much greater effect. The condition is found only in young patients and, contrary to what might be expected, particularly in myopes. An actual or relative myopia is produced and in these cases subjective testing without a cycloplegic indicates too high an error. Spasm of accommodation is produced artificially by the instillation of miotics.

In spontaneous spasm of accommodation there is nearly always some error of refraction and the eyes have usually been subjected to too much near work in unfavourable circumstances which may include such factors as bad illumination, bad posture, mental stress and anxiety and so on. The condition should not be diagnosed unless proved to be present by the use of cycloplegic drugs such as atropine.

Treatment consists of the correction of refractive error and if still necessary, use of cycloplegics for several weeks together with reassurance and, if indicated, psychotherapy.

THE CORRECTION OF ERRORS OF REFRACTION

The detection of errors of refraction has already been briefly described. It will be well, however, to outline the steps to be adopted in systematically examining for and correcting these errors, and to indicate the requirements which should be satisfied by spectacles.

1. Visual acuity is ascertained, uniocularly and binocularly; unaided, with previous spectacles (if available) and with a pinhole *(see* Chapter 10, p. 98).
2. External examination in diffuse light (*see* Chapter 11, p. 111).
3. Examination of the motility of the eyes *(see* Chapter 26).
4. Cover test to elicit heterophoria and squint *(see* Chapter 26) This is best done at this stage. The detection of a squint may account for a marked deficiency of vision in the deviating eye, which, if it is not recognized early in the examination, may give rise to some concern.
5. The examination of the eyes by focal illumination and ophthalmoscopic examination by the indirect and direct methods *(see* Chapters 11 and 12).
6. Trial frames are put on and centred.
7. Retinoscopy.
8. Subjective verification of retinoscopy findings, with test-types, astigmatic fan and cross-cylinder.
9. With full correction in place, the testing of muscle balance for distant vision.
10. With full correction in place, the determination of the near point of accommodation and convergence.
11. The addition of a correction for near work (if necessary), and the testing of the acuity with the near types, uniocularly and binocularly.
12. With the additional correction for near work, the estimation of muscle balance for near vision.

If the patient is less than 5 *years of age:* Steps 1-5 are done on the first visit. Then order atropine eye ointment 1% to be instilled three times a day for 3 days. The ophthalmoscopic examination is repeated and steps 6, if possible, and 7 are done. The spectacles may then be ordered based on retinoscopy alone, with the appropriate deduction for working distance and additional deduction for cycloplegia if clinically indicated.

If the patient is between 5 *and 20 years of age:* The same procedure should be undertaken but the entire examination can be done at one visit using homatropine (2%), cyclopentolate (1.0%) ortropicamide (1%) as a cycloplegic. Atropine must be used if the patient has a convergent squint or has high hypermetropia; a post-cycloplegic test is advisable.

If the patient is between 20 and 40 years of age: Cycloplegia is usually not required, but may be used if indicated *(see* pp. 66, 152). Steps 1-10 should be performed as a routine.

If the patient is above 40 years of age: Cycloplegia is rarely necessary and should only be used with care, after checking for narrow angles. Mydriasis (as with phenylephrine) may be employed in difficult cases. Steps 1-12 should be performed as a routine.

SPECTACLES, SUNGLASSES AND CONTACT LENSES

Optical correction for refractive errors can be done with spectacles, contact lenses and refractive surgeries.

Aspheric lenses have curves that flatten away from the centre, reducing the peripheral prismatic effects. They have the highest power density among other forms of lenses having an equivalent focal length.

Correction of high refractive errors would require very thick lenses of the usual refractive index, giving the patient poor peripheral vision and poor cosmesis. High index lenses in both glass and plastic have a higher refractive index and the lenses are therefore thinner, flatter and lighter.

Presbyopic patients with refractive errors for distance can use bifocal, multifocal progressive or variable focus lenses. Progressive addition lenses provide a smooth transition from distance viewing, through intermediate to near, with clarity at all distances in between. Some designs of presbyopic lenses are shown in Fig. 8.5.

Contact lenses are thin optical corrective lenses worn on the eye resting on the surface of the cornea. They are made of various materials.

Spectacles and sunglasses

Optical correction for refractive errors fitted in a frame constitute spectacles. *Spectacle frames* should be light in weight and a comfortable fit. Lenses are fitted in the frame with their optical centre exactly opposite the centres of the pupils when the visual axes are parallel in distant corrections. It is important that the lenses are fitted in the frame with the optical centre coinciding with the visual axis and not merely at the geometrical centre of the frame, to avoid unwanted prismatic effects. For near vision the lenses are decentred slightly inwards and tilted so that the surfaces form an angle of 15° with the plane of the face: they then approximate the visual axes when the eyes are directed downwards as in reading. In children, spectacles with large round or oval lenses should be ordered, otherwise the child may look over them. For children, tough plastic lenses, spring hinges and silicone nose-pads make spectacles comfortable. In patients with astigmatism rigid spectacles will keep the cylinder at the desired axis.

Spectacle lenses are made of two main types of materials—plastic or glass. Glass lenses come in a variety of refractive indices, designed to minimize the thickness. Lenses are usually made of crown glass of refractive index 1.52. Glass lenses offer optimum visual clarity, and do not scratch easily. Plastic lenses are often CR39. They are half the weight of glass and do not shatter but can get easily scratched or warped. Polycarbonate lenses are very light and thin, have a high refractive index, are scratch-resistant and unbreakable. They offer total ultraviolet protection. Polycarbonate is 10 times stronger than plastic and is ideal for children as well as for activities such as squash, cricket and tennis.

All these lenses can be tinted, coated or photochromatic. Tints prevent damaging ultraviolet rays from entering the eye and also reduce the amount of light entering the eye, making the patient more comfortable in very bright sunlight. Anti-reflection coating improves the patient's clarity of vision especially when driving at night, as it reduces glare from oncoming headlights, and for people who work on computers. Photochromatic

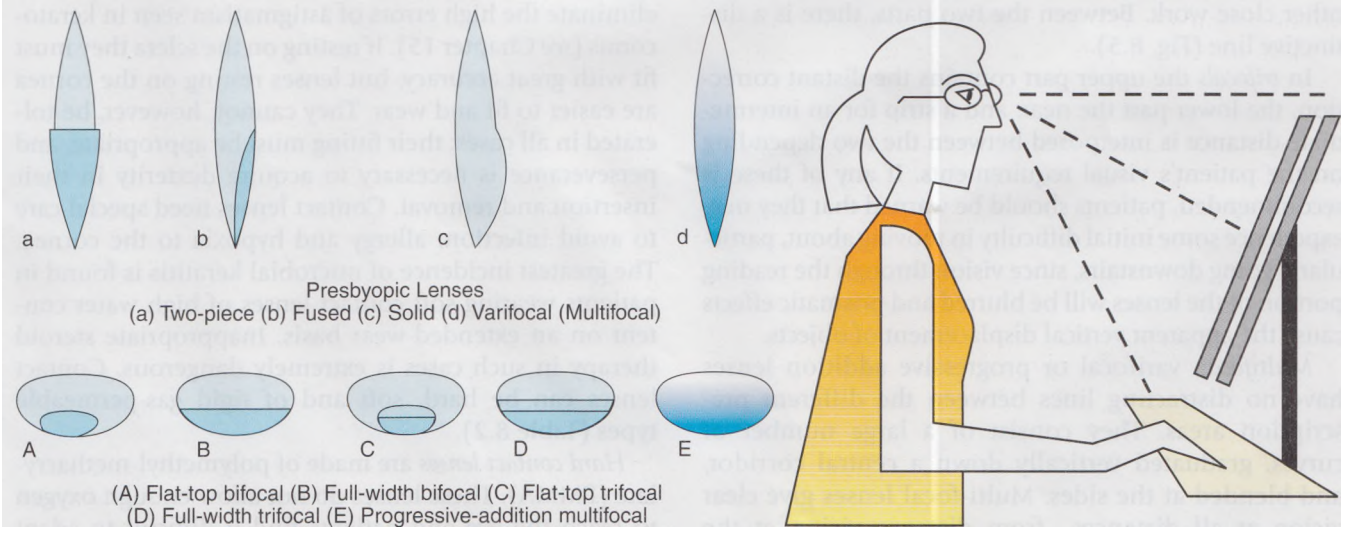


Fig. 8.5 Different designs of spectacle lenses used to correct presbyopia. The figure on the right shows the advantages of multifocal glasses.

lenses provide maximum comfort in ametropia by darkening and lightening according to lighting conditions. These are lenses that darken in sunlight when short-wavelength light (300-400 nm) interacts with chemicals incorporated in the glass lenses by the conversion of silver ions into elemental silver. On continued exposure the lenses progressively darken to absorb about 80% of the incident short-wavelength light. The reaction is reversible so that when the illumination decreases the lenses lighten, taking longer to lighten than darken. Photochromatic lenses can also be made of plastic in which case they are coated with an organic molecule which changes shape when illuminated and consequently light absorptive properties increase in bright light and decrease in dim light. They offer protection from harmful ultraviolet rays and are especially useful against harsh glare, fluorescent lights and video display screens. Scratch-resistant coatings allow plastic lenses to remain clear for a longer period of time.

Patients with high refractive errors require very thick lenses of crown glass, providing poor peripheral vision and cosmesis. *High index lenses* that are available in glass or plastic have a refractive index of 1.56 to 1.67, as compared to 1.52 for crown glass. The lenses are therefore thinner, flatter and lighter. *Aspheric lenses* have curves that flatten away from the centre, limiting diffraction. They have the highest power density among lenses of an equivalent focal length. They are specially designed for long-sighted people who would have needed thick lenses. They are thinner, flatter and make the eyes look more natural.

A *bifocal* lens contains two optical corrections. The most common use of a bifocal is for presbyopes who need assistance with both close work and distance vision. The upper part of the lens is used to correct distant vision, while the lower half assists with reading or other close work. Between the two parts, there is a distinctive line (Fig. 8.5).

In *trifocals* the upper part contains the distant correction, the lower part the near, and a strip for an intermediate distance is interposed between the two depending on the patient's visual requirements. If any of these is recommended, patients should be warned that they may experience some initial difficulty in moving about, particularly going downstairs, since vision through the reading portion of the lenses will be blurred and prismatic effects cause the apparent vertical displacement of objects.

Multifocal, varifocal or progressive addition lenses have no distracting lines between the different prescription areas. They consist of a large number of curves, graduated vertically down a central corridor, and blended at the sides. Multi-focal lenses give clear vision at all distances—from distance vision at the top of the lens, through intermediate vision for closer objects, to near vision at the bottom of the lens. They are particularly useful for computer work, and are available in high index, plastic, glass and polycarbonate material.

In high-illumination situations such as a bright sunny day, particularly in areas where there is excessive light reflected from surfaces such as on the sea or over snow, *sunglasses* allow better visual function by reducing glare, improving colour contrast and contrast sensitivity. Sunglasses can be either plane lenses or could be made with a refractive correction for use in ametropia. In addition to absorbing a major proportion of the incident, ambient light, sunglasses absorb most of the harmful incident ultraviolet radiation and prevent light-induced damage to the lens and retina.

Contact lenses

In cases of irregular corneal astigmatism and high myopia, great improvement of vision occurs when a suitably curved meniscus is in actual apposition to the cornea or separated from it by a thin fluid meniscus. Contact lenses are thin optical corrective lenses worn on the eye, resting on the surface of the cornea. As optical aids they undoubtedly form the theoretically ideal correction for ametropia and are free from many of the disadvantages of spectacles. The prismatic effects of spectacles are eliminated and the field of clear vision is greatly increased. They are therefore particularly valuable in high errors of refraction, especially myopia or aphakia. Moreover, their effect in maintaining the size of the image, approximately equal to that of the emmetropic eye, makes them useful in cases of anisometropia, in which the refractions of the two eyes are widely different and hence the image sizes are different (aniseikonia). The most dramatic example of this is unilateral aphakia. Another specific advantage is that these lenses eliminate the high errors of astigmatism seen in keratoconus (*see* Chapter 15). If resting on the sclera they must fit with great accuracy, but lenses resting on the cornea are easier to fit and wear. They cannot, however, be tolerated in all cases; their fitting must be appropriate, and perseverance is necessary to acquire dexterity in their insertion and removal. Contact lenses need special care to avoid infection, allergy and hypoxia to the cornea. The greatest incidence of microbial keratitis is found in patients wearing soft contact lenses of high water content on an extended-wear basis. Inappropriate steroid therapy in such cases is extremely dangerous. Contact lenses can be hard, soft and of rigid gas-permeable types (Table 8.2).

Hard contact lenses are made of polymethylmethacrylate (PMMA). These lenses do not allow enough oxygen to reach the eye and patients find it difficult to adapt to them. However, visual clarity is good and they can be used in astigmatic corneas. Hard contact lenses are

Table 8.2 Properties of various types of contact lenses

	Hard contact lenses	Soft contact lenses	Rigid gas–permeable lenses
Oxygen delivery	Poor	High	Moderate to high
Visual clarity	Good	Need to refocus after a blink	Clear vision
Use in astigmatism	Possible	Less suitable	Possible
Adaptation	Required	Not required	Required
Deposits	Few	Accumulate over time	Few
Durability	May scratch	Tend to tear	Do not scratch or tear

associated with substantially less acute infective complications. Indications for their use are now restricted.

Soft contact lenses are made from a gel-like plastic, hydroxyethylmethacrylate (HEMA) that contains as much as 79% water. They offer better initial comfort, but are prone to deposits, are difficult to keep clean and are difficult to handle. Deposit problems with soft lenses can lead to discomfort in the long term and therefore they are now used as disposables, being discarded every day, weekly or monthly. Daily disposables are designed to be worn for just a day, up to 15 hours. Weekly or monthly disposal programmes allow for the use of soft contact lenses on a daily basis with the necessity to clean them rigorously every day; however, they are discarded before excessive deposits make them unsuitable for wear. Continuous-wear lenses have an increased water content and oxygen permeability and allow up to six times more oxygen to the cornea than ordinary soft contact lenses. They can be worn continuously for up to 30 nights and days, but are associated with a higher risk of infection compared to daily-wear lenses.

Oxygen-permeable or *rigid gas-permeable lenses* are made of a firm, durable plastic that transmits oxygen, e.g. a copolymer of PMMA and silicone and cellulose acetate butyrate. As they do not contain water, they resist deposits and are less likely than soft contact lenses to harbour bacteria. Oxygen-permeable lenses are easy to clean and disinfect, do not dehydrate and last longer than soft lenses. The rigidity of oxygen permeable lenses also means that they are easier to handle than soft lenses. As they retain their shape better, they provide sharper vision.

Fitting of contact lenses requires a prior retinoscopy followed by keratometry to measure the anterior curvature of the cornea, as contact lenses have to fit on the corneal surface. If the lenses are too flat or too steep they will be uncomfortable and can damage the cornea. The tear film and cornea are evaluated by a biomicroscope for a baseline assessment, and to rule out pathological conditions such as a dry eye, blepharitis or pre-existing keratopathy.

Trial lenses are then applied to the cornea and the 'fitting' evaluated at the slit-lamp. Dyes such as fluorescein that highlight the tear film are useful in fitting rigid lenses. An ideal fit should show a minimal, uniform film behind the contact lens. Pooling of dye in the centre denotes a steep fit and the absence of any dye in the central area, a flat fit. The movement of lenses with each blink is evaluated and should not exceed 1 mm, as a very mobile contact lens may lead to a variable and distorted vision. If the lens does not move at all, the 'fit' is too tight. Sometimes lenses appear to fit fine when first applied, but can tighten up after several hours of wear. Checking the fit several times is important to ensure that there are no adverse effects on the cornea. Visual acuity is assessed through the contact lenses and their power adjusted to provide the best vision possible. The duration of wear and an understanding of the proper care of contact lenses is extremely important.

The final contact lens prescription should include contact lens material, power, base curve and diameter. Patients and contact lenses need to be examined regularly to avoid problems such as allergies, infections and protein deposits on the lenses.

REFRACTIVE SURGERY

Over the years, several different types of refractive surgery have been devised to correct refractive errors in individuals who wish to avoid the use of contact lenses or glasses. The need for optical aids can be reduced or eliminated by various means such as by modifying the curvature of the cornea, changing the intrinsic refractive status of the eye by implanting a refractive IOL, or removing the natural crystalline lens with or without replacement with an IOL of a suitable dioptric power or changing the length of the eyeball. Some have fallen into disrepute due to their unpredictable results and unacceptably high rate of complications, while others have been further refined with newer technology (*see* p. 75).

Refractive keratoplasty

Refractive keratoplasty has been introduced to modify the refractive power of the cornea itself. This may be done by: (i) *radial keratotomy* whereby radial incisions

are made in the cornea; (ii) *arcuate keratotomy* by arc-shaped incisions in the steeper or more myopic meridian to reduce astigmatism; (iii) *keratomileusis,* in which tissue is resected and modified in shape before replacement and (iv) *epikeratophakia,* whereby donor corneal tissue is attached to the host cornea after removal of the epithelium. Keratomileusis has been redesigned so that a superficial lamella of tissue is removed from the recipient cornea. A measured-in-depth central button is then dissected from the stroma of the recipient and the original lamella is sewn back with a continuous suture. This method avoids the need for freezing of corneal tissue and gives immediate and excellent acuity. The excimer laser has now supplanted all these methods as it modifies the shape of the cornea with great accuracy and without inflammatory reaction.

Excimer laser refractive surgery is of two types. In *photorefractive keratectomy* (PRK) the surface of the cornea is ablated by the laser leading to a flatter cornea to neutralize myopia. The other and now more popular method is LASIK or *laser-assisted in situ keratomileusis* in which a superficial circular flap of epithelium and stroma cut with an automated sharp blade called a microkeratome, leaving an attachment as a hinge on one side. The hinged flap thus created is 120-150 |j.m thick, is lifted up with a smooth blunt spatula and the stromal bed ablated with a laser which precisely sculpts the cornea to the desired extent ensuring a minimum residual stromal bed thickness of 250|jim to maintain adequate corneal biomechanical stability and prevent iatrogenic ectasia (*see* p. 75). Following this, the flap is reposited and remains in place without sutures. LASIK has the advantages of quicker visual rehabilitation, clearer vision as Bowman's membrane is not damaged, and the ability to correct higher degrees of refractive error.

Technological advances to minimize microkeratome-related complications include use of alcohol to lift a thin flap of epithelium (laser-assisted epithelial keratomileusis or LASEK), use of a special microkeratome designed to cut and separate a thin flap of epithelium and Bowman's layer (Epi-LASIK) and use of a Femtosecond laser to pre-fashion the anterior flap to a desired size and depth without using a surgical blade.

Advancements to match patients requirements and expectations to lead a spectacle-free existence include measurement of higher order aberrations of the optical system of the eye and use wavefront-guided or wavefront-optimized LASIK to correct or neutralize their effect and yield better visual quality in addition to 'supervision' or eagle eye vision better than 6/6.

Refractive lens surgery

See p. 75-77.

Surgical correction of presbyopia

This includes the following:

1. Bifocal or multifocal IOLs are implanted after lens extraction.
2. Insertion of special foldable silicone plate lenses in the capsular bag with the belief that in some patients they behave as an accommodating IOL. This provides a pseudo-accommodative effect by virtue of an anterior movement of the IOL on attempted accommodation which increases the refractive power.
3. 'Monovision' with IOLs, with one eye corrected for distance and the other for near vision after bilateral cataract surgery.
4. Techniques which actually restore some range of accommodation such as insertion of intrascleral segments of collagen or silicone expansion plugs or some other material overlying the ciliary muscle to indent the sclera and ciliary body. These assist accommodation by improving the ability of the ciliary body to contract and cause steepening of the central part of the crystalline lens anteriorly.
5. Additional measures include clear lens extraction or refractive lens exchange where the natural crystalline lens is removed using standard cataract surgery or lens extraction techniques and a presbyopia correcting IOL is implanted. These lenses provide clear vision for both distance and nearby either optical (refractive or diffractive bifocal or multifocal IOLs) or accommodative mechanisms.

LOW VISION AIDS

Low vision is a term used to signify an impairment of sight that is not fully correctable. It has a variety of causes including eye injury, diseases and heredity. Low vision could involve a blurring of central vision, tunnel vision or blind spots. Common causes are macular degeneration, glaucoma, diabetic retinopathy and retinitis pigmentosa.

Low vision aids are available for reading and for distant vision. For reading purposes, hand-held magnifiers, with or without in-built reading lamps, are commonly used. Height-adjustable stand magnifiers are advisable for reading over long periods of time or for people with tremors. Reading telescopes can be hand-held or mounted onto spectacle frames. They incorporate the optical principle of a Galilean telescope, but their use is difficult and they have a small visual field. Videomagnifiers project printed material onto a screen or computer. Scanners attached to a computer can 'read' printed material through a voice synthesizer.

During activities outside the house, visually impaired people commonly complain of light and glare sensitivity for which glare-reducing and blue-blocking lenses provide some relief. Hand-held monocular and binocular telescopes or spectacle-mounted telescopes also increase distant vision in a limited field.

SUMMARY

Eyes that are unable to focus parallel rays of light onto the retina are termed ametropic and the condition is known as ametropia or a refractive error. The common refractive errors are myopia (short sightedness with a finite far point), hypermetropia (long sightedness with a virtual far point) and astigmatism (variation of refraction in different meridians).

Unlike ametropia, in emmetropia there is absence of refractive error, the axial length of the eyeball matches the dioptric power of the eye and the far point is at infinity. The axial length, curvature of the cornea and lens and index of the ocular refracting media can vary in different proportions from person to person. If the abnormalities are appropriately matched to compensate each other, the eye remains emmetropic or in other words there is a physiologic variation in the states of ametropia. If an imbalance remains, the resultant is ametropia, which then needs to be corrected with spectacles, contact lenses or refractive surgery.

Aphakia and pseudophakia are situations that result from cataract surgery without and with IOL implantation which also can lead to varying degrees of ametropia and are accompanied by a loss of accommodation.

SUGGESTED READING

1. Optics and refraction (David Miller section editor). In: Yanoff M, Duker IS (Eds.). *Ophthalmology.* London: Mosby, 1999.
2. Refractive surgery (Dmitri Azar section editor). In: Yanoff M, Duker IS (Eds.). *Ophthalmology.* London: Mosby, 1999.

Section III

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Ocular Symptomatology

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The eyes are extremely sensitive structures, not only to light and images but also to touch and pain. It is therefore found that ocular diseases frequently lead to symptomatic disturbances, some of which are non-specific, but others could be diagnostic. Ocular symptomatology can be categorized into those caused by anomalies of ocular motility, anomalies of the ocular surfaces and abnormalities affecting the visual apparatus.

Most of the symptoms will be covered in each of the relevant chapters. In this chapter a review of common symptoms and an approach to their differential diagnosis is discussed.

ANOMALIES OF OCULAR MOTILITY

Disturbances of the extraocular muscles may manifest as eyestrain or asthenopia—a sensation of heaviness or tiredness of the eyes, blurring of vision after reading for a while, diplopia or a visible squint.

Asthenopia

Anomalies of ocular motility frequently result in asthenopia. This is defined as weakness or fatigue of the eyes commonly following prolonged close work but may also occur after extended viewing at a~distance, such as watching a film or television. This is generally seen in patients having an insufficiency of convergence, phorias or other extraocular muscle imbalances, an uncorrected refractive error or an incorrect refractive correction especially of astigmatism, or early presbyopia. The patient complains of an aching or burning of the eyes, heaviness of the eyelids, together with a headache. This is sometimes associated with complaints of a blurring of vision or 'doubling' of letters after reading for about 20-30 minutes. The latter is more specifically due to an insufficiency of convergence.

Binocular diplopia

Binocular diplopia is the subjective impression of two images of the same object seen by the patient when both eyes are open, but one image disappears on closing either-eye. The is due to the inability of the two eyes to move together synchronously, such that their foveas are both directed towards a target. This complaint is encountered in patients with an extraocular muscle paresis, restrictive squint or a displaced globe.

DISORDERS OF THE OCULAR SURFACE

Diseases affecting the cornea, conjunctiva and eyelids, i.e. the ocular surface of the eye, frequently present with symptoms of redness of the eye, a foreign body sensation, swelling of the lid, photophobia and irritation. The corneal and conjunctival surfaces are extremely sensitive. This is probably a protective mechanism and helps to avoid or detect minimal trauma at an early stage. They

are also extremely smooth, an attribute enhanced by the lubrication provided by the tear film. Miniscule changes in the surface contour, such as the exposed knot of a 10-0 monofilament nylon suture or a few papillae, cause severe tearing or lacrimation, a sensation akin to that of a foreign body on the eye, redness and visual disturbances. Chronic disorders of the ocular surface alter the tear film and can lead to a complaint of heaviness of the eyes by the latter half of the day, fluctuation in visual clarity and a gritty sensation.

Ocular irritation

Ocular irritation is often described as a sandy or gritty sensation which is generally worse in the morning.[1] The patient may also complain of tiredness of the eyes or a 'burning' sensation.

Lacrimation

Lacrimation is a term used to denote a reflex increase in the production of tears, as opposed to epiphora, which signifies an overflow of tears due to an obstruction to the outflow of tears. Lacrimation may be caused by irritation of the ocular surface due to the presence of a foreign particle, inflammation, chemical injuries or psychogenic factors.

Photophobia

Photophobia is defined as discomfort caused by an abnormal sensitivity to ambient light conditions. This intolerance to light may be due to pain induced by pupillary constriction and ciliary spasm because of inflammations ot the anterior segment, or stimulation of the terminal fibres of the trigeminal nerve in the cornea. Photophobia is generally encountered in patients having abnormalities of the corneal surface or anterior uveitis. The ophthalmologist should scan the eye for the presence of a corneal abrasion, oedema, foreign body or ulcer, using fluorescein staining to highlight epithelial defects, as well as look for evidence of anterior uveitis. Mild photophobia may also occur in keratoconiunctivitis or even posterior uveitis. Some drugs and poisons which dilafp the pupil *r.^a.*give rise to symptoms similar to photophobia.

True photophobia must be distinguished from 'glare' as well as decreased vision in bright light. Glare or excessive awareness of light could be due to conditions which allow excess light to enter the eye such as aniridia and qcu I a r albinism, or those which produce excessive irregular scattering of light in the eye such as a posterior subcapsular cataract. Decreased vision in bright hghtr3ue-K5~ conditions such as posterior subcapsular cataract, congenital cone dystrophy and other central macular disorders may also be.mistaken, for photophobia because ot the occasionally reported symptom of having to partly close the eyes in bright light. This is particularly true of cone dystrophy.

If the ocular examination is normal and photophobia persists, the patient should be investigated for migrameT meningitis, trigeminal neuralgia or other cranial disorders such as a suba rach noiciTiaemorrhage.

Red eye

The final |common response\to any anterior segment disease is redness ot the eye, irrespective of whether the basic cause lies in the conjunctiva, cornea or anterior uvea. It is therefore important to be able to identify the cause, gain is a prominent symptom in anterior uveitis, keratitis, and acute angle-closure glaucoma. Photophobia is pathognomonic of corneal affection, directly as in keratitis or keratoconjunctivitis, or indirectly due to corneal oedema in acute glaucoma and uveitis. Blurring of vision is a feature of keratitis and uveitis. The distinguishing features between conjunctivitis, iritis and glaucoma are given in Table 9.1 (Flowchart 9.1).

The differential diagnosis of a red eye should include the following:

Conjunctivitis	Infectious
	Viral
	Bacterial
	Non-infectious
	Allergic
	Dry eye
	Toxic or chemical reaction
	Foreign body
Keratitis	Infectious
	Bacterial
	Viral
	Fungal
	Protozoal, e.g. *Acanthamoeba*
	Non-infectious
	Recurrent epithelial erosions
	Foreign body
Uveitis	
Acute angle-closure glaucoma	

VISUAL PHENOMENA

Glare: Glare occurs when too much light either shines directly or reflects into the eye, reducing vision, e.g. bright light reflecting from shiny surfaces. It can also occur when a visual impairment causes light entering the eye to 'jump around' rather than come into focus. Glare increases the difficulty in distinguishing objects from their background and makes it hard to identify faces. Sunlight is often a major cause, both outside and indoors. High gloss paper such as that used in many magazines can also be hard to read because of glare, as can computer monitors. Ability to recover from glare

Table 9.1 Differential diagnosis of the common causes of a red eye

Clinical features	Conjunctivitis	Acute anterior uveitis	Acute angle-closure glaucoma
Onset	Acute	Rapid, over a few days	Sudden
Vision	Good	Fair	Poor
Pain	Mild discomfort	Moderate in the eye and along the first division of the trigeminal nerve in iritis	Severe pain in the eye and entire trigeminal area
Secretion	Mucopurulent	Watery	Watery
Photophobia	Absent	Usually present	Usually absent
Coloured halos around lights	Absent	Usually absent	Commonly present
Conjunctival congestion	Superficial	Deep ciliary	Deep ciliary
Pupil	Normal	Small and irregular	Larae and vertically oval
Tenderness	Absent	Present	Present
Depth of the anterior chamber	Normal	Normal	Shallow
Intraocular pressure	Normal	Usually normal but may be raised, sometimes low	Raised
Systemic symptoms	Absent	Referred pain	Prostration and occasional vomiting

or bright lights decreases after 50 years of age due to changes in the lens of the eye and in retinal sensitivity.

Floaters: With age, the normally transparent vitreous gel Ji^uefies and breaks up, leading to the presence of little particles and fibrous strands floating in the vitreous cavity. This debris casts shadows onto the retina. Patients complain of seeing black dots, rings, strands, 'spider-like' images that are more noticeable against a bright background and 'move' even when the eye is stationary. Floaters indicate some form of vitreous degeneration and liquefaction and are usually benign and age related; they are also common at a younger age in myopes. However, showers of dots or a sudden increase in their numbers could indicate the formation of a retinal tear, especially if associated with rihotopsia. Alternatively, sometimes the onset of new floaters is secondary to vitreous haemorrhage, often caused by advanced diabetic retinopathy, although several other retinal conditions could present in a similar manner. A thorough retinal examination must be performed to determine the cause of any new floaters, so that proper management is instituted.

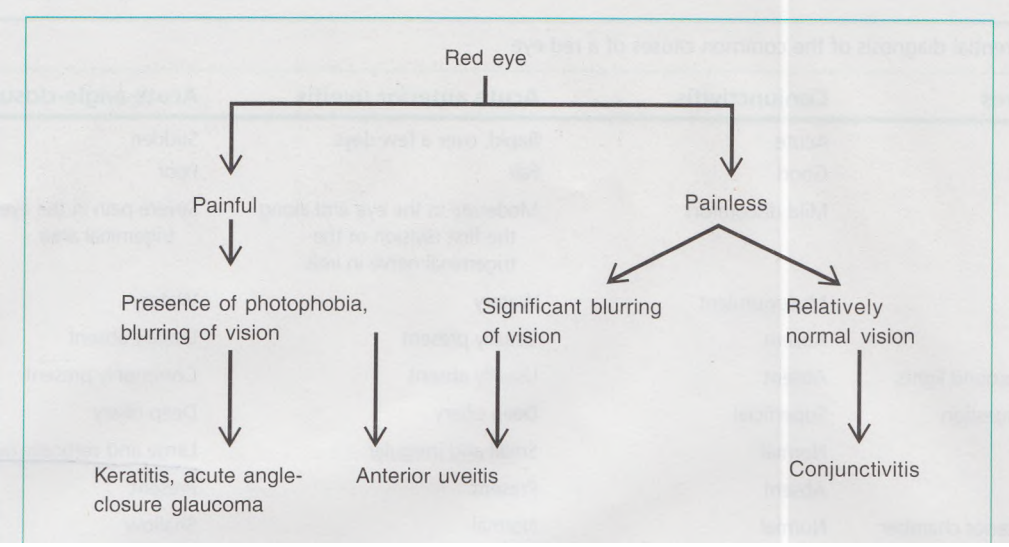
PhotoVsia is a phenomenon in which the patient perceives flashes of light or has a sensation of flickering lights. This occurs due to vitreous shrinkage or liquefaction, which causes a pull on the vitreoreti nal attach ments, irritating the retina and causing it to discharge electrical impulses. These impulses are interpreted by the brain as 'flashes'. This phenomenon is usually benign and age-related, but could be an indicator of a developing retinal tear or an early retinal detachment. The patient should undergo an indirect ophthalmoscopic examination and any peripheral retinal degeneration should be looked for, particularly if photopsia is accompanied by floaters.

JAetamorphopsia is a phenomenon wherein the patient perceives objects to have an altered, irregular contour or shape. For example, graph paper lines may be bent or obscured in areas. This can be reviewed for any changes over time using an Amsler grid (Fig. 9.1), which tests the central 10° of vision. It is associated with diseases affecting the macula such as central serous choroidopathy, age-related macular degeneration, diabetic macular oedema and macular hole. A variant ol this is *micropsia* when ordinary, everyday objects look smaller than normal. This / symptom is seen in central serous chorioretinopathy due to a separation of retinal elements by a collection of subrptinal fluid.

Coloured halos are seen as rainbow-coloured rings around lights at night. These commonly occur in acute angle-closure glaucoma, cataracts or in the presence of corneal oedema or mucus on the surface of the conjunctiva. This phenomenon is due to the prismatic dispersion of light brought about by these conditions.

A history of halos, particularly if associated with periodic obscurations of vision, should therefore always excite the liveliest suspicion; this suspicion should not be diminished by the observation that in the early stages of the disease the eye (apart from its narrow angle) is normal, its tension between attacks is not raised, there is no cupping of the disc and its function (visual acuity and fields) unimpaired, while the facility of the drainage of the aqueous as measured tonographically is undiminished.

The halos are due to the accumulation of fluid in the comeal epithelium and to alterations in the refractive condition of the corneal lamellae. The colours are distributed as in the spectrum with red outside and blue innermost.



Flowchart 9.1 Approach to diagnosis of a case with an acute red eye.

If the patient gives a vague history, their appearance can be demonstrated to him by his looking through a .thin layer of lycopodium powder enclosed between two glass plates made up as a trial lens.

Halos induced by corneal diseases and early cataractous changes in the lens may be differentiated by the Fincham tesA A stenopaeic slit is passed before the eye across the line of vision. As it passes, a glaucomatous halo remains intact but diminished in intensity, whereas a lenticular halo is broken up into segments which revolve as the slit is moved (Fig. 9.2).

Visual hallucinations are objects, shapes or lights 'seen' by patients which are not visible to other persons in the vicinity and arejairly specific for disorders involving the cerebral cortex. Unformed visual hallucinations consist of seeing distorted lights as in flashes and spots, lines, objects, or shapes and are symptoms of lesions affecting the occipital cortex such as migraine and arteriovenous malformations. Formed visual hallucinations are reported as seeing animals, objects, or people and have specific localizing value, indicating a lesion affecting the temporal lobe cortex as in temporal lobe tumours and epilepsy. The formed images could also represent misinterpretation of information in the brain due to the disruption of areas needed to process the information. In thaftTharles Bonnet syndrome^people having a gross diminution of vision segl detailed images. This probably represents an attempt by the brain to interpret any visual information received and form a mental picture corresponding to the stimulus. Visual hallucinations can also be due to transitory or chronic abnormalities in the brain, caused by changes such as electrolyte disturbances, high fevers, liver or kidney failure or drugs such as diazepam, alprazolam, LSD, etc. They are frequently reported by patients with parkinsonism.

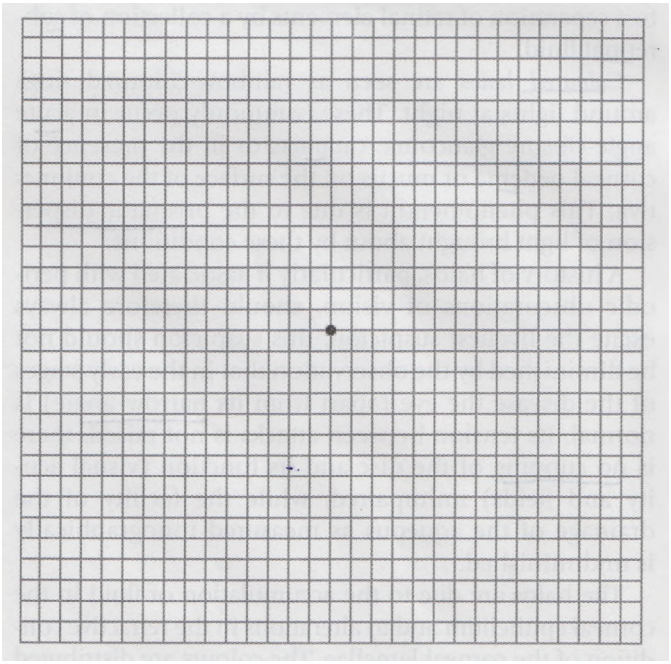


Fig. 9.1 Amsler grid.

Scintillating, scotomata of various kinds occur in migraine. In typical migraine the patient feels unusually well before the attack. A positive scotoma appears in the field of vision and while obscuring sight it has a peculiar shimmering character. It gradually increases in size until ultimately one-half of the field is clouded, the fixation point remaining relatively clear. In the dark field bright spots and rays of various colours are often seen, frequently arranged in zigzags, when they are called 'fortification spectra' (*teichopsia*). Both half-fields are usually affected, so that there is homonymous hemianopia In other cases the whole field becomes clouded, but in spite of this the fixation point is usually seen momentarily,

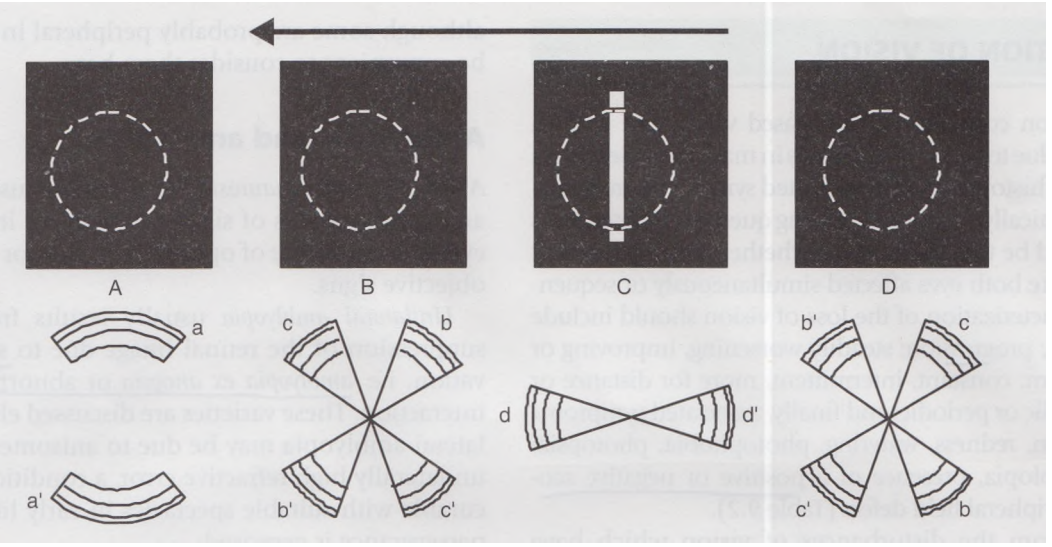


Fig. 9.2 The stenopaeic test for coloured halos. When a stenopaeic slit is passed before the eye in the direction of the arrow the successive appearances of the lenticular halo are represented. At (A), when only the lateral margin of the pupil is exposed, and only the horizontal radial fibres of the lens are implicated, the horizontal portions a, a', of the halo are visible. At (B), when the oblique fibres are involved, the portions a, a', appear to divide, forming b, c and b', c'; as the slit is moved these rotate, b, b' in a clockwise direction, and c, c', anticlockwise. When (C) is reached only vertical fibres are involved, and the portions appear to reunite in d, d'. On continuing the motion of the slit, the portions b', c and c' b, appear and revolve similarly, until finally, at the other extreme position, they become amalgamated as a, a' in (A). (By courtesy of Emsley and Fincham)

and then becomes obscured until the eyes are moved to a fresh spot. Vision usually clears in ahaut-»-auartei~of an hour, but the attack is soon followed by violent headache, generally intensified on the side of the head opposite the hemianopic field fhemicrania), and accompanied by nausea and evensickness (bilious attack).

During the attack numbness in the mouth and tongue as well as slight aphasia are frequent, as well as a copious secretion of urine of low specific gravity. Attacks occur periodically, but vary greatly in number and severity. In mild attacks, and especially as age advances, the scotoma may occur without thp headache or the headache without scotoma.

Migraine is attributed to vasomotor changes in the brain. Vasodilatation, associated with a feeling of well-being, is followed by vasoconstriction, especially in the occipital lobes. Rest, warmth and sleep are the best measures to combatthe attacks; they can sometimes be warded off or alleviated by/ergotamine tartrate/

Occasionally people who suffer from ordinary migraine have attacks in which, without any scotoma, the headache is followed by partial paralysis of the third nerve (*ophthalmoplegic migraine*) on the same side as the hemicrania. Slight ptosis, diplopia and sluggishness of the pupillary reactions continue for some hours and then gradually disappear. The paresis is worse and persists longer with succeeding attacks, and has sometimes eventually become permanent. Probably most of these cases are not migrainous, but due to some organic nerve lesion such as pressure on the third nerve by a distended artery.

Uniocular diplopia occurs relatively frequently in early senile cataracts with patients seeing multiple images of distant objects such as the moon when light is refracted through the wedge-shaped areas of hydration in immature senile cataract. Patients with a subluxated lens may see two images of an object, one through the aphakic area and one through the phakic zone. Large iridotomies, especially if not below the upper lid may also cause shadowing or uniocular diplopia. Ajrare\cause of uniocular diplopia is the folded-over retinal flap in giant retinal tears. One image is seen by the macula and projected straight ahead. The other image is due to stimulation of the displaced retina and is projected to the point in the visual field normally subserved by that region of the retina.

Coloured vision fchromatopsia) is a rare symptom. *Erythmpva f* rpH vir.~~inn~~)'ormrs in some patients after cataract extraction if the eyes are exposed to bright light. Objects look red, but the visual acuity is not affected, and no permanent damage results. Patients should be warned of the possibility of erythropsia, as it is somewhat alarming and suggestive of haemorrhage. On the other hand, some patients report an excessive 'bluish' appearance of objects after cataract extraction because hhip lipht was filtered out by the yellowish cataractous nucleus before surgery. It is also met with in snow-blindness. Chromatopsia also occurs in some cases during the resolution of optic neuritis when the ensuing atrophy is not omplete. In normal people black print will sometimes suddenly turn deep red owing to strong lateral light entering the eye through the sclera.

DIMINUTION OF VISION

The common complaint of decreased vision can give an important clue to accurate diagnosis in many eye diseases on the basis of history alone, if associated symptoms are analysed systematically. Important leading questions related to its onset would be the age at onset, whether it was gradual or sudden; were both eyes affected simultaneously or sequentially. Characterization of the loss of vision should include its duration; progression: steadily worsening, improving or static; pattern: constant, intermittent, more for distance or near, episodic or periodic; and finally, associated symptoms such as pain, redness, watering, photophobia, photopsia, floaters, diplopia, presence of a positive or negative scotoma or peripheral field defect (Table 9.2).

Apart from the disturbances of vision which have been described above and have their origin in the eye itself, there are others dependent upon lesions in the visual nervous paths. There are also some visual defects, the cause and origin of which are imperfectly elucidated; although some are probably peripheral in origin, it will be convenient to consider them here.

Amblyopia and amaurosis

Amblyopia and *amaurosis* are the terms used for partial and complete loss of sight, respectively, in one or both eyes in the absence of ophthalmoscopic or other marked objective signs.

Unilateral amblyopia usually results from psychical suppression of the retinal image due to sensory deprivation, i.e. *amblyopia ex anopsia* or abnormaTBinocular interaction. These varieties are discussed elsewhere. Unilateral amblyopia may be due to anisometropia, with a unilaterally high refractive error, a condition sometimes curable with suitable spectacles in early life if sufficient perseverance is exercised.

Bilateral amblyopia can be due to bilateral sensory deprivation as in bilateral cataracts or corneal opacities or bilateral high refractive error. Bilateral visual loss due to various exogenous toxins with a normal fundus used

Table 9.2 Frequent causes of decreased vision

Causes of gradual, painless and progressive diminution of vision	
Age less than 40 years	Age more than 40 years
Refractive error*	Presbyopia*
Keratoconus*	Age-related cataract*
Corneal dystrophy*	Chronic simple glaucoma (primary open-angle glaucoma*)
Developmental cataract	Dry type of age-related macular degeneration
Juvenile glaucoma	Diabetic retinopathy*
Retinitis pigmentosa*	Corneal dystrophies*
Compressive optic neuropathy	Retinitis pigmentosa*
Hereditary macular degeneration*	Drug-induced maculopathy or optic neuropathy*
Sudden and painless causes of diminution of vision	
Unilateral	Bilateral
Retinal detachment	Bilateral occipital infarction
Retinal vascular occlusion	Atypical optic neuritis
Vitreous haemorrhage	Diabetic retinopathy
Retinal haemorrhage	Grade IV hypertensive retinopathy with macular star
Exudative age-related macular degeneration	Toxic optic neuropathy
Subluxation or dislocation of the lens	Posterior uveitis
Diminution of vision associated with pain and/or an acute red eye	
Uveitis	Endophthalmitis
Corneal ulcer	Retrobulbar neuritis
Acute angle-closure glaucoma	
'Usually bilateral but can be asymmetrical.	

to be termed 'toxic amblyopia', but is presently more accurately termed as toxic retinopathies or neuropathies. Bilateral visual loss also occurs in uraemia, meningitis and hysteria.

Bilateral amaurosis occurs particularly in acute nephritis, especially complicating pregnancy or after scarlet fever, but is also found in association with chronic renal disease. The onset of blindness is sudden or rapid (8-?4honrs):-it is bilateral and complete. The fundi show no changes, unless, as in some cases, there is a coincident hypertensive retinopathy. Vision usually improves in 10-18 hours, and is fully restored in about 48 hours. In uraemic amaurosis the pupils are dilated, but generally react to light, showing that the lower centres are not affected. The condition is probably due to circulation of toxic material, which acts upon the cells of the visual centres. In cases occurring during pregnancy there is usually eclampsia.

Amaurosis fugax is a transient monocular blindness caused by a temporary lack of blood flow either to the brain or retina. It is related to atherosclerosis in the blood vessels that supply the brain, and is thought to be the result of emboli from plaques in the carotid artery. These block an artery for a while and then move on, resulting in a loss of vision for the duration of blockage. The onset is acute and the episode usually lasts for several minntes. 'I*he sudden loss may appear like a curtain falling from above or rising from below and vision mayTje completely absent at the height of the attack. Recovery occurs in the same pattern. Examination during or shortly after an attack may reveal retinal ischaemia in the form of retinal oedema, small hapmorrhapes and, in some cases, visible emboli in the retinal vessels. The emboli are fibrin-platelet aggregates originating on the irregular surfaces of an ulcerating atheroma within the carotid artery or the aorta, or cholesterol crystals. Repeated attacks of amaurosis fugax indicate the need for arteriography, especially if associated with transient cerebral symptoms.

Cardiovascular abnormalities such as valvular defects or arrhythmias may cause similar visual phenomena. Prolapse of the mitral valve, a congenital cardiac abnormality, is associated with a similar history. Fibromuscular hyperplasia is a disease occurring in young females. In these patients proliferation of the medial muscular coats of medium-sized blood vessels occurs causing carotid artery, renal artery and vertebral artery stenosis. Arteriography shows a characteristic 'string of beads' sign. Migraine is an occasional cause of unilateral visual loss. Some patients with migraine have retinal manifestations presumed to be secondary to vasospasm in the retinal vessels and this may be substantiated by the presence of oedema in the retina.

Patients with optic nerve head oedema experience brief or 'transient' obscurations of vision lasting



Fig. 9.3 Venous stasis retinopathy in the left eye of a patient with angiographically proven occlusion of the left internal carotid artery. Note the dilated, dark and irregular veins.

30-60 seconds. It may occur bilaterally or unilaterally in patients with asymmetric disc oedema due to increased intracranial pressure or to giant cell arteritis.

Venous stasis retinopathy (Fig. 9.3) may also present this way and consists of microaneurysms, small punctate haemorrhages and patches of neovascularization. The symptom of visual obscuration originates from ischaemia and resultant anoxia and its presence indicates either occlusion or severe stenosis of the internal carotid artery. The retinal artery pressure is invariably low on the affected side. Ischaemic orbital pain may be produced by anoxia, lessened by lying down.

Treatment with aspirin or Persantine may alleviate symptoms due to platelet emboli. Disobliteration of the carotid is indicated for an isolated atheromatous plaque but often such plaques are multiple. Patients with transient ischaemic attacks of retinal origin are much less likely to develop a hemiplegia than those who suffer from similar attacks of cerebral origin.

Gaze-evoked amaurosis is defined as transient monocular loss of vision occurring in a particular direction of eccentric gaze. It is pathognomomcoF orbital disease, commonly an optic nerve sheath meningioma. The possible mechanism is an inhibition of axonal impulses or transient optic nerve ischaemia.

Visual field defects

See Chapters 12, 19 and 31.

Night blindness

This occurs most frequently in pigmentary retinal dystrophy and in xerophthalmia,but in rare cases it is a familial congenital affection. Night blindness is to be

attributed to interference with the functions of the retinal rods. In xerophthalmia the symptom is a manifestation of a deficiency of ftusolul^ the diet. It also occurs in diseases of the liver, especially cirrhosis, and may appear as a functional nervous disorder associated with other symptoms of neurosis or malingering.

Colour blindness or achromatopsia

This may be congenital or acquired. *Acquired colour blindness* may be partial, as in cases with relative scotomata; or complete, as in disease of the optic nerve. In most diseases of the retina and choroid, changes in colour perception affect mostly th^ blue end of the spectrum. Slight diminution in acuity of perception of these rays is also caused normally, owing to their physical absorption, by the increase offamber pigmenpin the nucleus of the lens *(blue blindness)TSndrtlnis* may be abnormally great in sclerosing lenses (black cataracti: it has been said to affect the pictures of artists in their old age.

Congenital colour blindness occurs in two chief forms—total and partial. The former is very rare and is generally associated with nystagmus and a central scotoma. All colours appear grey, of different brightness. The spectrum appears as a grey band like the normal scotopic spectrum, seen with the maximum brightness at 510 microns It is probable that total colour blindness is caused by a central defect.

The partial form is seldom discovered unless special tests are undertaken, since the subjects compensate for their defect by attention to shade and texture, combined with experience. Gross cases occur in 3-4% of males, but are rare in females (0.4%); milder cases are more common in males. Colour blindness is an inherited condition, being transmitted as X-linked recessive through the female who is usually unaffected, and is probably due to the absence of one of the photopigments normally found in the foveal cones. In most cases reds and greens are confused, so that the defect is a source of danger in certain occupations, such as in engine-drivers and sailors. The red-green cases fall into two chief groups, *protanopes* and *deuteranopes* For the former the red end of the spectrum is much less bright than for normal people and is often actually shortened; in deuteranopes the green sensation is defective. These groups are said to have *dichromatic* vision. In both groups the defects may not be complete and these cases are called *protanomalous* and *deuteranomalous,* respectively. It is clear that theoretically there might be other cases of colour blindness due to absence of the blue sensation, and such cases have been described, but are very rare (*tritanopes*).

Word blindness

Also termed *dyslexia,* this occurs as a not very uncommon congenital anomaly, due to defects in the association areas of the brain, and often runs in families. It affects 0.1% of primary schoolchildren, being much commoner in boys than girls. Owing to backwardness in learning to read, the children are often brought to the ophthalmic surgeon because a visual defect is suspected. In spite of normal fundi and often normal acuity of vision, the patients fail to recognize printed or written words. The auditory memory of words is unimpaired, and generally numerals and music can be read. Hence the patients learn well orally and are good at arithmetic. They are often quite intelligent and may be wrongly punished for inattention and stupidity. The defect is not necessarily complete, and much improvement can be obtained by careful individual tuition and perseverance. Acquired dyslexia is a part of an *aphasia* which is commonly found after a cerebrovascular accident.

Non-organic 'functional' visual loss

Aetiopathogenesis

Non-organic 'functional' visual loss can be either due to (i) wilful 'blind' behaviour, i.e. feigning of symptoms *(malingering)* or (ii) subconscious expression of non-organic signs and symptoms of defective vision *(hysteria).* Differentiation of the two requires careful observation of visual behaviour, but is sometimes difficult and help may be needed from psychiatric experts.

Malingerers are frequently involved with some form of financial gain in the form of an insurance claim, financial compensation, employment benefits, request for job transfer or early retirement or, in the case of children, an excuse to avoid examinations.

On the other hand, patients with hysterical neuro-ophthalmic complaints have little or no insight into their infirmity and may sometimes display a complete lack of concern over their incapacitating symptoms *(la belle indifference).*

Clinical features

The most common presentations of functional non-organic visual loss are (i) decreased visual acuity in one or both eyes, and/or (ii) constricted visual fields.

Malingeritig: Cases occasionally occur of people who hope to gain some advantage by pretending to be visually defective. It is rare for complete blindness to be assumed, and such cases can only be detected by constant watching of the person's behaviour. When one eye is said to be blind, in spite of the absence of sufficient objective evidence to account for the condition, the demonstration of malingering resolves itself into a contest of wits between the surgeon and the individual.

On clinical examination, no ocular or neuro-ophthalmic findings are detectable which can account

Table 9.3 Conditions which produce visual loss with a normal fundus

Condition	Differentiating features
Amblyopia	May suddenly notice poor vision in one eye though the onset is usually in early childhood. It is important to identify an amblyopiogenic factor such as anisometropia, manifest squint, microtropia, etc.
Cortical blindness	Must be ruled out by a detailed history, careful observation and examination of the patient with relevant investigations
Retrobulbar neuritis	A definite or relative afferent pupillary defect will be present
Cone-rod dystrophy	Positive family history, photophobia in bright light, abnormal dark adaptation and abnormal cone dystrophy electroretinogram
Chiasmal tumour	Sometimes visual loss may precede optic atrophy. Pupils show a sluggish reaction to light, with characteristic visual field defects

for the symptoms. Pupillary light reactions are normal. The subject should be observed when brought into the examination room and the eye movements of the patient and his/her reaction to the surroundings noted. The menace reflex should be tried to see if the eyes blink or the patient flinches when threatened. An attempt should be made to elicit optokinetic nystagmus (OKN) by rotating an optokinetic tape or drum in front of the patient. The pattern visual evoked potentials should be recorded. It is to be noted, however, that a wary patient may not attempt to fixate or 'look' at the pattern but may fixate beyond the pattern stimuli, obliterating the Pioo response and thus confusing the picture.

Differential diagnosis

This essentially includes disorders presenting with visual loss with a normal fundus, and are discussed below in Table 9.3.

Many tests have been devised, and several should be employed in each case.

1. A low concave or convex glass (0.25 D) is placed before the 'blind' eye, and a high convex (+ 10 D) before the 'good' eye, and the examinee is told to read the distant types. If he succeeds, malingering is proved.
2. A prism is placed base downwards before the 'good' eye and the examinee is told to look at a light. Malingering is proved if the patient admits to seeing two lights.
3. The surgeon stands behind the patient and covers the 'blind' eye with his hand, at the same time holding a prism of 10° base down before the 'good' eye in such a manner that the edge of the prism passes horizontally across the centre of the pupil; uniocular diplopia results. The surgeon then simultaneously removes his hand from the 'blind' eye and shifts the prism so that the whole pupil is covered by it. If the examinee still admits to seeing two lights, malingering is proved.
4. While the examinee looks at a light a prism of 10° is placed base outwards before the 'blind' eye. If the eye moves inwards in order to eliminate diplopia it is not blind.
5. The Worth four-dot test or Snellen coloured types may be employed. The letters are printed in green and red. If a red glass is placed before the 'good' eye, and the patient reads all the letters, the other eye is not blind, for the eye looking through the red glass can only see the red letters. Care must be taken in this test that the red glass cuts off all the rays from the green letters, as tested by the surgeon's own' vision.

Hysteria, as might be expected, exhibits protean manifestations. It may be unilateral, but is more commonly bilateral. There is usually concentric contraction of the fields, with or without colour defects; very characteristic is a spiral field, which continually diminishes while it is being taken, so that it may be finally limited to the fixation point. The patients, however, get about perfectly well unaided, an impossibility in cases of genuine contracted fields. Sometimes there are irritative symptoms—blepharospasm, blinking and lacrimation. The pupillary reactions are perfect, affording an invaluable objective diagnostic sign. Great care must be taken to eliminate organic disease before the diagnosis is finally accepted.

Treatment

Discrepancies should be conveyed to the patient tactfully. Sometimes it may be necessary to suggest that the subject has a symptom which will improve on its own over time or with special drops. Help with psychotherapy and counselling is sometimes needed and psychiatric referral becomes necessary.

It is important to remember that some patients with organic disease have a strong functional overlay and there is danger that a casual diagnosis of a purely functional disease may overlook a potentially serious one. A diagnosis

of non-organic functional visual loss should, therefore, be made only after careful documentation of a mismatch between subjective and objective findings. If there is any doubt regarding the authenticity of the clinical features, appropriate neuroimaging studies should be carried out and further consultation sought.

SUMMARY

Ocular symptoms can highlight the involvement of different zones of the eye. They also relate to central nervous system and other systemic diseases which affect the eye directly or indirectly. Asthenopia, binocular diplopia and squint relate to problems with ocular motility and binocular coordination. Irritation, foreign body sensation, watering, pain, photophobia and redness occur in diseases affecting the ocular surface and anterior segment.

Visual loss or visual disturbances of different kinds can present in simple or complex form and relate to disorders that affect the different parts of the eye, its refractive apparatus and the visual pathways.

SUGGESTED READING

1. Differential diagnosis of ocular symptoms. In: Douglas JR, Mark FP (Eds.). *The Wills Eye Manual.* Philadelphia: Lippincott Williams & Wilkins, 1999.

10

Assessment of Visual Function

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The functiona\ examination of the eye consists of testing all forms of visual perception—the form sense and the field of vision, the light sense and colour sense. Each eye must be tested separately throughout.

VISUAL ACUITY

Visual acuity is a measure of the spatial resolution of the eye or, in other words, an estimation of its ability to discriminate between two points. If two objects are so close that two adjacent cones are stimulated, the patient would appreciate them as a single target. Therefore, there must be an unstimulated cone between stimulated ones to allow for the resolution of two targets or edges. Foveal cones are separated by 2 |xm, corresponding to a visual angle of 25 seconds of arc. The acuity of *distant central vision* is commonly tested by means of visual acuity test-types (Fig. 10.1).

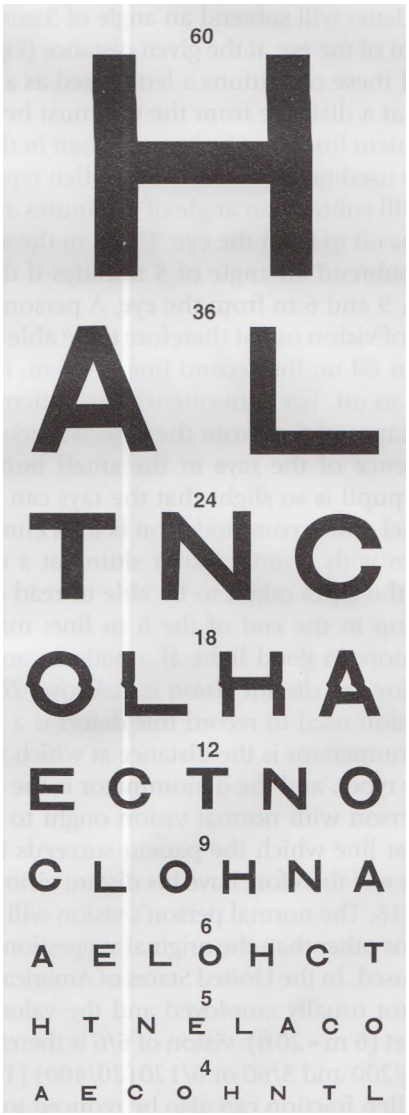


Fig. 10.1 Snellen distanttest-types. The lines, from above downwards, should be read at 60, 36, 24, 18, 12, 9, 6, 5, 4 m, respectively. At these distances the letters subtend a visual angle of 5 minutes.



Fig. 10.2 Widening effect of the visual angle with distance.

Visual acuity test-types consist of a series of letters arranged in lines, each diminishing in size. The breadth of the lines of which the letters are composed is such that the edges will subtend an angle of 1 minute at the nodal point of the eye at a particular distance. Each letter is shaped such that it can be placed in a square, the sides of which are five times the breadth of the constituent lines. Hence the whole letter will subtend an angle of 5 minutes at the nodal point of the eye at the given distance (Fig. 10.2).

To fulfil these conditions a letter used as a test-object presented at a distance from the eye must be larger and the constituent line must be broader than in the case of a letter to be used nearer the eye. In Snellen types the largest letter will subtend an angle of 5 minutes at the nodal point if it is 60 m from the eye. Those in the subsequent lines will subtend an angle of 5 minutes if they are 36, 24, 18, 12, 9 and 6 m from the eye. A person with average acuity of vision ought therefore to be able to read the top letter at 60 m, the second line at 36 m, the third at 24 m and so on. For convenience the patient is kept at a fixed distance of 6 m from the type. At such a distance the divergence of the rays in the small bundle which enters the pupil is so slight that the rays can be considered parallel and accommodation is thus eliminated.

A person with normal vision sitting at a distance of 6 m from the types ought to be able to read every letter from the top to the end of the 6 m line; many people can read more in good light. If a patient can only read the 18 m line, his distant vision is defective. The numerical convention used to record this defect is a fraction in which the numerator is the distance at which the patient is from the types, and the denominator is the distance at which a person with normal vision ought to be able to read the last line which the patient succeeds in reading. The patient will therefore have his distant vision recorded thus: V=6/18. The normal person's vision will be *V=6/6*.

Notations other th an the original suggestion of Snellen are widely used. In the United States of America the metric system is not usually employed and the values are converted to feet (6 m = 20ft): vision of 6/6 is therefore 20/20; of 6/60, 20/200 and 3/60 or 6/120(20/400) (Table 10.1).

The Snellen fraction can also be reduced to a decimal number, and then is known as *decimal acuity* (Table 10.1). In this system a higher visual acuity is represented by a numerically larger number, which is reverse in the Snellen grading.

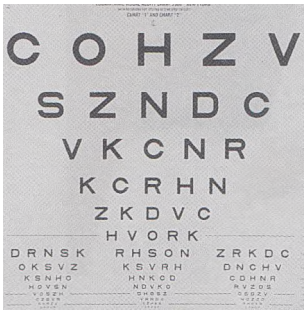
Minimum angle of resolution

The denominator in Snellen grading is an indirect measure of the size of the letters read and the angle they subtend. A notation of visual acuity that has the same clinically significant difference between each line and allows easy recording of every letter read is the log minimum angle of resolution (MAR) scale. The MAR is arrived at by dividing the denominator by the distance at which the letters were read, i.e. the Snellen fraction is inverted and reduced. A Snellen acuity of 6/12 or 20/40 therefore corresponds to a MAR of 2 minutes of arc. Log MAR, or a logarithm of the MAR allows for constant geometric progression over each step. The progression of difficulty from one line to the next is uniform. The lines

Table 10.1 Notations for recording visual acuity

Snellen equivalent (m)	(feet)	Decimal equivalent	Log MAR* equivalent
6/3	20/10	2.00	−0.3
6/4	20/12.5	1.50	−0.2
6/5	20/16	1.20	−0.1
6/6	20/20	1.00	0.00
6/7.5	20/25	0.80	+0.1
6/9	20/30	0.6	+0.2
6/12	20/40	0.50	+0.3
6/15	20/50	0.40	+0.4
6/18.9	20/63	0.32	+0.5
6/24	20/80	0.25	+0.6
6/30	20/100	0.20	+0.7
6/36	20/120	0.17	+0.8
6/37.5	20/125	0.16	+0.8
6/48	20/160	0.13	+0.9
6/60	20/200	0.10	+1.0
6/75	20/250	0.08	+ 1.1
6/96	20/320	0.06	+ 1.2
6/120+	20/400	0.05	+ 1.3
6/150	20/500	0.04	+ 1.4
6/600+	20/2000	0.01	+2.0
6/6000§	20/20000	0.001	+3.0

The figures in blue indicate the letters on most standard visual acuity charts.
'Log of minimum angle of resolution.
+Vision < 6/20 (3/60) is the WHO definition for blindness.
*6/600 = count fingers at 2 feet.
§6/6000 = hand motion at 2 feet.



Fig, 10.3 Modified Bailey–Lovie type visual acuity chart.

progress in 0.1 log MAR steps and every letter read by the patient counts as 0.02 of each line. A Snellen acuity of 6/12 or 20/40 or a MAR of 2 minutes of arc, corresponds to a log MAR of 0.3, i.e. $\log_{10}2$. If the patient reads two alphabets in the next line, the log MAR visual acuity will be recorded as 0.3+ (2x0.02), i.e. 0.34. This derivation has been used in the construction of charts such as the Bailey-Lovie chart. This chart has 10 letters known to have relatively equal legibility, DEFHNPRUVZ. These letters are structured in a ratio of 5:4, and there are five letters in each row (Fig. 10.3). The chart has a constant geometric progression, with the size of letters in each row decreasing by a factor of $\log_{10}10$. The distance between each letter is equal to the width of the letter. The chart used in the Early Treatment of Diabetic Retinopathy Study (ETDRS) is based on similar principles, and uses a combination of 10 alphabets with a ratio of 5:5.

The amount of illumination on the test card has a considerable influence on the visual acuity recorded. It has been found that the acuity rises rapidly as the illumination is increased from zero up to 5-10 foot candles (ft cs); and more slowly up to 1000 or more ft cs. The illumination of the test card should never be allowed to fall below 20 ft cs, and to allow for the deterioration of lamps with use, a standard of 100 ft cs is used.

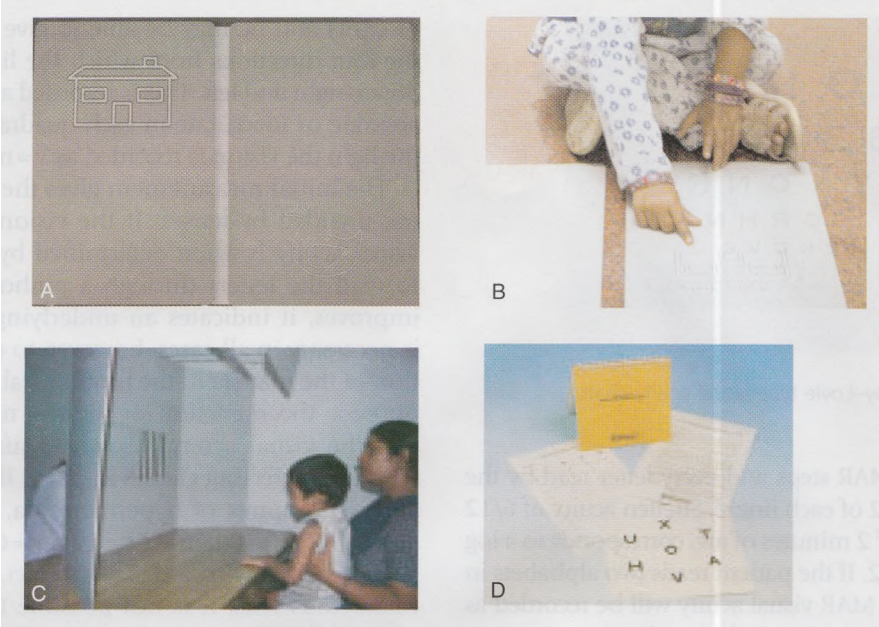
If the patient cannot read the largest letter on any distant acuity chart he is told to walk slowly towards the types. At a certain distance he may be able to see the top letter. He should then be moved back a little, since he may not have understood exactly where to look. In this manner, the furthest point at which he can distinguish the top letter is determined. If this is 3 m, the vision is recorded thus: V=3/60. If he is unable to see the top letter when close to it, he is asked to count the extended fingers of the surgeon's hand, held up at about 1 m against a dark background; this is recorded thus: V= ability to count fingers at 1 m. If he cannot count fingers the surgeon's hand is moved in front of the eye; if he can distinguish the movements, the vision is recorded as V=hand movements. If he is unable to see these he is taken into the dark room and a light is focused on his eye and he is asked to say when the light is on and when it is off. If he succeeds in doing this, V= PL (perception of light) and he may be able to give some indication of the four directions from which the light is directed—up, down, right and left. This is recorded as projection of light, accurate or inaccurate in each quadrant. If he fails to see the light the vision is recorded as V=no PL.

The initial measurement gives the visual acuity of the eye unaided by lenses. If the vision is subnormal, the visual acuity is again determined by asking the patient to read the letters through a pinhole *(see* p. 80). If it improves, it indicates an underlying refractive error. It is necessary in all cases, however, to determine the function of the macula in the best optical conditions; for this purpose the refraction of the eye must be determined and the visual acuity assessed again in the same way with the correcting glasses in place. If, for example, there are two dioptres of hypermetropia, *best corrected visual acuity* (BCVA) is then written as: V= 6/12 + 2 D = 6/6.

In patients with a dense cataract, i.e. totally opaque cataractous lens, it is not possible to test visual acuity as above. The laser interferometer forms a diffraction pattern of parallel lines on the retina even through a moderate cataract. The patient is asked to identify the orientation of progressively finer lines, to establish the visual acuity likely to be regained after surgery. A similar instrument, the potential acuity meter, projects a tiny Snellen chart onto the retina around a lens opacity and the patient is required to read the alphabets.

The ordinary test-types cannot be used with young children who are easily distracted and may not know their alphabets. Maturation of infant visual function has been studied by two techniques, the pattern visual evoked potential (VEPs; *see* p. 112) and preferential looking behaviour. In children younger than 2 years the VEP test proves more successful; in children over 2 years who can manage both tests the results from the VEP conform more nearly to the findings of Snellen and 'E' acuity testing than do the forced-choice preferential looking test results.

Other tests include the Keeler-Elliot and Kay picture test, Cardiff acuity cards (Figs 10.4A and B) and Ffooks symbols, preferential looking test, and its simplified version, the Teller acuity test (Fig. 10.4C). Given a choice, an infant prefers to look at patterned rather than unpatterned stimuli. The infant's preference may be quantified by incorporating patterns which vary in stripe width. Teller's method of estimation is used in very young, preverbal children (1-3 years of age). The Teller acuity card system consists of 17 cards, one half is a set of vertical black-and-white bars of varying width and spatial frequency; and the other half has a uniform grey background. The Teller cards are presented in the centre of a large grey 'stage', after first drawing attention to the stage with a toy. There is a small hole in the centre of each card, through which the examiner judges the preferred side of the card by noting the infant's fixation. If the infant fixates on the side of the card with the grating, a smaller grating size is shown



Fig, 10,4 Tests for recording visual acuity in children. (A and B) Cardiff acuity cards for children 2–4 years of age; (C) Teller acuity cards for children below 3 years of age; (D) Sheridan–Gardiner test for children 4–6 years of age. (By courtesy of Keeler)

till no preference for fixation is observed. The grating size (spatial frequency) of the card can then be converted to the equivalent of Snellen visual acuity.

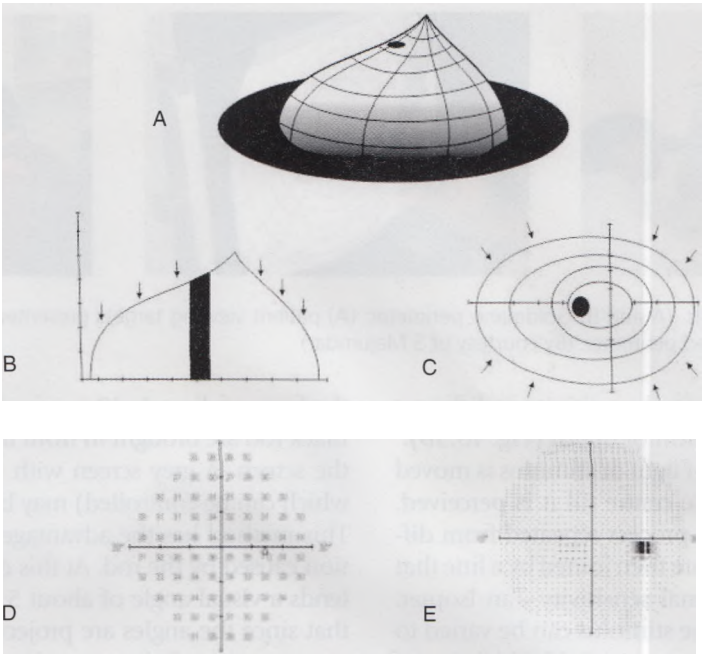
With toddlers and slightly older 'verbal' children, simple pictures constructed on Snellen's principles may be used. A very effective test is the 'E-test' in which the examiner holds cards on which the letter E is printed, in various positions and in various sizes. If the test is treated as a game, the child standing 6 m away will readily respond on request by indicating the direction of the letter with his hand or by holding a similar card in the same position so long as he sees it. A similar test is the Landolt C chart. The system of character matching is exploited by the Sheridan-Gardiner (Fig. 10.4D), STYCAR (sight testing for young children and retards) and HOTV tests, in which children match Snellen letters on a hand-held card.

An objective measure of the visual acuity may also be made by utilizing the phenomenon of *opticokinetic nystagmus.* If a white drum with vertical black stripes is rotated before the eyes, patients follow a stripe with a slow motion and as it disappears, switch suddenly back to pick up a new stripe. This is an automatic reflex which persists as long as the individual stripes are seen. By varying the breadth of the stripes or the distance of the patient from the drum, an assessment of the acuity can be made, particularly in uncooperative or malingering patients. It is worth noting that in cases of hemianopia due to lesions of the parietal lobe the response is absent.

Exposure to a bright light prior to recording visual acuity may result in a fallaciously low reading in retinal disorders. The extent of involvement can be assessed clinically by recording vision before and after exposure to a bright light or photostress. The *photostress test* is performed by covering one eye and asking the patient to read the smallest possible line on the near chart. A bright light is shone into the eye for 15 seconds, following which the patient is asked to read the same line of print and the recovery time noted. The test is repeated with the other eye. In normal people and those with optic nerve disease there is no significant difference in the time taken for the two eyes to recover from the photostress. In a subject with macular disease the recovery time is prolonged. If the difference is at least one-third longer than the recovery time of a normal eye it is considered significant. When photoreceptors are diseased there is a marked delay in the visual pigment regeneration process so that the after-image of the light persists longer on the diseased side. The test is useful in early macular disease, particularly central serous retinopathy, where there may be minimal deterioration in visual acuity and yet an easily detectable decrease in photoreceptor reserve capacity.

FIELD OF VISION

The extent of the normal visual field is limited in an individual by anatomical features such as the brow superiorly, the nose nasally and the cheek inferiorly. It is seen that the field for a white target extends 60° upwards, rather more than 90° outwards, 70° downwards and 60° inwards (Fig. 10.5). The extent varies with illumination, size of the test-object, contrast of the test-object *vis-a-vis* the background, and the state of adaptation of the eye.



Fig, 10.5 (A) Three-dimensional representation of the normal visual field as an island of vision in a sea of darkness; (B) meridional two-dimensional representation of the visual field in any axis as obtained by static perimetry; (C) two-dimensional representation of the sensitivity of the visual field as obtained by kinetic perimetry; (D) numerical values of the retinal threshold at different areas of the visual field; (E) grey-scale representation of the threshold values in different areas of the visual field.

Confrontation test

A rough, but very useful, method is the *confrontation test*, which can be applied in the clinic or at the patient's bedside, if there is a suspicion of a gross visual field defect.

The surgeon sits facing the seated patient with his head level with that of the patient, at a distance of about 60 cm. The patient is asked to cover his left eye with the palm of his hand, and is told to look straight into the surgeon's left eye. The surgeon closes his right eye, and then moves his hand in from the periphery towards the common line of vision of the patient's right and his own left eye, keeping his hand in the plane half-way between the patient and himself. As soon as the surgeon sees it himself, the patient ought to say that he also sees it. The movement of the hand is repeated in various parts of the field—above, below, to the right, to the left and so on. The other eye is also tested similarly.

This method is extremely simple and rapidly applied. It will be seen that the surgeon tests the range of the patient's field by a comparison with that of his own, which may be considered normal; moreover, he is continually watching the patient's eye, so that he can at once observe any deflection from the point of fixation. Better results are obtained by face-outline perimetry. The object is brought from behind forwards into the patient's field at a distance of several centimetres from the face. This is repeated in 10-12 meridia. A hemianopic defect can be easily detected if the surgeon extends each hand to either side and asks the patient how many hands he sees.

If any defect is indicated by these methods, or is suspected from other features of the case, it must be accurately mapped out and recorded by perimetry.

Perimetry

The term *perimetry* is used to describe techniques employed to examine and quantify the visual field using targets of various sizes and colours. Because of the subjective nature of the patient's responses, efforts have been made to standardize the many aspects of testing to eliminate as many variables as possible. Despite this, when interpreting a visual field defect, it is still very important to take into account the patient's reliability.

The *threshold of differential light sensitivity* measures the ability of a given eye to discern a small spot of light projected on a uniformly illuminated background. *Differential light sensitivity* decreases slowly from the macula to the periphery, but not as abruptly as visual acuity. This is described as the *'hill of vision'* (Fig. 10.5), with the elevation representing differential light sensitivity at different points.

Two techniques of testing are commonly employed to determine the profile of this 'hill of vision': (i) kinetic, in which a target is moved across the field to map out the two-dimensional extent of the field (Fig. 10.5C) and
(ii) static, utilizing stimuli of varying luminance in the

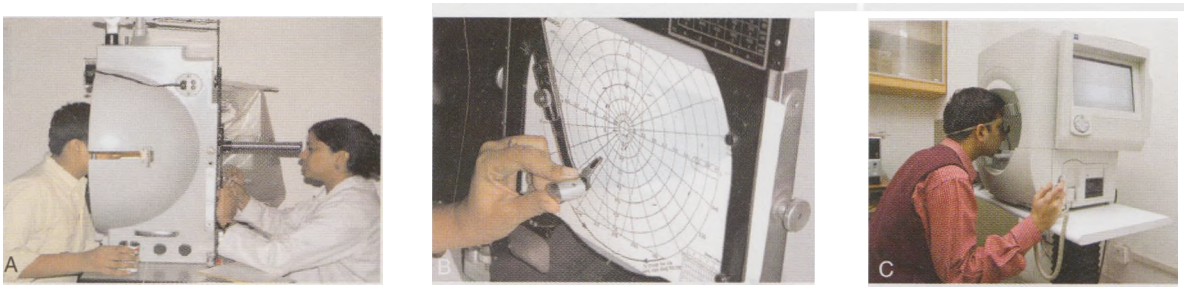


Fig. 10.6 Recording the visual fields. (A and B) Goldmann perimeter: (A) patient viewing targets presented; (B) perimetrist recording the responses; (C) Humphrey automated perimeter. (By courtesy of S Majumdar)

same position to determine retinal sensitivity at different points, adding a third dimension of depth (Fig. 10.5B).

In kinetic perimetry, a spot of light or stimulus is moved from the periphery towards the centre till it is perceived. This point is recorded and the process repeated from different directions. These points are then joined by a line that represents a given level of retinal sensitivity—an isopter. The size and illumination of the stimulus can be varied to allow assessment of areas of the visual field which are of interest to the ophthalmologist, e.g. the central 30^0.

The *perimeter* is commonly a half-sphere, situated at the patient's near point, within which a spot of light can be moved to test for retinal sensitivity, e.g. Goldmann perimeter, or computerized, automated perimeters (Fig. 10.6).

During perimetry, stimuli may be presented in three different ways:

1. In kinetic perimetry, a target of given luminance is moved from a non-seeing area until the patient sees it, as in the *Bjerrum screen* and *Goldmann perimeter.* Targets of different luminance are used to plot the various isopters. The brightest target will have the largest isopter and dimmest the smallest. The target will be of threshold intensity for the limits of the isopter but suprathreshold for points tested within the isopter.
2. In static, suprathreshold perimetry, targets of a given slightly supranormal intensity explore the visual field and should be seen by a normal eye. In the presence of a moderate-to-gross loss of sensitivity, the supranormal stimulus is not seen. However, milder deficits may be missed. The *Friedmann analyser* and automated screening strategies on other automated perimeters use such stimuli.
3. In static, threshold perimetry, targets of different and increasing intensities are presented at designated points in the visual field until just visible, to determine the patient's threshold for that point. This is used in computerized, automated perimeters.

Kinetic perimetry

Bjerrum target screen: The patient is seated 2 m from the centre of a large black screen, 2 m or more in diameter. He fixes a spot in the centre of the screen and small white targets in the form of discs, 1-10 mm in diameter, attached to a long black rod are brought in from the periphery on a level with the screen. A grey screen with a spot of light (the size of which can be controlled) may be used in a similar fashion. This method has the advantage of eliminating the distraction caused by the rod. At this distance a 3 mm object subtends a visual angle of about 5 minutes. It will be noticed that since the angles are projected onto a flat surface, tangents are recorded, not angles themselves as with the arc (Fig. 10.7). Hence only a small area can be investigated, and distortion must be taken into account. The kinetic perimetry chart has circles marked upon it, concentric to the macula (Fig. 10.8), corresponding to degrees marked on the arc. The arc is under the observer's control at the back of the perimeter (Fig. 10.6). The patient is seated with his chin upon the chin-rest and face vertical with one eye occluded. The other eye fixes the central white dot, situated at the centre of an illuminated hemisphere, around which the arc revolves.

The field is first charted with a large, white spot of light—the stimulus—which is gradually brought in from the periphery of the arc towards the centre at a moderate pace. The patient is asked to press a buzzer when the object and not a 'blur' is identified. The patient has to be constantly reminded to keep his eye fixed on the central target. At least eight meridians must be investigated, preferably 16, and the object should be carried up to the fixation point,

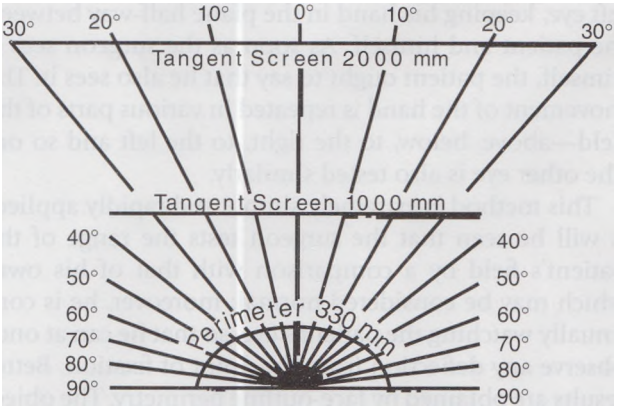
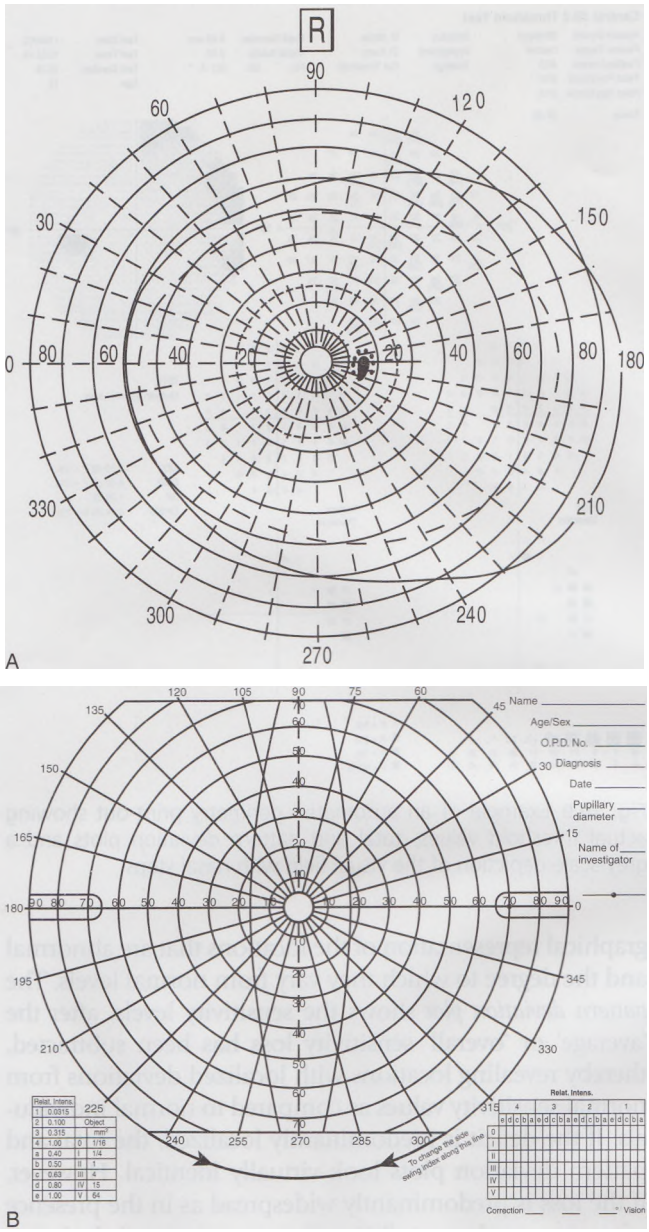


Fig. 10.7 Diagram of the right field, showing the relationship of the retina to the degrees of the perimetric arc, and the relative value of the latter when projected on a tangent scale.



Fig, 10,8 (A) The right visual field for a white object determined by kinetic perimetry (5/330, 1/330, 1/2000 in good daylight). Numerator size of object in mm; denominator distance of testing in mm. (B) Kinetic perimetry. Plotted with Goldmann perimeter.

as there may be areas inside the limits of the field which are 'non-seeing' (*scotomata*). These should be mapped out with the same accuracy as the limits of the field, and the plotting should always be from a 'non-seeing' to a 'seeing' area. If the scotomata are small, the limits are determined with a smaller stimulus. The size of the test object and its luminance are recorded as isopters or lines joining points of equal retinal sensitivity. With small, dim stimuli, *relative scotomata* can be found which are not demonstrable with large bright objects. *Absolute scotomata* are those which are demonstrable with all light intensities.

Perimetry is purely subjective. The normal physiological response to an object in the peripheral field is to turn the eyes towards it. In charting the field of vision this normal response must be suppressed, fixation being rigidly maintained centrally while 'attention' is directed to an object at the periphery. Hence the first fields taken should be interpreted with caution. With good illumination an object subtending a visual angle of 5 minutes will give the full normal field for white. A 5 mm object used at the usual distance of 33 cm (5/330), corresponds to a visual angle of approximately 1 °. The extent of the normal field, with a 5 mm object in good illumination, is shown in the chart of Fig. 10.8. In comparison to the wide field recordable by this method, a tangent screen can only record changes in the central 30° of visual field (Fig. 10.8). If the charts of the two eyes are superimposed there will be a large central area which is common to both eyes: this is the *field of binocular vision.*

Having mapped out the field for white, the process may be repeated with coloured objects of similar size. The limit of the field for a colour is the point at which, passing from the periphery to the centre, the colour first becomes evident. Peripheral to this limit, the object is perceptible but appears grey in ordinary illumination. The exact limit is difficult to determine, for most colours appear to change in hue and saturation as the object passes from the fixation point towards the periphery. Red or green should be used first, then blue or yellow. In ordinary conditions, the blue field is largest, slightly smaller than the white, then follow the yellow, red and green, in the order named. The field for blue and yellow' is roughly 10° less in each direction than that for white, and that for red and green another 10^0 less. The limits of the colour fields vary not only with the intensity of the light, but also with saturation of the colour and, above all, with the size of the object. If these are sufficiently great, colours may be recognized almost, if not quite, at the periphery. Deductions made from variations in the colour fields are particularly unreliable, except in compressive lesions when the red field is affected first.

Static perimetry

Static perimetry is usually done with computerized, automated perimeters. It can be plotted with the Goldmann perimeter as well, keeping the location and size of the target stimulus constant and gradually increasing its intensity till the patient sees it, and then similarly testing at different locations. This is time-consuming and needs a very experienced perimetrist. Goldmann perimetry is now reserved for kinetic perimetry alone.

Suprathreshold static perimetry uses stimuli readily visible to normal controls, and these are presented at selected locations throughout the visual field. The machine records the locations where the target is 'seen' and 'not seen'. This quickly screens the visual field for gross anomalies and if

the stimulus is not visible in any area, further evaluation with threshold testing should be done.

Threshold perimetry records incremental threshold measurements at different visual field locations that are typically arranged in a grid pattern or along meridians. Static perimetry performs a sampling of 50-100 locations of the visual field in specific areas known to be commonly affected in ocular pathology. A staircase threshold determination strategy or 'bracketing' technique is used to measure threshold values at each location. The light intensity is increased in large steps till perceived by the patient, and is then decreased in smaller steps to the point where it cannot be identified. *Threshold sensitivity* measurements recorded at a given point indicate that this stimulus can be seen by the patient 50% of the time.

Automated perimeters

Automated perimetry has made perimetric examination simpler, more accessible and more reproducible, and has therefore become a major screening, diagnostic and review modality in patients having any visual field defect.

Automated perimetry has many advantages over manual ways of recording the field.

- Points in the visual field are tested randomly so that the subject cannot 'anticipate' where the next stimulus will be presented.
- The visual field is tested by a static method which quantifies retinal sensitivity and is more accurate than manual perimetry.
- Examiner bias is eliminated.
- There is constant monitoring of fixation.
- Abnormal points are re-tested automatically.
- Built-in, custom-made programmes can be selected or further programming done to perform customized visual field testing.

The patient is seated, with his head at the centre of an illuminated hemisphere or screen (Fig. 10.6). An appropriate corrective lens is placed in front of the eye to be examined, and the other eye is occluded. The patient is instructed to maintain constant fixation at a specific fixation target, and press a button when he perceives a light stimulus within the visual field. A computer randomly presents stimuli of varying luminance at different locations. The threshold values of an individual are then compared by the computer to age-matched normal values.

Abnormal areas, together with the density of the visual field defect, are computed. These comparisons are shown in numerical form, box plots and a grey-scale (Fig. 10.9). The *total deviation box plot* presents one of a group of symbols at each location tested, indicating whether the sensitivity there is within age-adjusted normal limits or has a probability of being seen in less than 5, 2, 1 or 0.5% of age-matched normal individuals, respectively. This provides an immediate

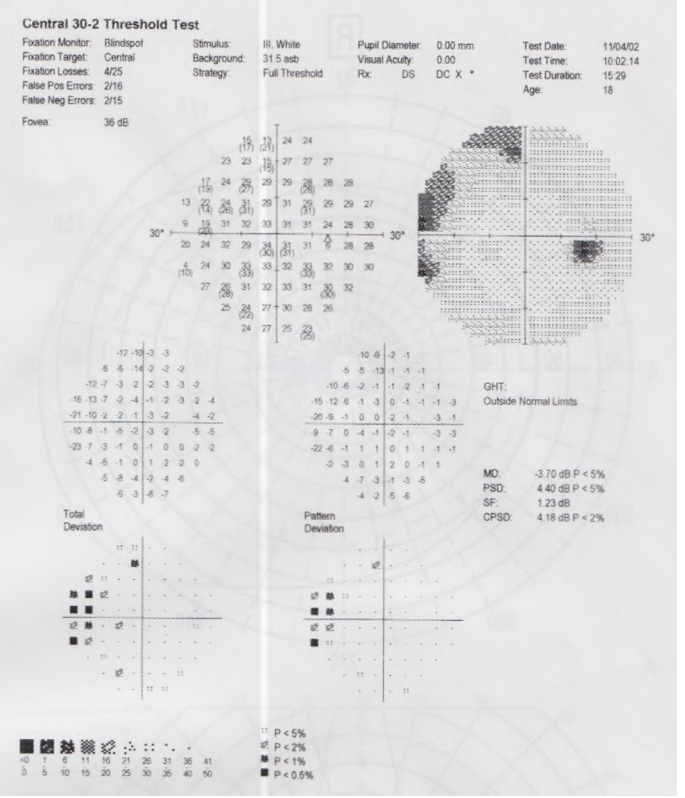


Fig. 10.9 Example of an automated perimetry print-out showing actual threshold values, total and pattern deviation plots and a grey-scale depiction of the visual field with nasal steps.

graphical representation of the locations that are abnormal and the degree to which they vary from normal levels. The *pattern deviation plot* shows the sensitivity levels, after the 'average' or 'overall' sensitivity loss has been subtracted, thereby revealing locations with localized deviations from normal sensitivity values as compared to normal individuals. If the deficit is predominantly localized, the total and pattern deviation plots look virtually identical. However, if the loss is predominantly widespread as in the presence of a cataract, abnormalities appear on the total deviation plot, but the pattern deviation plot is virtually normal. On the *grey-scale,* areas of high sensitivity near the peak of the 'hill of vision' are denoted by a lighter hue, and areas of low sensitivity by a darker tone.

Automated perimeters such as the Humphrey field analyser and the Octopus provide a summary of statistical analysis of the plotted visual field, known as *visual field indices.* The mean deviation (MD) on the Humphrey field analyser or mean defect on Octopus perimeters is the average deviation of sensitivity at each test location from age-adjusted normal population values. It indicates the degree of generalized or widespread loss present in the visual field. Pattern standard deviation (PSD) on the Humphrey field analyser or loss variance (LV) on the Octopus system is a calculation of the average deviation of individual visual field sensitivity values from the

normal slope of the visual field after correcting for any overall sensitivity differences, that is, MD. PSD is a measure of localized visual field loss, or scotomas. Corrected pattern standard deviation (CPSD) and corrected loss variance (CLV) take into account the short-term fluctuations (STF), if any, exhibited by the patient, which are derived from testing a sample of 10 locations twice, to determine the average deviation of repeated measures. The CPSD reduces the effect of intra-test variability in the patient's responses on the local deviation measures.

- The first step in the interpretation of an automated field print-out is to ensure that the right strategy was used as ordered, and that the basic parameters allowing visualization of the targets are met—refraction, visual acuity, pupil size, etc.
- Reliability parameters, i.e. fixation losses, false-positive and false-negative results have to be reviewed before continuing the examination. The duration should be noted as the patient may get fatigued during long tests.
- As compared to age-matched controls, the total deviation plot allows an assessment of all problems of visual perception in a given patient.
- The pattern deviation plot is the one that provides information about a localized defect in the visual field after subtracting for any overall depression. Abnormalities in this have to be carefully examined to ascertain if their degree, density and position correspond with other clinical findings. A scotoma is diagnosed when three contiguous points on two consecutive visual fields have a probability of <5% of being normal. At least one of these three points should have a probability of 1% of being normal. The location of all these points should neither be peripheral nor contiguous with the blind spot. The CPSD should have a probability of <5% of being normal, which is confirmed on two consecutive tests. To diagnose glaucoma, the glaucoma hemifield test and GHT should be 'outside normal limits'.
- The pattern defect should be correlated with actual threshold measurements to offset the possibility that the whole field could be grossly defective and a residual small area of vision be highlighted as a pattern defect.
- A quick look at the *grey-scale* helps to reconfirm gross abnormalities.
- The *glaucoma hemifield test* should be read in patients having or suspected to have glaucoma.
- Finally, the *global indices* provide information on how often such changes are likely to be present in the normal population, statistically helping to diagnose the field as normal or abnormal.

Charting of the visual fields is useful in the diagnosis of many disease conditions such as glaucoma, neurological disorders, retinal diseases (e.g. retinitis pigmentosa), and following laser treatment for diabetic retinopathy. Kinetic perimetry with the Goldmann perimeter is useful in detecting neurological field defects as it gives a quick assessment of both central and peripheral fields. In some countries, visual standards for driving include documentation of a 120° extent of field horizontally binocularly. This is plotted with both eyes open using a special programme on the Humphrey visual field analyser.

A significant change in the visual fields over time can be computed by various programs available, but it is sometimes not possible to distinguish subtle visual field changes from long-term variations.

DARK ADAPTATION

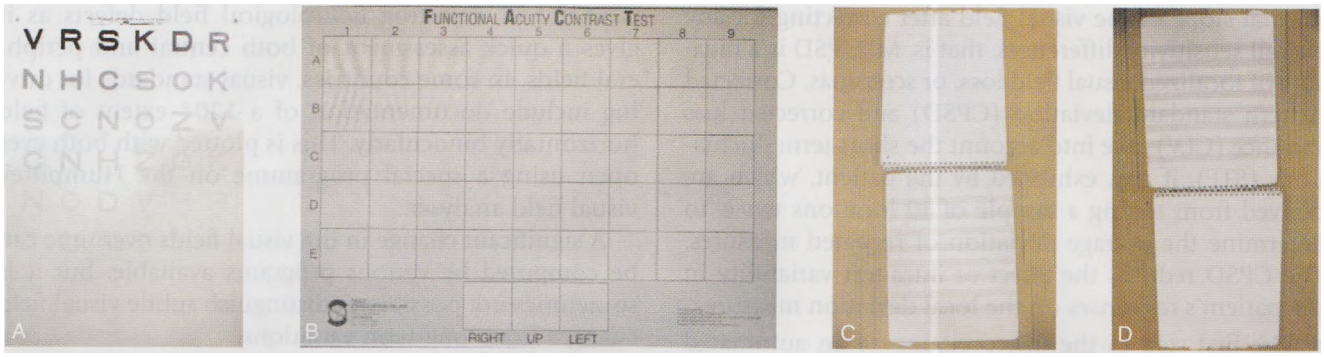
Ocular sensitivity can be determined by measuring the least luminance required to produce a visual sensation, the absolute intensity threshold. Above a certain luminance, about 0.03 cd/m^2, the cones are responsible for photopic vision. As a person enters a dark environment, the light sensitivity of the retina increases while rod activity progressively replaces that of cones, providing scotopic vision. Both the photoreceptors work together at the mid range of illumination, the mesopic range. When the rods function alone, coloured objects appear colourless, as only the cones perceive colour. Dark adaptation is plotted by an adaptometer as the light sensitivity response against a function of time. After 5 minutes of light adaptation at 780 cd/m^2, the subject is seated in the dark. A test spot of increasing luminance is presented until seen by the subject. The adaptation curve normally shows two successive phases. The adaptation of cones is represented by a sharp decrease in the light sensitivity threshold that stabilizes after a few minutes. The sensitivity of the rod pathway improves considerably after 5-10 minutes in the dark and is reflected by the second part of the dark adaptation curve with an increase in sensitivity and a plateau after approximately 20 minutes.

This is utilized in the evaluation of retinal disorders in which the electroretinogram (ERG) is flat, for metabolic diseases and for assessing the scotopic performance in pilots and drivers.

There are individual differences in the rate of development of dark adaptation and facility of behaviour under low illumination which must be considered normal, but the rate of dark adaptation may be prolonged in pathological conditions such as pigmentary dystrophy of the retina, vitamin A deficiency or glaucoma.

CONTRAST SENSITIVITY

Contrast sensitivity is a measure of the smallest distinguishable contrast, and indirectly assesses the 'quality' of vision. Visual acuity is routinely tested under the



Fig, 10.10 Charts for testing contrast sensitivity: (A) Pelli–Robson contrast sensitivity chart; (B) functional acuity contrast test; (C and D) Cambridge contrast sensitivity gratings.

best possible conditions, and does not reflect the visual problems present when driving at night, or on a cloudy day. Contrast sensitivity can be assessed by *letter contrast sensitivity* or the use of *contrast sensitivity gratings* (Fig. 10.10).

Letter contrast sensitivity is measured using visual acuity charts, but with the contrast reduced from 50 to 4% of normal. The *Pelli-Robson* (Fig. 10.10A) and *Regan charts* are most commonly used. They measure the contrast threshold of letters of a certain size. The letters show a gradual decrease of contrast down the chart. The charts are placed at 1 m from the patient, and he is asked to read the smallest letter possible.

Sinusoidal pattern gratings in the form of bars can be shown to the patient who has to identify the direction of tilt of each series of bars, which get progressively smaller. Figure lO.ll(A-C) show examples of sinusoidal gratings and D shows a square grating, together with their diagrammatic representation. Of all the gratings in the figures, the two main variables are the degree of blackness to whiteness, the *contrast,* and the distance between the repeats of the pattern. The distance between the repeats varies, in terms of the retinal image, as the observer moves towards or away from the page. It is usually, therefore, specified in terms of the visual angle, i.e. the number of grating periods, or *cycles per degree* of visual angle. Diagrams on the right of the figure show the output of an ideal reflection microdensitometer as it traverses the grating on the left in a horizontal direction.

Cambridge contrast *sensitivity gratings* require the subject to identify the gratings on a blank card. Gratings of decreasing contrast are presented until the observer cannot distinguish the grating from the blank page (Fig. 10.10).

Assessment of contrast sensitivity is indicated for patients who have visual problems despite a normal visual acuity. It is affected in early cataract and after refractive surgery. It is also a measure of optic nerve disease and its change over time, as in optic neuritis, multiple sclerosis, papilloedema and possibly glaucoma.

COLOUR VISION

Testing colour vision requires elaborate apparatus for its scientific investigation. There are two objectives in testing for colour blindness: (i) the exact nature of the defect and (ii) whether the subject is likely to be a source of danger to the community. The first is an exhaustive investigation involving stringent tests with a pure spectrum. In testing for danger, it is obvious that the names given to the colours are of value, for if a man repeatedly calls 'red', 'green' or *vice versa,* he is unsuited to be an engine-driver or look-out man on a ship. Whatever the object in view, several of the following tests should be employed.

1. *The lantern test*: The subject names various colours shown by a lantern, and is judged by the mistakes he makes. Much here depends upon the size of the apertures of the lantern (i.e. the size of the retinal areas stimulated) and the nature and intensity of the light source. Many lanterns are worse than useless. The Edridge-Green lantern is efficient if used by an expert.
2. *Holmgren wools:* These consist of a selection of skeins of coloured wool from which the candidate is required to make a series of colour matches. This test has been much criticized, but if properly carried out, gross defects of colour vision are easily recognized and an expert will be put on his guard in almost every case of even a minor defect.
3. *The Farnsworth-Munsell 100-hue test:* It identifies hue discrimination by an error score; the greater the score the poorer the colour vision. Patients with toxic optic neuropathy display a characteristic pattern.
4. *Isochromatic charts:* These consist of coloured litho graphic plates in which bold numerals are

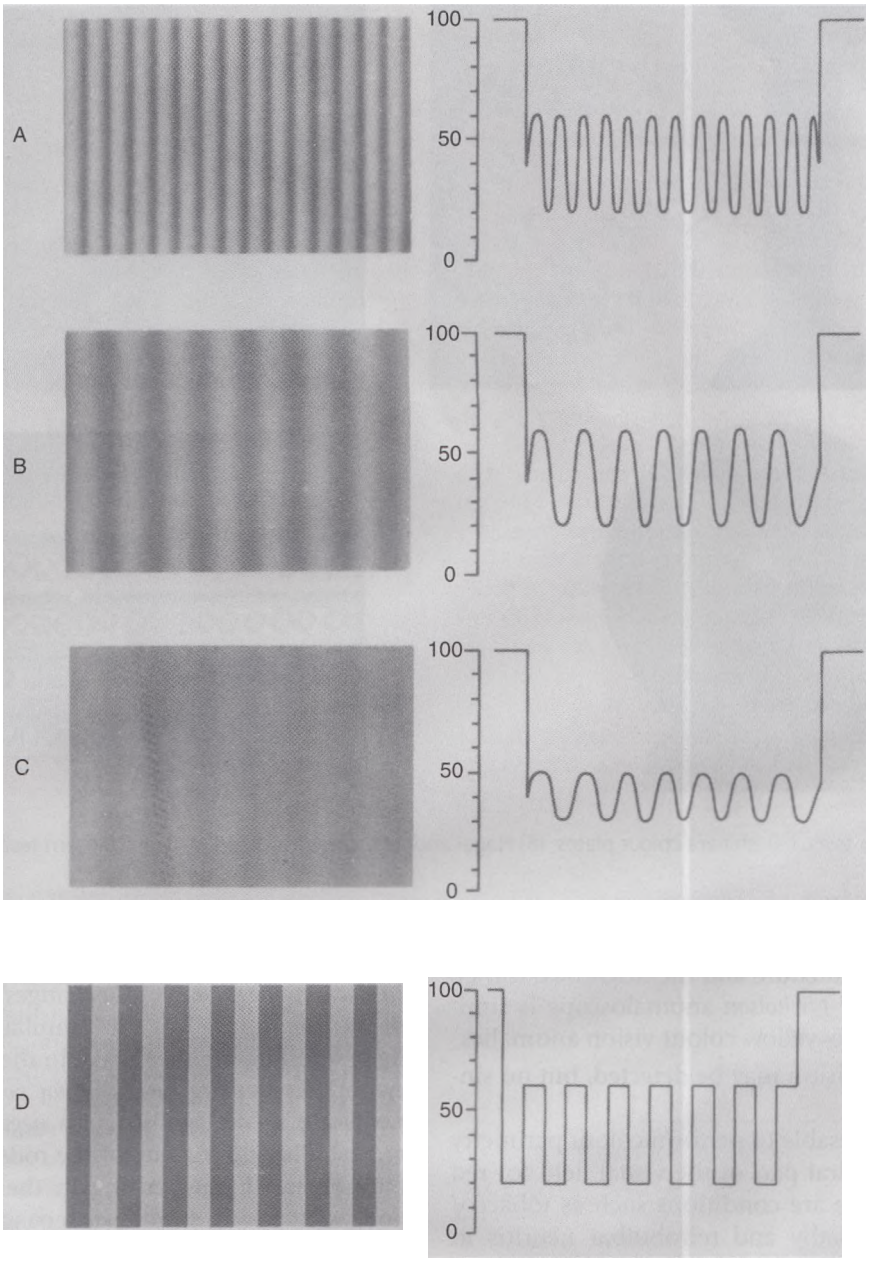


Fig. 10.11 (A, B and C) Sinusoidal grating patterns; (D) square grating pattern. (A) and (B) differ in spatial frequency, (B) and (C) in contrast, defined as (Lmax−Lmin)/(Lmax + Lmin) where L is the light intensity recorded by a photocell scanning across the gratings, as indicated in the diagrams to the right of the illustrations. (By courtesy of Professor GB Arden)

represented in dots of various tints set amid dots of the same size but of tints which are most readily confused with those of the figures by colour defective people. Normal trichromats can easily read the numbers, some of which cannot be distinguished by the various types of colour defectives. Tests are also included in which the numbers can be read by colour defectives, but not by the normal sighted. Stilling's original tests have now been largely replaced by the Japanese test of *Ishihara* (Fig. 10.12), which largely identifies red-green anomalies. The American *Hardy-Rand-Ritler* (H-R-R) test identifies blue-yellow anomalies.

5. *Anomaloscopes:* These are instruments in which on looking down a telescope a bright disc is seen, divided into two halves by a horizontal line. In the *Nagel* anomaloscope one half is illuminated by the light of the sodium line of the spectrum (yellow), and this has to be matched by a mixture of red (lithium line) and green (thallium line) in the other

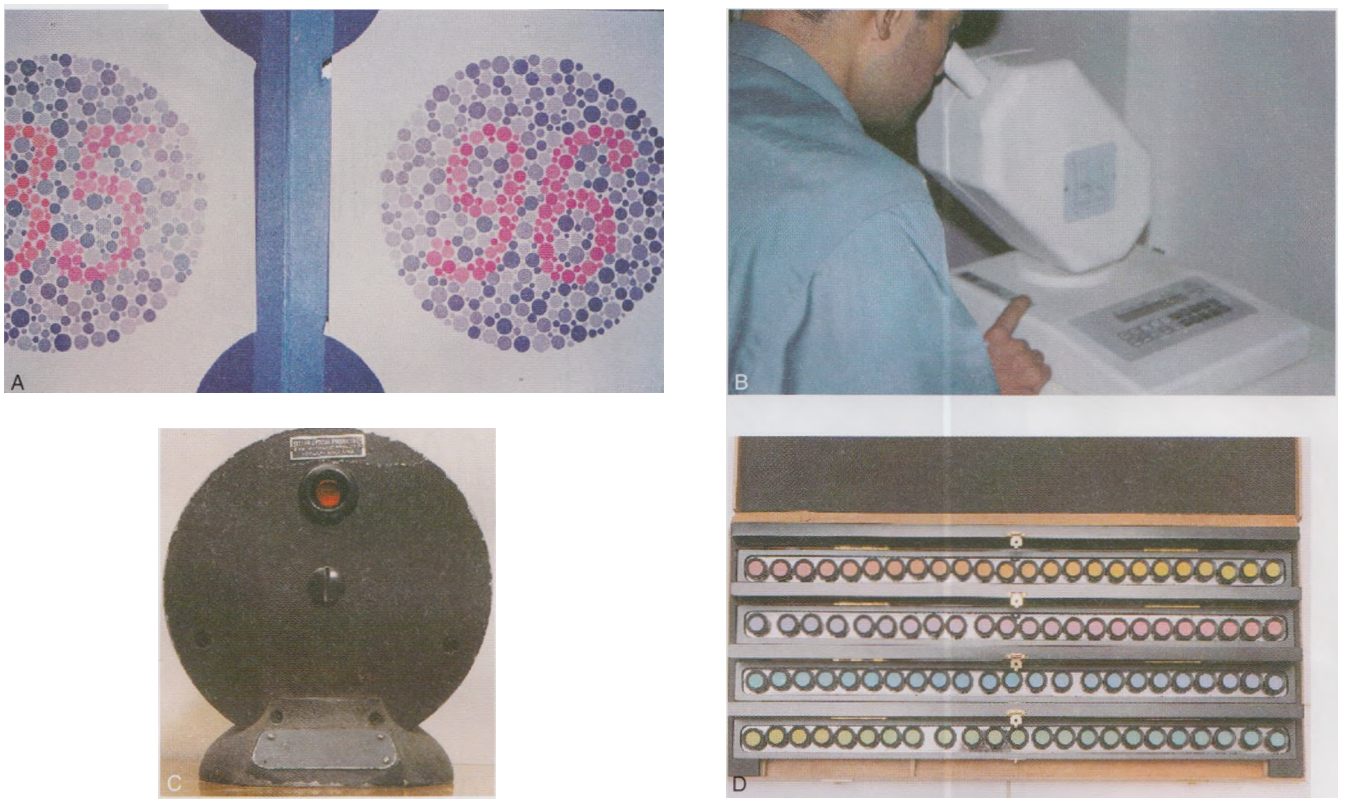


Fig. 10.12 Colour vision tests. (A) Ishihara colour plates; (B) Nagel anomaloscope; (C) Edridge-Green lantern test; (D) Farnsworth-Munsell 100-hue test.

half. By turning knobs, the relative amounts of red and green in the mixture and the brightness can be varied. A *Pickford Nicholson* anomaloscope is similarly used for blue-yellow colour vision anomalies.

Defects of colour vision may be detected, but no single test is infallible.

It is frequently advisable to perform colour perimetry to investigate the central part of the visual field for red and green, since there are conditions such as tobacco/alcohol optic neuropathy and retrobulbar neuritis in which these colours are not recognized, causing *central relative scotomata.* In such a test it is sufficient to use perimetric targets (5 mm in diameter) of the appropriate colour. It will be found that blue and yellow will frequently be recognized as such, but not red and green.

ELECTROPHYSIOLOGICAL TESTS

The tests previously described all require the patient's subjective expression of visual function. However, a truly objective, i.e. totally independent of the patient's psyche, recording of visual perception can be obtained by certain tests. Such objective recording of visual functions is achieved by what are known as *electrophysiological techniques.*

Electroretinography

In *electroretinography* (ERG) changes in the *resting potential* of the eye, induced by the stimulation of the eye with a light stimulus, are measured. In the normal *dark-adapted eye,* after a fleeting *early receptor potential,* three components are seen (Fig. 10.13); a *negative a-wave,* possibly representing the activity of the rods and cones; a *positive* (composite) *b-wave* arising in the inner retinal layers; and, with strong stimuli, a secondary rise in potential and *c-wave,* related not to visual processes but to retinal metabolism, associated particularly with the pigmentary epithelium. Clinically the simplest technique investigates

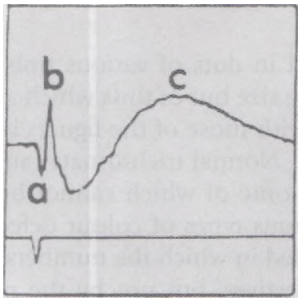


Fig. 10.13 Typical electroretinogram showing a, b and c waves. The dip in the lower line indicates the point of stimulation.

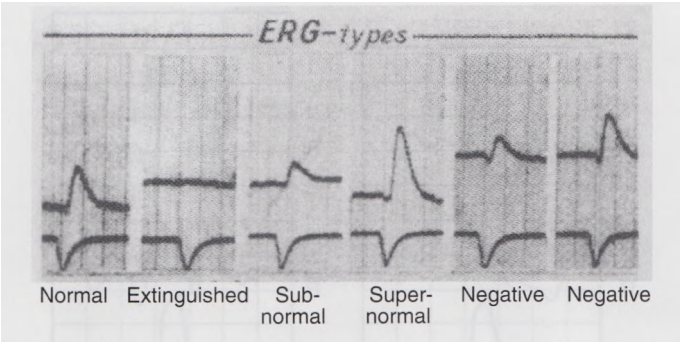


Fig. 10.14 Types of electroretinogram. Upper curve, ERG. Lower curve, photometric record of light–flash.

the dark-adapted eye in which a minute a-wave is followed by the positive b-wave (Fig. 10.14). It is measured in dark adaptation with the active electrode incorporated into a contact lens and the reference electrode attached to the forehead so that a monopolar recording is obtained of the electric potentials picked up from the corneal surface. The response is *extinguished* when there is complete failure in the function of the rods and cones (pigmentary retinal dystrophy complete occlusion of the retinal artery, complete old retinal detachment or advanced siderosis). It is *subnormal* in those conditions in which a large area of the retina does not function; and *negative* in gross disturbances of the retinal circulation (Fig. 10.14).

The ERG measures a global response and essentially gives an indication of the activity of the entire retina, that is, of the rods and cones and their immediate connections. The rod response is selectively tested in the dark-adapted state with a blue light stimulus (scotopic ERG). The cones are tested in bright light (photopic ERG) or with a flickering light stimulus of >20 Hz, which is higher than the critical fusion frequency of rods. The pattern ERG indicates the activity of the central macular region and its corresponding nerve connections; it is used to diagnose early glaucomatous damage. By using a red filter and sharply focused light, an ERG can be obtained from the fovea by the use of averaging techniques, and in this way macular degeneration can be diagnosed in cases of cataract.

Electro-oculography

In the technique of *electro*-oculography (EOG), changes in the resting ocular potential are picked up by electrodes placed at the inner and outer canthi when the eyes are moved from side to side. Changes in the potential thus obtained with changes of illumination are indicative of the activity of the pigmentary epithelium and the outer segments of the visual receptors. These changes are often diminished or absent in retinal dystrophies and degenerations before visual symptoms are evident. The patient is asked to alternately look towards two targets placed in

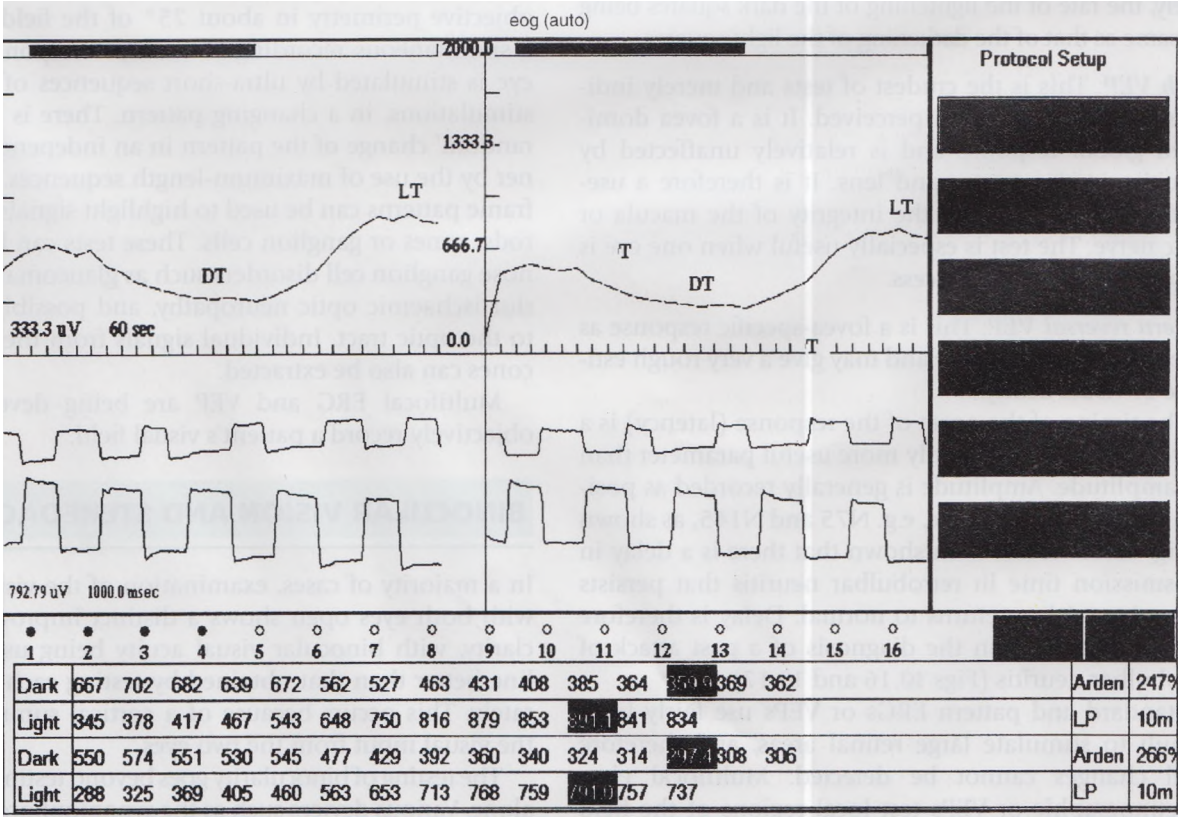


Fig. 10.15 Electro-oculographic recording of a patient with night blindness. DT, dark trough; LT, light trough.

front of him to the right and to the left, and the potentials recorded by the electrodes are printed. The potentials are continuously recorded for a fixed time interval in a light-adapted and dark-adapted state. The ratio of the light peak (Fig. 10.15) over the dark trough is known as the *Arden index*. A value above 185 is normal, below 150 abnormal and 150-185 borderline. The technique is of value in diagnosing objectively the early stages of retinal diseases, especially those that affect the retinal pigment epithelium, or in cases where the fundus cannot be clearly seen. The electrodes and apparatus used for EOG can also be used to measure the change in potentials produced by ocular movements and record the pattern of eye movements in nystagmus (*electronystagmography* or ENG).

Visual evoked potential

The development of the electronic averager has made it possible to detect specific alterations in the electroencephalogram caused by sensory stimuli. The visual response is known as visual evoked response (VER) or VEP. The visual stimulus may be unstructured, as in a flashing light, or structured, as in some form of pattern to the flash stimulus or the stimulus may be patterned, as in a checkerboard presented on a video display unit. The essential feature is that while the pattern changes, the overall illumination remains the same. Black squares go white and white become black alternately, the rate of the lightening of the dark squares being the same as that of the darkening of the light squares.

Flash VEP: This is the crudest of tests and merely indicates that light has been perceived. It is a fovea dominated global response and is relatively unaffected by opacities in the cornea and lens. It is therefore a useful test to grossly assess the integrity of the macula or optic nerve. The test is especially useful when one eye is involved in a disease process.

Pattern reversal VEP: This is a fovea-specific response as it depends on form sense and may give a very rough estimate of visual acuity.

The timing of the onset of the response (latency) is a more reliable and generally more useful parameter than the amplitude. Amplitude is generally recorded as positive, e.g. P100, or negative, e.g. N75 and N145, as shown in Fig. 10.17. It has been shown that there is a delay in transmission time in retrobulbar neuritis that persists even when vision returns to normal. Delay is therefore an important sign in the diagnosis of a past attack of retrobulbar neuritis (Figs 10.16 and 10.17).

Standard and pattern ERGs or VEPs use fairly large stimuli to stimulate large retinal areas, and therefore focal changes cannot be detected. Multifocal electroretinographic or VEPs test local regions of the field with focal stimulation and can be utilized to record an

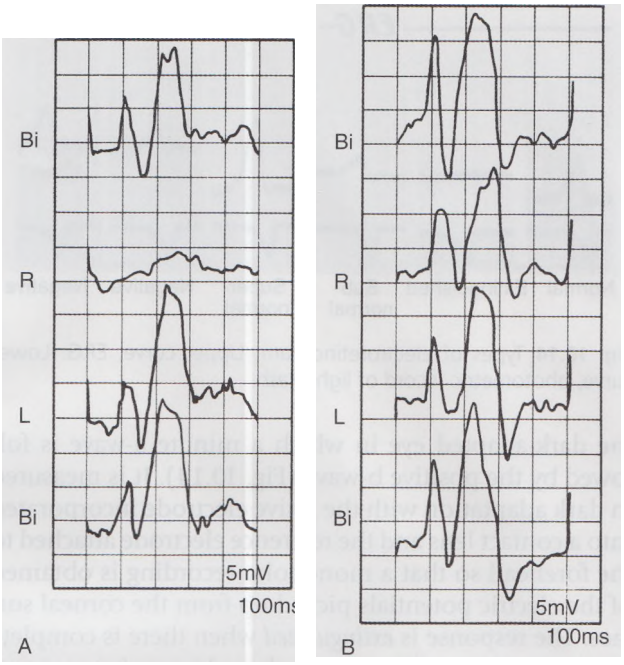


Fig. 10.16 (A) Visual evoked response (VER) in a patient suffering from an acute attack of retrobulbar neuritis in the right eye. Note the markedly reduced amplitude on the right side. (B) VER in the same patient after he had recovered from an attack of retrobulbar neuritis in the right eye. Note that the first negative peak in particular is very slightly delayed compared with the left. The difference is small but significant. (By courtesy of Galloway)

objective perimetry in about 25^0 of the field. There is a simultaneous recording of multiple responses as the eye is stimulated by ultra-short sequences of 250-500 stimulations, in a changing pattern. There is a pseudo random' change of the pattern in an independent manner by the use of maximum-length sequences. Different frame patterns can be used to highlight signals from the rods, cones or ganglion cells. These tests can help diagnose ganglion cell disorders such as glaucoma and anterior ischaemic optic neuropathy, and possible damage to the optic tract. Individual signals from the rods and cones can also be extracted.

Multifocal ERG and VEP are being developed to objectively record a patient's visual field.

BINOCULAR VISION AND STEREOACUITY

In a majority of cases, examination of the visual acuity with both eyes open shows a distinct improvement in clarity, with binocular visual acuity being usually one line better than that obtained by testing each eye separately. This occurs because of a cortical summation of the visual input from the two eyes.

The testing of binocularity goes beyond testing of acuity alone. Various devices such as the synoptophore, Bagolini striated glasses, polarized projectors and binocular visual

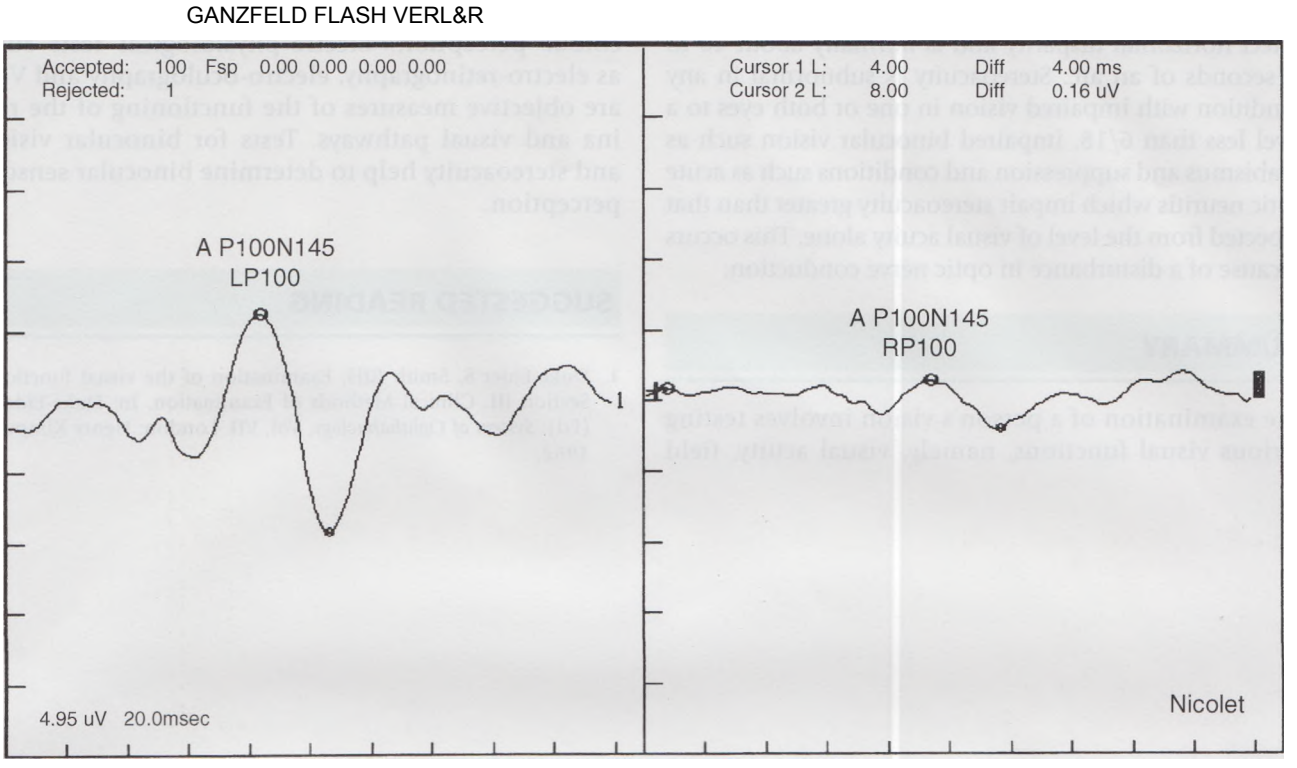


Fig. 10.17 Print-out of the flash visual evoked potential of a patient with optic neuritis in the right eye, showing a reduced amplitude and increased latency.

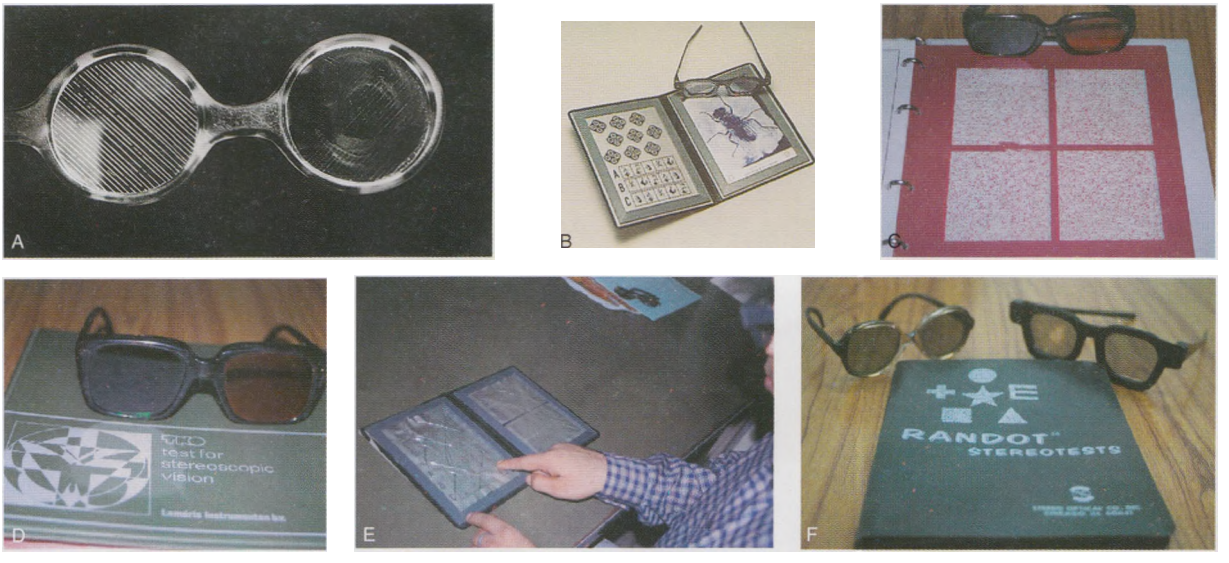


Fig. 10.18 Tests for binocular vision and measuring stereoacuity. (A) Bagolini striated glasses; (B) Wirt stereo fly test (By courtesy of Keeler); (C and D) TNO test; (E and F) Randot stereoacuity test. Wirt and Randot stereoacuity tests are performed with the patient wearing a pair of polaroid glasses with the right and left lenses having a different plane of polarization. The TNO test is performed using red and green glasses.

fields (tested with different coloured glasses in front of the two eyes) are used to assess if the two eyes are functioning together. Tests to further quantify the extent of stereopsis, i.e. measure stereoacuity, include various means of dissociating the images presented to the right and left eye by using different coloured glasses or polarized lenses and appropriately designed pictures such as the Titmus fly test, TNO test and Randot stereoacuity test (Fig. 10.18).

Stereoacuity is a measure of the ability of the eye to detect horizontal disparity and is normally about 40 to 60 seconds of an arc. Stereoacuity is subnormal in any condition with impaired vision in one or both eyes to a level less than 6/18, impaired binocular vision such as strabismus and suppression and conditions such as acute optic neuritis which impair stereoacuity greater than that expected from the level of visual acuity alone. This occurs because of a disturbance in optic nerve conduction.

SUMMARY

The examination of a person's vision involves testing various visual functions, namely, visual acuity, field of vision, dark adaptation, contrast sensitivity and colour perception. Electro-physiological tests such as electro-retinography, electro-oculography and VEP are objective measures of the functioning of the retina and visual pathways. Tests for binocular vision and stereoacuity help to determine binocular sensory perception.

SUGGESTED READING

1. Duke-Elder S, Smith RJH. Examination of the visual functions. Section III. Clinical Methods of Examination. In: Duke-Elder S (Ed): *System of Ophthalmology,* Vol. VII. London: Henry Kimpton, 1962.

11

Examination of the Anterior Segment

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Examination of the anterior segment of the eye requires a combination of techniques: (i) general inspection with diffuse light; (ii) examination in focal (or oblique) illumination using a slit-lamp or magnifying loupe; (iii) examination of the recess of the angle of the anterior chamber with a gonioscope and (iv) estimation of intraocular pressure by tonometry.

General inspection of the eye performed with the diffuse light of a torch or ophthalmoscope to acquire a gross picture of the eye and to identify possible areas of abnormality.

Focal or oblique illumination using a binocular loupe is carried out with the help of a small electric torch, the beam of which can be focussed to a point or converted into a slit. With a *binocular loupe* light is focussed on the area of interest, and a stereoscopic effect is obtained, so that the depth of opacities can be determined. The degree of magnification is three- or fourfold. The *slit-lamp* is a more sophisticated instrument and is essential for a thorough examination of the eye (Fig. 11.1). It employs the same principles of focal illumination, in which a brilliant light is brought to focus as a slit or a point by an optical system supported on a movable arm, and observations are made through a binocular microscope. The magnification can be varied by changing the power of the eye pieces and the objective lenses. The slit-lamp has a binocular viewing system that is co-pivotal with the illumination arm, allowing for the use of various angles while viewing and illuminating the eye. The biomicroscope and illumination arms are parfocal or can be simultaneously focussed at the same point at all angles.

SLIT-LAMP BIOMICROSCOPY

Slit-lamp biomicroscopy is a dynamic examination in which the eye is scanned anteroposteriorly and horizontally. Ocular problems can be identified by different methods of examination, which differ in the positioning of the illuminating light and the angle between the illumination and observation arms. Various permutations and combinations of these techniques are used, some simultaneously and others sequentially.

1. *Diffuse illumination* allows an observer to obtain a direct and tangential view of the anterior segment of the eye. A direct, diffuse illumination examination with low magnification is undertaken first, which is later replaced by higher magnification for viewing areas of interest (Fig. 11.2). Diffuse illumination allows determination of general features, such as colour, size and relative position of structures. This is followed by tangential illumination with a large angle of illumination, which helps to increase contrast and highlight the texture of ocular tissues.
2. *Focal illumination* is used for direct observation of the illuminated point, *direct focal* examination, or to allow observation of an adjacent area, *indirect*

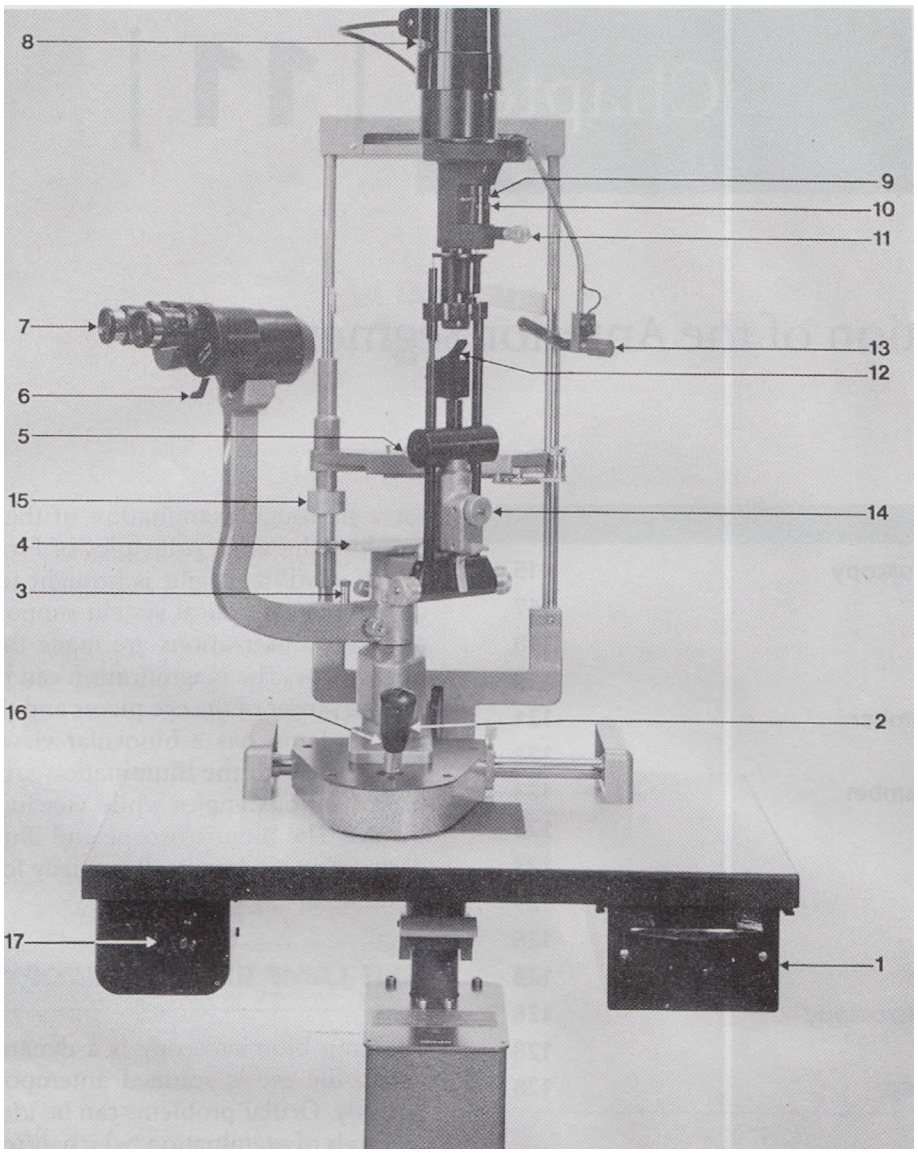


Fig. 11.1 The Haag-Streit slit-lamp 900.

1. Accessory box
2. Joy-stick lever for horizontal coarse and fine adjustments
3. Roll for setting the angle between microscope and illumination unit
4. Guide-plate for preset lenses and applanation tonometer
5. Chin support
6. Lever for changing objectives
7. Interchangeable eye-pieces
8. Lamp-casing
9. Lever for four different light filters
10. Lever for six different diaphragms
11. Ball-handle for turning slit-image
12. Interchangeable illumination mirror
13. Fixation lamp with annular fixation marker
14. Centring screw
15. Level adjustment control for chin support
16. Height adjustment control of slit-lamp
17. Transformer with switch

focal viewing. This permits the observer to cut an optical section of the anterior segment at any angle. Fig. 11.3 shows a general view of the eye illuminated by a slit-lamp beam of light of moderate width, entering the eye from the left side. Optically the homogeneous media appear quite black; structures such as the cornea, lens and suspended particles in the aqueous scatter light and appear opalescent. On the left of both Fig. 11.3A and B is seen the illuminated portion of the cornea forming a parallelepiped, the brighter areas corresponding to the surfaces, the darker to the section of the cornea. The black space on the right is the anterior chamber. Then follows the 'phantom' of the lens. A dim central interval can be distinguished, formed by the embryonic nucleus with

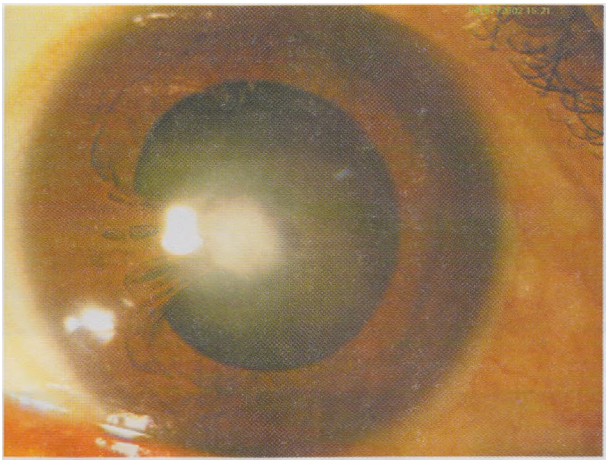


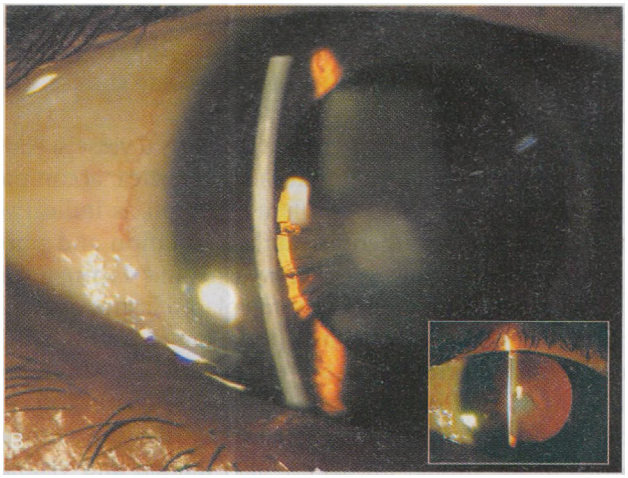
Fig. 11.2 Slit-lamp view of a corneal opacity (adherent leukoma) in diffuse illumination.

its Y-sutures. Outside this are the successive 'zones of discontinuity'— the fetal nucleus, the infantile nucleus, the adult nucleus and the cortex. Focal illumination permits an assessment of the depth of any ocular abnormality.

3. *Retroillumination:* In this form of examination the illuminating and viewing arms of the slit-lamp are placed along the same axis, coaxially, or nearly the same axis, paraxially. (i) Direct retroillumination uses an axial or paraxial light beam that shines into the pupil and reflects off the retina. The fundal glow highlights the presence of opacities in the media, such as cataracts (Fig. 11.3B), comeal scars, deep corneal vessels (Fig. 11.9B), transparent cysts and refractile bodies. It also highlights the presence of defects in the integrity of the normally opaque iris, e.g. an iris hole, (ii) Indirect retroillumination from the iris is achieved by directing the light beam to the iris at an angle of 45^0 and focussing on the cornea. The light reflected off the iris allows visualization of subtle, transparent corneal irregularities, such as ghost vessels or keratic precipitates.
4. *Specular reflection* allows the observer to visualize the corneal endothelium by viewing light reflected back from this interface. The illuminating and viewing arms are adjusted so that each forms an angle of about 30° to the central perpendicular, the slit-lamp beam is narrowed to a height of 2 mm and focussed onto the central corneal endothelium. This is placed immediately adjacent to the reflection of the slit-lamp bulb on the cornea. A golden sheen with darker lines outlining the hexagonal endothelial cells is seen (Fig. 11.4). An approximate count of the endothelial cells is possible using an Eisner grid.
5. *Scleral scatter:* This is an indirect form of illumination, created by decentring the beam after releasing the central locking screw and directing a broad beam to the temporal limbus. This light is totally internally reflected through the thickness of the cornea, like a fibre-optic light pipe, and emerges at the opposite limbus. Any opacities in the central cornea are highlighted, e.g. nebular corneal opacities, vortex dystrophies and early corneal oedema.

THE CONJUNCTIVA

To examine the entire conjunctival sac it is necessary to expose the palpebral conjunctiva and the fornices. The lower fornix is easily exposed by drawing the lower lid down while the patient looks up. The upper palpebral conjunctiva is exposed by everting the upper lid, which requires practice.



Fig, 11.3 (A) Slit-lamp examination with direct focal illumination where the slit is placed over the specific area of interest. (B) Slit-lamp examination with indirect focal illumination where the slit is placed adjacent to the specific area of interest, and retroillumination (inset) where the beam is aligned to allow the light to be reflected back from behind the area of interest.

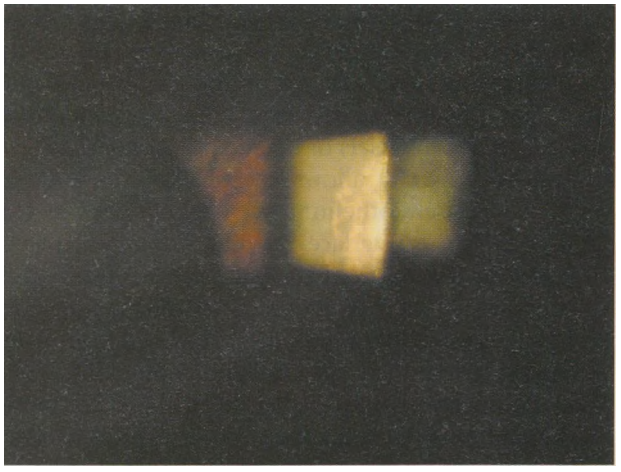


Fig. 11.4 Slit-lamp view of examination in the zone of specular reflection showing hexagonal endothelial cells and central guttate spots in a patient with Fuchs endothelial dystrophy.

Eversion of the upper lid: A probe or a thin pencil is placed along the skin of the upper lid at the level of the upper border of the tarsus with the patient looking towards his feet. The eyelashes are grasped between the index finger and thumb, and the lid is drawn away from the globe, using the probe as a fixed point. The lid is rotated in a vertical direction round the probe, and the probe withdrawn (Fig. 11.5A and B).

The upper palpebral conjunctiva can now be examined, but the upper fornix still cannot be seen, where occult foreign bodies could possibly be lodged. This can be exposed by double eversion of the upper lid in adults under local anaesthesia. A lid retractor is placed on the anterior surface of the already everted lid, above the superior border of the tarsus. The lashes are used to evert the lid onto the retractor, which is then gently pulled away from the globe to expose the upper fornix (Fig. 11.5).

The conjunctiva is examined for congestion, presence of any foreign bodies or inflammation, reactions in the form of papillae or follicles, cysts, concretions and tumours. The general status of the ocular surface and tear film are also assessed.

In general, congestion of the conjunctival vessels, leaving a relatively white zone around the cornea, accompanied by mucus or mucopurulent secretion, is indicative of conjunctivitis. If there is marked irritation and photophobia with some blepharospasm and lacrimation, the presence of a foreign body, misplaced lashes or some other irritation of the cornea (abrasion, erosions, ulcer and forms of keratitis) is more likely. Careful examination shows that in such disorders the vessels in the circumcorneal zone are bright red, and that the corneal loops of the limbal plexus are also dilated and visible. In ciliary congestion, which indicates involvement of the inner eye, particularly inflammation of the iris or the sclera, the pink perilimbal injection is supplemented by a

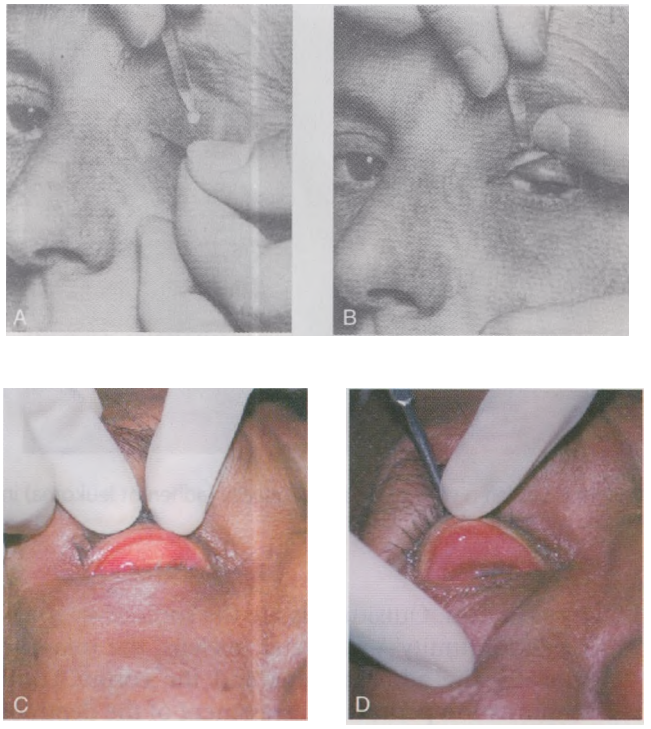


Fig. 11.5 (A and B) Eversion of the upper lid (By courtesy of Hansell). (C and D) Double eversion of the upper lid using a Desmarre retractor.

dusky, lilac tint due to congestion of the deeper, anterior ciliary vessels. As opposed to ciliary congestion, conjunctival congestion reduces after instillation of vasoconstrictors such as 10% phenylephrine, and blanches on direct pressure with a finger through the lid, the vessels fill from the fornix inwards on releasing such pressure.

These types of conjunctival congestion, however, are frequently combined so that they then cease to have special diagnostic importance.

THE SCLERA

Inspection of the sclera around the cornea may reveal the raised, congested, painless nodules of episcleritis, while deep scleritis is seen as a deep red, almost dusky congestion, with associated peripheral keratitis and uveitis.

Definite blue coloration of the circumcomeal sclera is pathological, except in very young children. It is most frequently seen as staphylomata, scleral ectasia with herniation of uveal tissue, owing to weakness of the sclera after injury or scleritis or increased intraocular pressure. Staphylomata may be anterior (situated between the cornea and ciliary body), ciliary (over the ciliary body), equatorial or posterior. Discoloration may also be due to pigmentation. Slight duskiness around the points where the anterior ciliary vessels perforate the sclera is not uncommon in people with dark complexions; otherwise pigmentation

in this area, either in the conjunctiva or sclera, should be regarded with suspicion as indicative of melanosis.

THE CORNEA

The corneal surface should be bright, lustrous and transparent. Any loss of substance, such as an abrasion, may easily be overlooked without special methods of examination.

An accurate assessment of the corneal surface may be made by a *Placido keratoscopic disc,* on which alternating black and white circles are painted. The observer looks through a hole in the centre at the corneal image reflected from a light behind the patient. A loss in the sharpness of the outline of the image denotes a loss of the normal 'polish' of the corneal surface, while irregularities in the rings reflect irregularities on the corneal surface (Fig. 11.6). Even minor degrees of keratoconus or corneal astigmatism deform the corneal rings. The image may be computerized in corneal topography mapping systems to provide an objective record of the optical and anatomical condition of the anterior corneal surface. The posterior surfaces of the cornea, the anterior chamber and the lens are additionally imaged in corneal topography systems using slit-scanning technology such as the Orbscan (Fig. 11.7).

To determine the state of the *corneal epithelium,* the technique of *corneal staining* with a vital dye is employed, by which lesions often minute and invisible to the naked eye are dramatically accentuated in vivid colours. Three dyes are usually employed. Fluorescein is the most useful to delineate areas denuded of epithelium (abrasions, multiple erosions, ulcers) which stain a brilliant yellowish green, when examined with cobalt blue light. Rose bengal stains diseased and devitalized cells red (as in superficial punctate keratitis). Alcian blue dye stains the mucus selectively and delineates excess mucus produced when there is a deficiency in tear formation.

Opacities of the cornea may be so faint that they require minute investigations, as do the details and depth of gross opacities. These can best be studied with the slit-lamp.



Fig. 11.6 Placido keratoscopic disc.

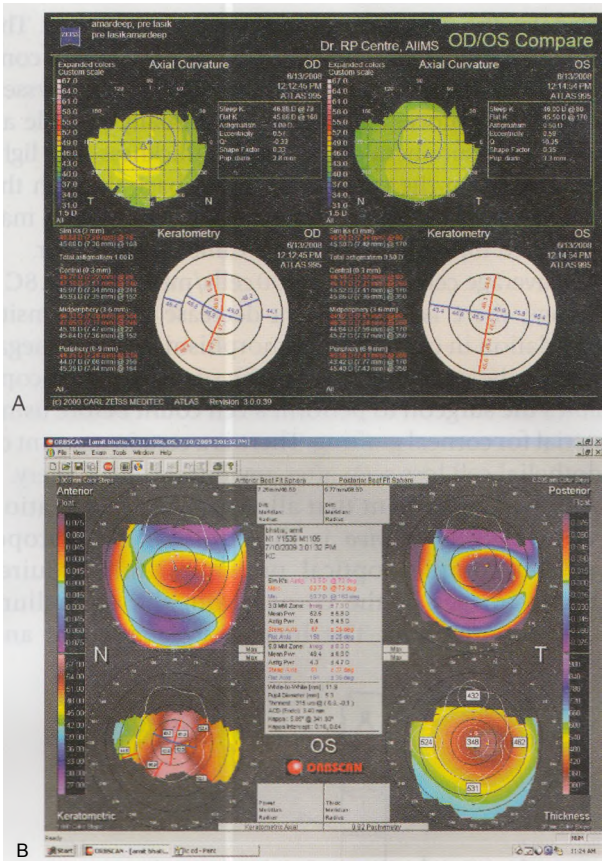


Fig. 11.7 Prints of corneal topography recorded with a system based on Placido disc showing normal cornea (A) and a slit-scanning system showing an abnormal cornea with keratoconus (B). The slit-scanning system also gives information about the corneal thickness (pachymetry).

Of particular importance is the detection of the minute epithelial or subepithelial lesions of *superficial punctate keratitis* and *keratic precipitates,* small accumulations of inflammatory cells derived from the uvea which adhere to the mid and inferior comeal endothelium. The presence of keratic precipitates indicates inflammation in the uvea. When fresh, they appear as white, round and dome-shaped; however, they become progressively flatter, smaller, crenated and pigmented. Large, waxy keratic precipitates are also described as 'mutton fat', and are seen in granulomatous uveitis, whereas fine keratic precipitates are present in Fuchs cyclitis and herpes zoster uveitis.

The *corneal endothelium* can be examined cursorily by the specular examination technique on the slit-lamp. Objective examination with the specular microscope (Fig. 11.8A) makes it possible to observe a relatively large number of endothelial cells, photograph them and study their morphology. In this instrument light passes through a slit aperture into a system of mirrors which direct the light into the cornea through an objective lens and its attached 'dipping cone'. The dipping cone lens has a flat surface extension on the water immersion objective that

applanates the cornea as in applanation tonometry. The focussing knob adjusts the excursion of the dipping cone to focus the image of the cornea for different thicknesses. The focussing process is used to additionally provide an objective measurement of the corneal thickness. The light is reflected from the endothelium and back through the objective lens eye-pieces at 200* magnification and may be observed through an eye-piece, camera or monitor.

The average cell count is 2800cells/mm^2 (Fig. 11.8C). With age, there is a significant decrease in cell density and variation in cell size (pleomorphism and polymegathism) of the endothelial cells. The specular microscope enables the surgeon to perform a cell count before using material for corneal grafting. There is a certain amount of endothelial cell loss seen after any intraocular surgery.

Another instrument that allows direct visualization of corneal cells *in vivo* is the confocal microscope. Based on complex optical principles, this acquires multiple images of the cornea from the epithelium to the endothelium. The images are magnified and show endothelial and epithelial cells and keratocytes. Analysis of these images provides detailed information regarding cell numbers, average cell area and cell density.

In many diseases *new vessels* are formed in the cornea. An exact knowledge of their position, whether superficial or deep; and their distribution, whether localized, general, peripheral, etc. is of diagnostic importance. The degree and depth of corneal vascularization are prognostic in keratoplasty. Deep vascularization in more than two quadrants is considered as a high risk factor for graft rejection following keratoplasty.

Superficial vessels in the cornea are distinguished from deep ones (Fig. 11.9) by the following features:

1. Superficial vessels can be traced over the limbus into the conjunctiva, while the deep ones seem to end abruptly at the limbus.
2. Superficial vessels are bright red and well-defined, while deep ones are ill-defined, greyish red or cause only a diffuse red blush.

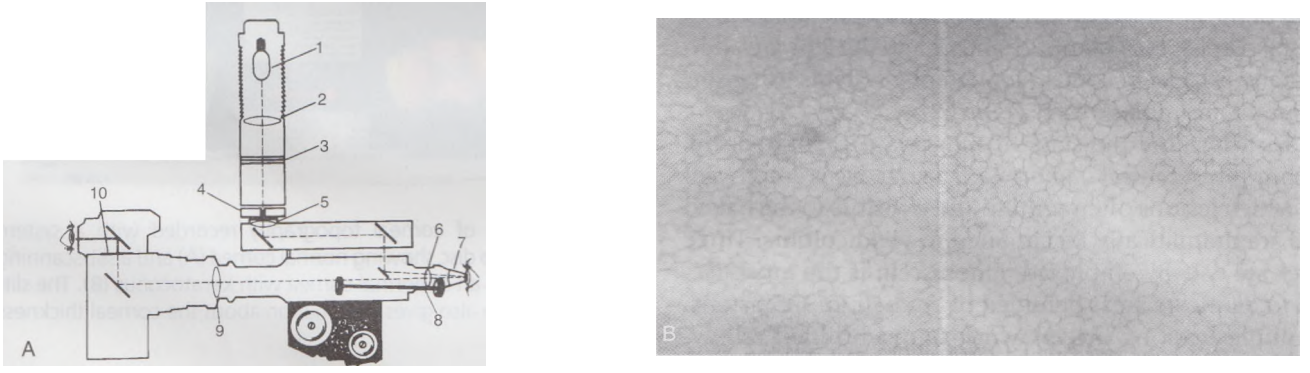


Fig. 11.8 (A) Diagram of the clinical specular microscope with: 1, viewing lamp; 2, condensing lens; 3; xenon flash tube; 4, slit aperture; 5, condensing lens; 6, objective lens; 7, dipping cone lens; 8, attachment for focussing; 9, eyepiece lens and 10, viewing screen. (By courtesy of WM Bourne and HE Kaufman. Published with permission from *Am J Ophthalmol* 1976;81:319–23. Copyright by the Ophthalmic Publishing Co., 24 April 1981.). (B) Normal corneal endothelial cells. (By courtesy of Keeler Instruments Ltd.)

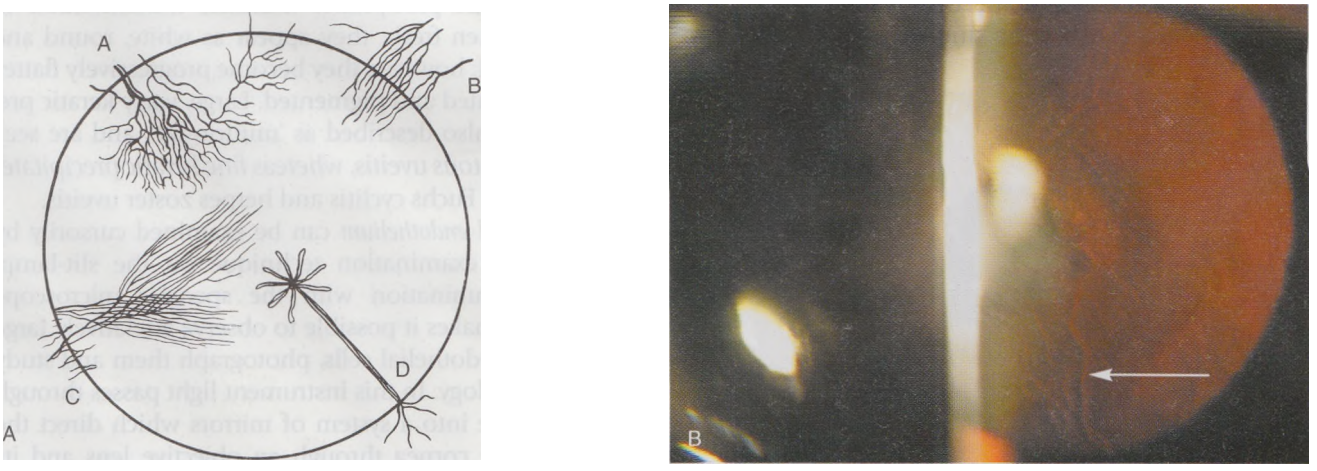


Fig. 11.9 (A) Types of corneal vascularization: A, arborescent (superficial) type; B, terminal loop type; C, brush type; and D, umbel type. (B) Slit-lamp photograph of deep corneal vascularization viewed by retroillumination.

3. Superficial vessels branch dichotomously, in an arborescent fashion, while deep vessels run more or less parallel to each other in a general radial direction, branch at acute angles and their course is determined by the lamellar structure of the substantia propria.
4. Superficial vessels may raise the epithelium over them so that the surface of the cornea is uneven, while with deep vessels the cornea, though hazy in appearance, is smooth.

Corneal sensitivity may be tested by touching it in various places with a wisp of cotton-wool twisted to a fine point and comparing the effect with that on the other, normal cornea. There is in general a brisk reflex closure of the lids. Corneal sensations are often diminished after any gross disorder, but the change is of diagnostic significance in certain cases, particularly herpes keratitis where minimal corneal changes are accompanied by a gross diminution of sensation. Quantification of the corneal sensation is possible to some degree by the use of a corneal aesthesiometer in which a single horse hair of varying length is used instead of a wisp of cotton-wool. The longest length which induces blinking is a measure of the threshold of corneal sensitivity.

The curvature of the anterior surface of the cornea can be measured by a keratometer and the corneal thickness by an optical pachymeter on a slit-lamp or an ultrasonic pachymeter.

THE ANTERIOR CHAMBER

The anterior chamber is shallow in the very young and in old age. At other periods of life it is normally about 2.5 mm deep. The iris is viewed through the cornea, which is a strongly refracting convex surface. The effect of this is to magnify the iris and pupil, and to make them appear closer than they really are. The depth of the anterior chamber is estimated as the distance between the posterior surface of the cornea and the anterior surface of the lens. The depth of the anterior chamber can be clinically evaluated by focussing a beam of light on the temporal limbus, parallel to the surface of the iris. In a normal or deep anterior chamber the beam will pass through directly, illuminating the opposite limbus (Fig. 11.10A). In eyes with a shallow anterior chamber, the anterior placement or bowing forward of the iris obstructs the light and a shadow is observed on the medial half of the iris and limbus (Fig. 11.10B). A comparison of the depth of the peripheral anterior chamber to the peripheral comeal thickness is used to determine the degree of shallowness of the anterior chamber in the van Herrick method. An optical section of the peripheral cornea and anterior chamber is made on the slit-lamp with the illumination and viewing arms at 60 ° to each other, and the viewing arm perpendicular to the cornea, using a magnification of 15. If the anterior chamber depth is equal to or less than a quarter of the thickness of the cornea, angle closure is possible, and if the anterior chamber is more than half the corneal thickness, closure is unlikely (Fig. 11.11). This is an approximate, subjective assessment. Objectively, the anterior chamber can be measured optically by the pachymetry attachment of a slit-lamp or Orbscan II ultrasonography.

The anterior chamber is usually shallow in angle-closure glaucoma. It is frequently unequal in depth in different parts—for example, it may be deeper at the periphery than in the centre in iridocyclitis; while on the other hand, when the iris is bowed forwards (iris bombe) it is funnel-shaped, the centre being deep, the periphery shallow. Tilting (subluxation) of the lens causes it to be deeper on one side than on the other. A similar deepening is seen adjacent to angle recession following trauma.

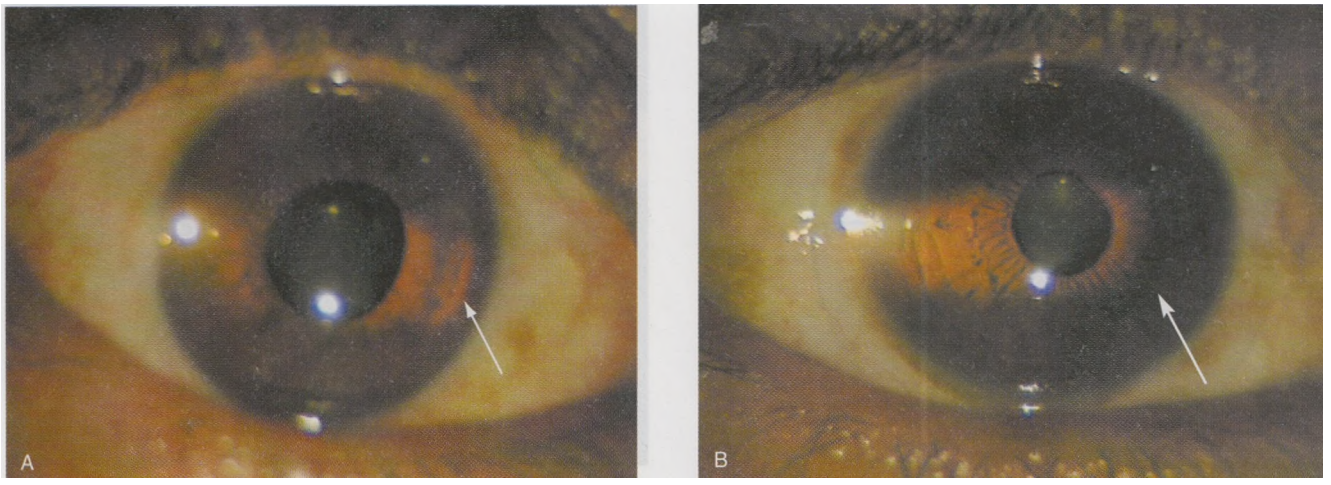


Fig. 11.10 Assessing the depth of the anterior chamber by shining a torch from the temporal side of the right eye. (A) Normal anterior chamber depth with good illumination of the nasal iris and (B) shallow anterior chamber with absence of illumination of the nasal iris, i.e. a nasal shadowing to the right.

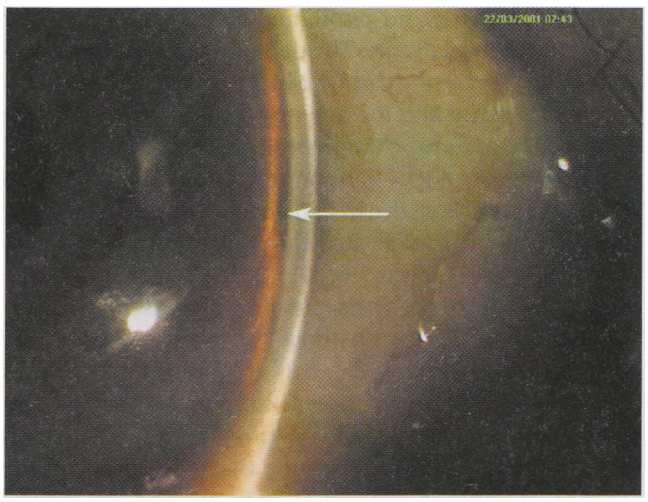


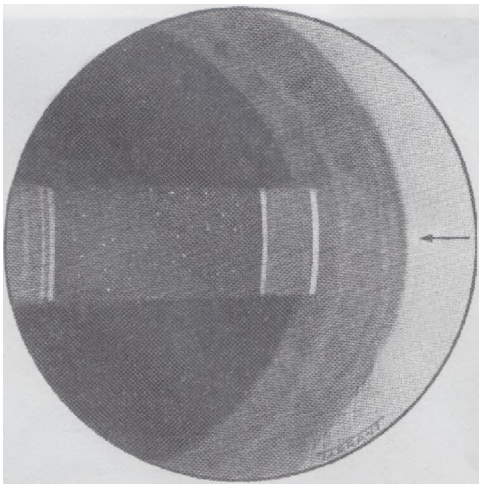
Fig. 11.11 van Herrick method of assessing the peripheral anterior chamber depth using a slit-lamp.

After considering the depth, attention must be paid to the contents. In inflammatory conditions of the uveal tract where the permeability of the vessels is increased, the aqueous may contain particles of protein or floating cells. These are of considerable diagnostic importance (Table 11.1). Protein transudation from the iris or ciliary vessels produces an opalescence of the aqueous, an *aqueous flare* (Fig. 11.12A), which may be visible on the slit-lamp, when its beam is narrowed to 2x1 mm. It is graded as being 1+ if barely present, 2+ if moderate, 3+ if it obscures visualization of the iris pattern and 4+ if fibrin is present in the anterior chamber. Floating cells in the aqueous are an indication of active uveitis and are graded by counting the number seen in 2 x 1 mm) beam on the slit-lamp. The aqueous cells are recorded as trace if 1-5 are present, 1+ if 5-10, 2+ if 10-20, 3+ if 20-50 and 4+ if more than 50. The presence of such an opalescence should lead to a careful examination of the posterior surface of the cornea to detect whether any protein material or cells are deposited on it (keratic precipitates, Fig. 11.12B). In infected wounds and ulcers of the cornea, and occasionally in iridocyclitis, there is a collection of lymphocytes in the anterior chamber forming a sediment at the bottom, the surface of which is level *(hypopyon).* A similar collection of blood may occur after contusions or spontaneously *(hj'phaema).* Micro-filariae may be observed in the anterior chamber in eyes with onchocerciasis.

THE IRIS

The colour of the iris and the clarity of its pattern should first be examined. The two irides or parts of the same iris may be of different colour, conditions which are known as heterochromia iridium or iridis, respectively. A dull iris with an ill-defined pattern or 'muddiness of the iris' suggests atrophy from iridocyclitis and sectoral patches of atrophy suggest an acute angle-closure glaucoma or herpes zoster. Freckles are darkly pigmented spots in the iris which are not raised above the surface. Brushfield spots are seen in Down syndrome and pedunculated nodules (Lisch) in neurofibromatosis. Flat nodules at the pupillary margin (Koeppe nodules) or at the peripheral base of the iris (Busacca nodules) or a 'muddy' iris with a small, irregular pupil and sluggish reaction to light are indicative of uveitis. In acute angle-closure glaucoma the pupil is usually large, immobile and oval, with the long axis vertical.

The *position* of the iris must be examined next, especially the plane in which it lies. Special attention should be



Fig, 11.12 (A) Aqueous flare, showing particles suspended in the anterior chamber as seen by a slit-lamp (light coming from the right) in a case of cyclitis. (B) Slit-lamp image showing fine keratic precipitates on the posterior surface of the cornea in a case of non-granulomatous anterior uveitis.

Table 11.1 Aqueous flare and cells measured by counting within the field visible with a slit-lamp keeping the beam at maximum intensity (modification of the technique originally described by Hogan *eta I.)**

Grade	Flare (beam 2 mm height, 1 mm width)	Cells per field (2 mm height. 1 mm width)
0	Absent	0
1+	Faint, barely detectable	5–10
2+	Moderate, iris and lens details clear	10–20
3+	Marked, iris and lens details hazy	20–50
4+	Intense flare, fibrinous aqueous	>50

'Hogan MJ, Kimura SJ, Thygeson P. Signs and symptoms of uveitis. Anterior uveitis. *Am J Ophthalmol* 1959;47:155–70

paid to any adhesions or *synechiae,* anterior to the cornea or posterior to the lens capsule. Tremulousness of the iris or *iridodonesis* is seen when the eyes are moved rapidly if this tissue is not properly supported by the lens. This occurs in absence, shrinkage, or subluxation of the lens, and is best appreciated in a dark room with oblique illumination, on asking the patient to move his eye.

THE POSTERIOR CHAMBER

The posterior chamber lies between the posterior surface of the iris and the anterior surface of the lens, is filled with aqueous and is not readily visible by direct observation due to the opaque iris.

THE LENS

The lens cannot be examined thoroughly without the assistance of a slit-lamp and an ophthalmoscope. Any opacities in the pupillary area can be seen by inspection, aided by focal illumination.

By direct slit-lamp examination, through the pupil of a young person's eye the lens substance seems almost perfectly clear; at most a faint bluish haze is seen. The haze is much more pronounced in an old person and the lens looks slighdy milky due to sclerosis of the nucleus. It is probable that the patient has a cataract, but examination by distant direct ophthalmoscopy shows a clear red reflex. The explanation is that the refractive index of the lens substance increases with age, and scattering of light from its surface is greater. The milkiness is due to rays of light which are reflected from the lens and enter the observer's eye.

Opacities in the lens itself are seen by oblique illumination as grey, white or brown-yellow areas, and by retroillumination or distant direct examination with the ophthalmoscope, they appear black. Various forms of cataract are diagnosed according to their distribution and nature but observation must always be confirmed by ophthalmoscopic examination, and the opacities localized with the help of the slit-lamp (Figs 11.3 and 18.3A). A spot in the centre of the pupil, looking as if it were on the surface of the lens, may be a pupillary exudate or an anterior polar cataract. Triangular spokes of opacity with their apices towards the centre are indicative of a cuneiform senile cataract. A white appearance over the whole pupillary area suggests a total or mature cataract; if it is yellowish-white, with white spots of calcification and the iris is tremulous, a shrunken calcareous lens should be suspected. Finally, the pupil may be blocked with uveal exudates forming an inflammatory pupillary membrane.

THE PUPILS

During routine examination of the eyes, the pupils should be examined at an early stage, before any mydriatic is employed. Such an examination should be careful, detailed and is best carried out with low background illumination using a bright focussed light with the patient looking into the distance.

While testing the pupillary reflexes the following points should be kept in mind:

- illumination in the examination room should be low;
- the patient should look into the distance and
- the light used should be focussed and bright.

The patient should face a diffuse light, so that both pupils are equally illuminated. The patient is asked to look into the distance to prevent accommodative constriction of the pupil. Note the size, shape and contour of each pupil, then test the pupillary reflexes. These reflexes are: (i) constriction of the pupil to direct or consensually presented light and (ii) accommodation—constriction on viewing a near target.

To elicit the *direct reaction to light,* cover both the eyes with the palms of the hands, preferably without touching the face. While the patient looks straight ahead remove one hand and watch the pupil, noting if its constriction to light is well maintained. Replace this hand and remove the other, observing the other pupil. The *consensual reaction to light* is determined by removing one hand so that this eye is exposed to light (it should be shaded from intense light) and watching the pupils as the hand is removed from the other eye. The process is repeated while observing the other pupil.

This method of examination is not always possible due to an absence of natural light or diffuse illumination. Moreover, when the reaction to light is feeble and the pupils are already small, it is difficult to be certain of the results in bright, diffuse daylight. In such cases the examination should be carried out in a dark room and light concentrated upon one pupil by focal illumination so that it shines upon the macula, the most sensitive area

from which to elicit the light reflex. By slight lateral movements the focus of light can be moved on or off the pupil, the pupillary movements being observed constantly. Still finer observations can be made with the slit-lamp, when the microscope is focussed on the papillary margin and the beam is abruptly switched from the side into the pupillary aperture. If there is no movement in these conditions it may be concluded that the reaction to light is absent.

The same method will elicit the *hemianopic pupillary reaction* (Wernicke) in the rare cases (lesion of one optic tract) in which it is present. The light is focussed first on the nasal side of the retina and the pupil observed, and then the light is focussed on the other side of the retina. The best source of illumination for this purpose is the focal beam of the slit-lamp reduced to a spot. If the reaction is present the pupil will react briskly when one half of the retina is illuminated, but very slightly when the other half is illuminated. This is so because it is impossible to prevent diffusion of light onto the sensitive half of the retina, so the test is rarely unequivocal.

'Swinging-flashlight' test: A bright light is shone onto one pupil and a constriction noted. After 2-3 seconds, the light is rapidly Uansferred to the opposite pupil. This swinging to-and-fro of the light is repeated several times while observing the response of the pupil to which the light is transferred. When the input through both optic nerves to the mid-brain is equal, the pupil to which the light is transferred will remain tightly constricted since the consensual response has the same magnitude as a direct response. Should there be a lesion of one optic nerve the input from that side is less than that from the normal side. In that case when the light is transferred to the diseased eye both pupils will dilate, and on swinging back to the normal side both the pupils will constrict. The dilatation or 'escape' that occurs is commonly called the *Marcus Gunn pupil* or an *afferent pupillary defect* and may be the earliest indication of an optic nerve disease such as retrobulbar neuritis.

The *reaction to convergence and accommodation* is determined by asking the patient to look to the far end of the room. While he does so an accommodation target is suddenly held up vertically at about 15 cm from the patient's nose and he is told to look at it. The movement of the pupils is studied while he converges.

When properly conducted, the above method provides reliable information as to the shape and relative size of the pupils and their reactions. A few of the common conditions are considered here.

Abnormal size of the pupil: The size of the pupil is determined by the afferent and efferent pathways for pupillary light reflexes, and the function of the sphincter and dilator pupillae muscles. Dilatation of the pupils with retained mobility is found sometimes in myopia and in conditions of impaired tone or nervous excitement. Conversely, the pupils are small in babies and in old people. Many pathological entities can lead to disturbances of the pupil (*see* Chapter 31).

Very large, non-reactive pupils will suggest that a mydriatic has been used, perhaps inadvertently, as when a patient has been using an ointment containing atropine, and has rubbed (usually) his right eye with soiled fingers. The pupils are usually immobile, and the patient complains of dimness of vision, especially for near work.

The pupils are also large and immobile in bilateral lesions affecting the retina and optic nerve causing blindness (*see* Fig. 4.7), as in optic nerve atrophy. Unilateral blindness due to these diseases never produces a dilated pupil because of the consensual light response elicited by the normal, fellow eye. Bilateral dilated pupils, in bilateral blindness, can be distinguished from a bilateral efferent pupillary defect, pupilloplegia, by eliciting the near reflex. Although the patient cannot see his thumb held close to the face, by proprioception he attempts to accommodate and causes constriction of both pupils. It is equally important to remember that the presence of a direct reaction to light does not eliminate the possibility of the patient actually being blind due to a central lesion affecting the visual pathways above the level of the lateral geniculate body (postbasal meningitis, haemorrhage, uraemia, bilateral occipital lobe infarction).

Opacities in the media such as dense cataracts or vitreous haemorrhage never lead to absent pupillary reflexes if tested with bright illumination.

Dilated and immobile pupils also result from third nerve palsies (*absolute paralysis of the pupil)-,* if the paralysis also affects the third nerve fibres to the ciliary muscle, accommodation is also paralysed (*ophthalmoplegia interna).* This results in lesions affecting the third nerve nucleus, diseases such as meningitis, encephalitis and cerebral syphilis, diphtheria, lead poisoning and orbital disease, or trauma affecting the third nerve, ciliary ganglion or the eye itself.

Unilateral dilatation may result from irritation of the cervical sympathetic nerves. This may be due to conditions such as swollen lymph nodes in the neck, apical pneumonia, apical pleurisy, cervical rib and thoracic aneurysm. It may also be due to syringomyelia, acute anterior poliomyelitis and meningitis affecting the lower cervical and upper thoracic part of the spinal cord and pressure on the sympathetic fibres leaving the cord in the lower cervical and upper thoracic ventral roots. Most of the conditions causing an irritative dilatation lead eventually to constriction from sympathetic paralysis. When all sympathetic function on one side is lost, resulting in miosis, a narrowed palpebral fissure and slight enophthalmos (due to loss of tone of Muller muscle), sometimes associated with unilateral absence of sweating, the condition is called the *Horner syndrome.*

Small immobile pupils suggest the use of drugs, either locally (miotics), or systemically (morphine). A small,

sluggish pupil with 'muddiness' of the iris is associated with an active iritis. A small, immobile pupil suggests old iritis with posterior synechiae, and should be investigated with a mydriatic such as cyclopentolate to ascertain if the pupil dilates regularly. Bilateral small pupils may be due to irritation of the third nerves, arousing suspicion of a central nervous disease in their vicinity. The condition can also be due to palsy of the sympathetic system, as in pontine haemorrhage.

Abnormal reactions of the pupil: These are equally important (*see* Fig. 31.9). As mentioned earlier, loss of light reflexes results from a lesion in the retina or optic nerve causing blindness while a hemianopic reaction results from lesions in the tract (Fig. 4.7). A lesion in the third nerve abolishes both light and convergence reflexes.

More complex lesions may result from damage to the relay paths in the tectum between the afferent and efferent tracts. The most important of these is the *Argyll Robertson pupil,* usually caused by a lesion, almost invariably syphilitic, in this region. In this condition, the pupils are small (spinal miosis) and do not react to light, but the contraction on convergence is retained. This is referred to as *light near dissociation.*

The *tonic pupil* (of Adie) somewhat resembles the Argyll Robertson pupil; it is of unknown aetiology, not associated with syphilis, occurs usually in young women, is often unilateral and associated with absent knee-jerks. This pupil is slightly dilated and always larger than its fellow; the unilateral Argyll Robertson pupil is always smaller. Although in the tonic pupil the reaction to light seems absent at first, careful examination shows it to be present as a vermiform, slight constriction. The reaction of the pupil on convergence is sluggish with a long latent period and is unduly sustained. The tonic pupil dilates well with atropine; the Argyll Robertson pupil does not; finally, the tonic pupil constricts with 0.1% pilocarpine.

The symptoms of Adie pupil fall into two groups; those due to the pupil size, which do not last longer than a few weeks, and those due to ciliary dysfunction. The affected eye usually has a slight accommodative paresis and asthenopia is often induced by near effort. Many patients can never get the two eyes to work together when reading and are best advised to use dilute pilocarpine and fix with the other eye.

GONIOSCOPY

The recesses of the angle of the anterior chamber are difficult to visualize since this region is covered by the projecting shelf of the sclera at the limbus and all emergent light undergoes total internal reflection. In many conditions such as glaucoma, foreign bodies or tumours, a close inspection of this region is important. It can, however, be observed by the slit-lamp provided the beam is diverted at an angle. For this purpose several types of *gonioscopes* have been developed, the simplest of which is the *indirect gonioscope* typified by that of Goldmann (Table 11.2). A contact lens is inserted between the lids to lie upon the anaesthetized cornea, and fitted with a mirror placed at an angle of 62^0 or 64 °, in which the image of the recesses of the angle is reflected (Fig. 11.13A and B). Gonioscopes with one, two or four mirrors are available, of which the 4-mirror gonioscope allows the examination of 360 ° of the angle without rotating the lens. A base of about 7 mm enables viewing of the angle using a tear film bridge, and also allows depression of the central cornea for indentation gonioscopy (Fig. 11.13C). In a narrow angle, aqueous is displaced from the centre peripherally, to push away the iris, and allow better visualization of the angle structures. A *direct gonioscope* consists of a dome-shaped glass contact lens which refracts light from the angle into the observer's eye, thus providing a clear view of the whole angle and is especially used to examine supine children under general anaesthesia.

Table 11.2 Commonly used contact lenses for gonioscopy

Lens	Description/use
I. Indirect goniolenses	
• Goldmann single-mirror gonioscope	Mirror inclined at 62°
• Zeiss four-mirror gonioscope	All four mirrors inclined at 64°; requires holder (Unger); fluid bridge not required
• Posner four-mirror gonioscope	Modified Zeiss four-mirror gonioprism with attached handle
• Sussman four-mirror gonioscope	Hand-held Zeiss-type gonioprism
• Ritch trabeculoplasty lens	Four mirrors; two inclined at 59° and two at 62° with a convex lens over two of the mirrors
II. Direct goniolenses	
• Koeppe	Dome-shaped lens
• Barkan	Quarter sphere surgical and diagnostic lens
• Swan-Jacob	Surgical goniolens for children

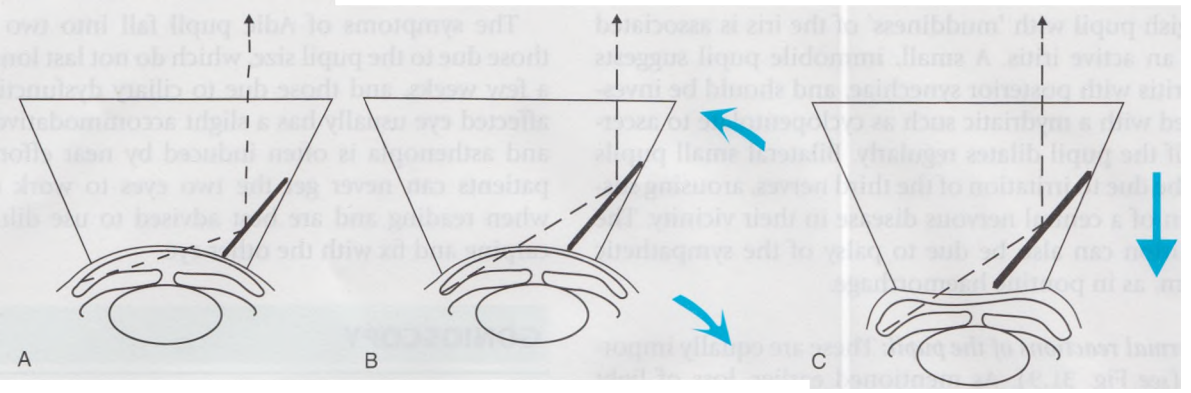


Fig. 11.13 The Goldmann contact lens used for gonioscopy with the slit-lamp microscope. (A) The figure shows the path of light rays through the lens. They are reflected by the mirror into the angle, and again, as they emerge, into the objectives of the slit-lamp microscope. (B) In a shallow anterior chamber the gonioscope may need to be moved towards the angle being viewed or the patient is made to look towards the mirror to allow visualization of the angle structures. (C) Indentation gonioscopy also allows visualization of the angle in an eye with a narrow angle, by displacing aqueous from the centre peripherally so that the iris is pushed backwards at the angle.

Fig. 11.14(A) and (B) show the main features of the gonioscopic picture. In an open angle the landmarks from behind forwards are: (i) the anterior surface of the iris; (ii) the grey coloured, anteromedial surface of the ciliary body; (iii) the white line of the scleral spur; (iv) the faintly pigmented trabecular meshwork covering the canal ofSchlemm; (v) Schwalbe line (a glistening white line corresponding to the peripheral extent of Descemet's membrane); and beyond this (vi) the posterior surface of the cornea which is seen as a convex dome.

Narrowing of the angle can be identified by a steep configuration of the iris and the angulation of a slit light reflex as it passes into the angle recess. The Schwalbe line can be identified by following the anterior and posterior surfaces of the corneal slit to the point where they meet.

TONOMETRY

Tonometry is the assessment of the intraocular pressure of the eye and is one of the pillar stones of diagnosis of glaucoma. It is also essential in the monitoring of anti-glaucoma medications. It may be done digitally in the same manner as testing for fluctuation in other parts of the body, i.e. by two fingers placed a short distance from one another above the superior tarsal plate.

Instruments known as *tonometers* have been devised for measuring the intraocular pressure of the intact eye and are of two types. The *indentation tonometer* of Schiotz measures the depth of the indentation of the anaesthetized cornea, produced by a weighted stylet and is measured by a lever which travels over a scale (Fig. 11.15). The depth

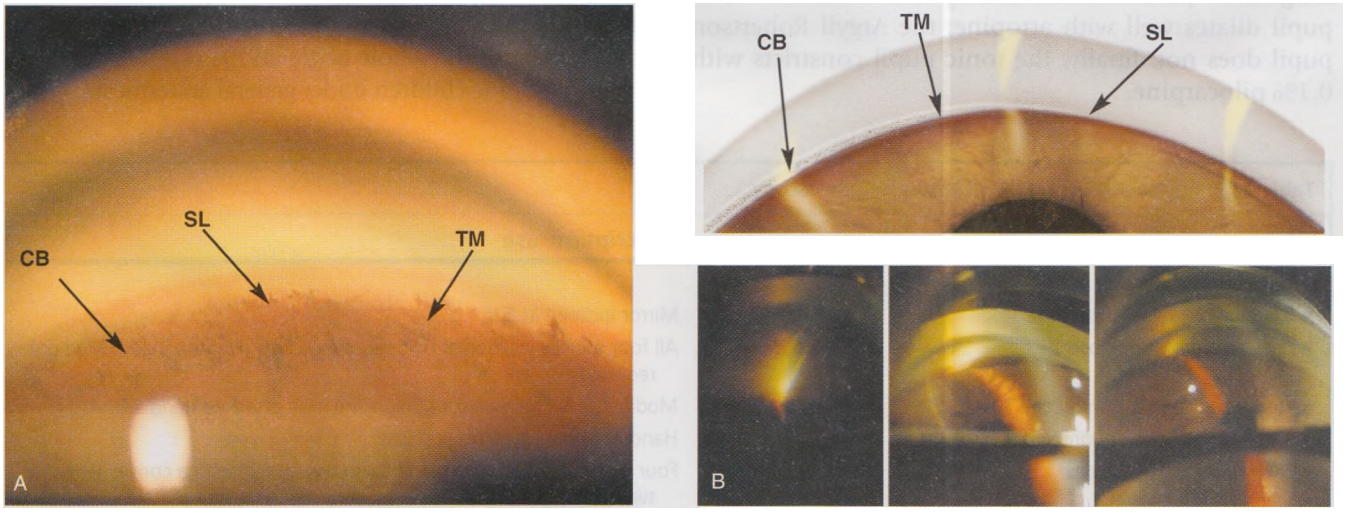


Fig. 11.14 (A) The angle of the anterior chamber seen with a gonioscope: SL, Schwalbe line; TM, trabecular meshwork; and CB, ciliary body band. The scleral spur is the white line seen between CB and TM. A slit (Fig. 11.14B) allows identification of the Schwalbe line (SL) as the point where the corneal epithelial and endothelial surfaces meet. The slit beam permits evaluation of the angle between the corneal endothelium and peripheral iris. (B) Diagrammatic representation of the anterior chamber angle (top) and gonioscopic view (below). The figure on the extreme left shows a fully open anterior chamber angle and on the extreme right a fully closed angle. The figure in the centre shows a narrow angle recess.

and the volume of the indentation are dependent on the intraocular pressure and the distensibility of the ocular walls. There are four weights (5.5, 7.5, 10 and 15g) that can be applied and the greatest accuracy is attained with the weight by which the lever is deflected by 2-4 mm. The instrument is calibrated so that the equivalent readings in millimetres of mercury can be read off a chart. The Schiotz tonometer is often inaccurate, largely because of wide individual variations in the rigidity of the corneoscleral coats. However, the tonometer is useful for obtaining approximate readings, particularly for comparative measurements, such as between the two eyes or for successive measurements on the same eye. To allow for this inaccuracy the type of tonometer should always be cited and the reading expressed in this form -20.6 mmHg (Schiotz 4/5.5g). The readings are not accurate in steep, thick or irregular corneas, high myopia or hyperopia, with the use of miotics, vasodilators or vasoconstrictors, or after any intraocular surgery, especially vitreoretinal surgery.

An *applanation tonometer* is more accurate than an indentation tonometer and is based on the Imbert-Fick principle. Instead of measuring the amount of indentation, the applanation tonometer assesses the amount of force needed to flatten or applanate a known area of the cornea. In this process, the factor of ocular rigidity is offset by an induced capillary force acting in the opposite direction. Therefore, no correction for the individual ocular rigidity is necessary. When the cornea is flanened by the application of a plane surface on it, the intraocular pressure is directly proportional to the pressure applied and inversely to the area flattened. Only 0.05 ml of aqueous is displaced by the applanation and the basal intraocular pressure is negligibly altered. The most popular applanation tonometer was designed by Goldmann for use with the Haag-Streit slit-lamp (Fig. 11.16). In it, a flat circular plexiglass plate 7 mm in area is applied to the anaesthetized cornea so as to flatten an area 3.06 mm in diameter at the posterior corneal surface. The constancy of the area of applanation is ensured by an ingenious duplicating optical device, formed by prisms placed apex to apex. This particular area of flattening is chosen, as with it a force of 0.1 g exerted by a spring-and-lever system corresponds to an intraocular pressure of 1 mmHg. The patient is seated at a slit-lamp after anaesthetizing the cornea and applying 1% fluorescein dye in the palpebral sac. On placing the plexiglass plate on the cornea, the circular meniscus of fluorescein is seen as two half-circles or mires, which have to be aligned carefully as shown in Fig. 11.17. The most accurate reading is obtained when the two inner edges of the mires coincide. The mires should not be too thick or too thin, because of excess or scarcity of fluorescein, as the intraocular pressure will then be over- or underestimated, respectively. In the presence of excessive corneal astigmatism two readings should be taken at right angles; the average is taken as the reading. The applanation tonometer cannot be used in scarred corneas. A hand-held version is available as the Perkin tonometer, which can be used in any position. Another technique of measuring intraocular pressure using the applanation principle is that of Mackay Marg. Movement of a plunger, which extends 10 micron beyond a plane footplate, is monitored by a transducer and recorded on paper. The average of several tracings is taken as the reading of the intraocular pressure. A digital, hand-held version of the same is available as the Tonopen tonometer, which provides a mean and standard deviation of 4-10 acceptable readings, automatically. Non-contact tonometers also utilize the principle of applanation, a calibrated, warm puff of air is projected on the cornea and a photoelectric cell measures reflected light obtained when a fixed area of cornea is applanated. The time taken for applanation is proportional to the intraocular pressure. The average intraocular pressure is approximately 15-17 mmHg (applanation).

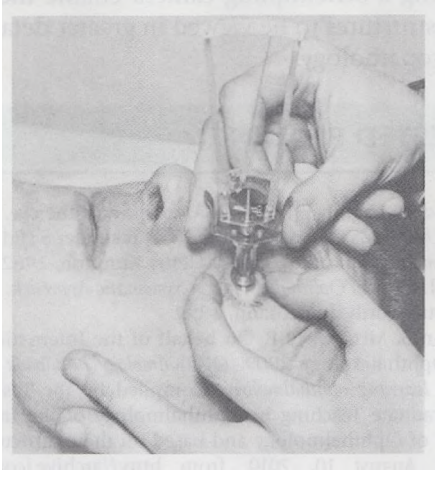


Fig. 11.15 Schiotz tonometer. (By courtesy of Hansell)

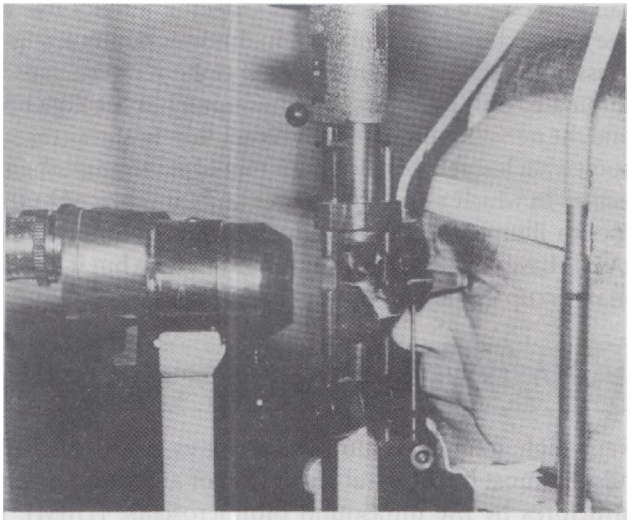


Fig. 11.16 The applanation tonometer. (By courtesy of Hansell)

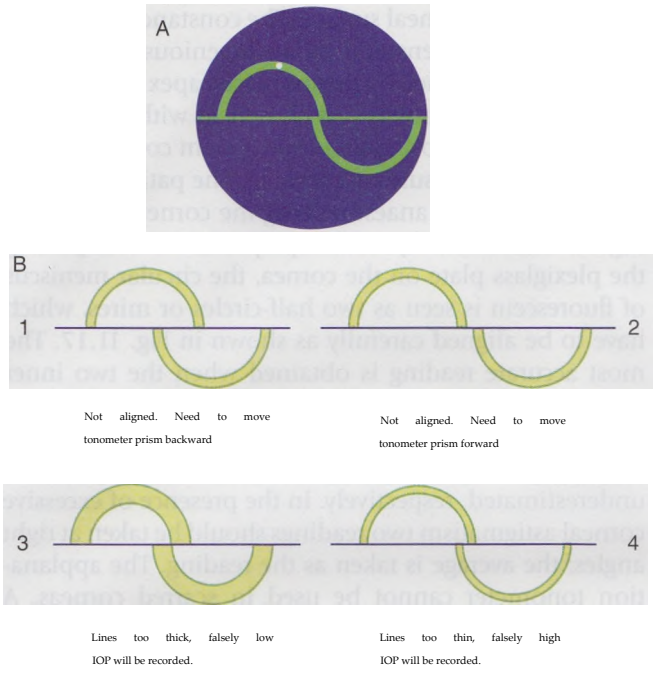


Fig. 11.17 (A) Fluorescein stained mires of the applanation tonometer. End-point of perfect alignment of mires when recording intraocular pressure with the Goldmann applanation tonometer. (B) 1–4: Incorrect alignment.

TRANSILLUMINATION

In this method of examination, an intense beam of light is thrown through the conjunctiva and sclera whereupon the pupil normally appears red. If, however, a solid mass lies in the path of the light, the beam is obstructed and the pupil remains black. For this purpose, special transilluminators maybe employed or, more simply, a cap with an open hole at the end may be fitted over the bulb of an electric ophthalmoscope. A solid mass can thus be delineated and a tumour differentiated from a cyst. An opaque foreign body can be seen in a cataractous lens. Only the anterior half of the eye can be transilluminated in this way, but if there is a mass in the posterior segment of the globe, it can be transilluminated only after the capsule of Tenon has been opened and the transilluminator inserted within it. In such a case, a somewhat less reliable method is that of *indirect transillumination,* in which a powerful source of light is placed in the mouth illuminating the eyes from behind. Normally the pupils have a strikingly luminous appearance but if a solid mass occupies the fundus, they appear black.

ULTRASOUND BIOMICROSCOPY

Very high frequency ultrasound waves of 50-80 MIIz allow almost histological resolution of anterior segment structures by the ultrasound biomicroscope (UBM). It is used specifically for defining abnormalities of the anterior chamber angle, limbus and anterior part of the retina (Fig. 11.18).

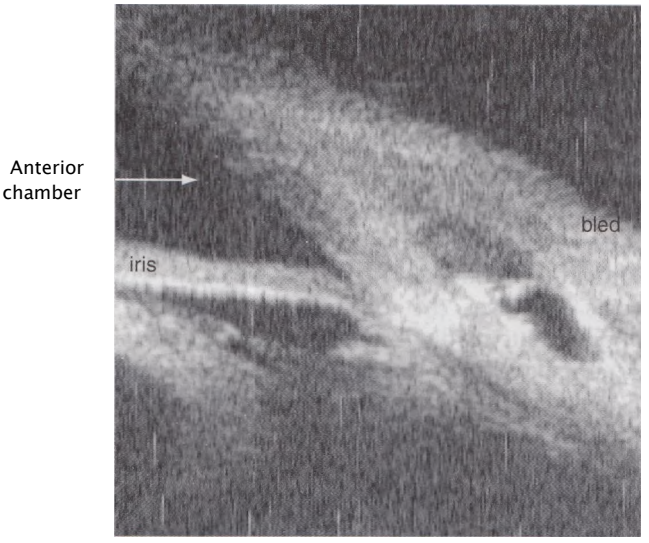


Fig. 11.18 Ultrasound biomicroscopy image of a trabeculectomy bleb.

SUMMARY

The external examination of the eye includes observation of the position of the eyes, their binocular alignment; the lids and adnexa inclusive of the lacrimal gland, lacrimal sac and drainage system; and the ocular surface including the tear film, conjunctiva, sclera and cornea. These structures are amenable to direct observation with a torch light and more detailed examination using magnifying aids such as a slit lamp biomicroscope. In case of obstruction of view by pathology, indirect observation is possible using ultrasound biomicroscopy. Modern technological advances like anterior segment optical coherence tomography, confocal microscopy and photography using a Scheimpflug camera enable the anterior segment structures to be viewed in greater detail akin to gross histopathology.

SUGGESTED READING

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Kanski JJ. *Clinical Ophthalmology: A Systematic Approach,* 5th ed. Oxford: Butterworth Heinemann, 1999.
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12

Examination of the Posterior Segment and Orbit

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The anterior segment of the eye is easily observed under some magnification with diffuse or focal illumination. Examination of the eye behind the crystalline lens requires a special arrangement of lenses or mirrors, so that light reflected back from the inside of the eye can be brought into the observer's eye to form an image. This is called ophthalmoscopy.

In ordinary circumstances the pupil looks black, and no reflex is obtained from the fundus. If, as in Fig. 12.1, there is a source of light L in front of the eye, and the eye is focused upon it or accommodated for it, the light and a spot on the retina are conjugate foci so that the image of the spot of light is a spot on the retina. Reversing the direction of the rays, all rays from the illuminated spot of the retina are brought to a focus at the source of light. It follows that no rays will enter an observing eye unless it is situated at the source of light. The problem of ophthalmoscopic examination is to simultaneously make the observing eye the source of illumination of the observed fundus.

If the eye is not focused for the source of light, the conditions are different, and some slight luminosity of the pupil may be seen. This is one cause of luminosity in the pupils of very hypermetropic eyes and in pathological conditions when the retina is displaced forwards as in detachment or by a tumour.

In hypermetropia the conjugate focus of the source of light, L, is a point, I, behind the retina (Fig. 12.2). Hence the emergent rays from the illuminated area of

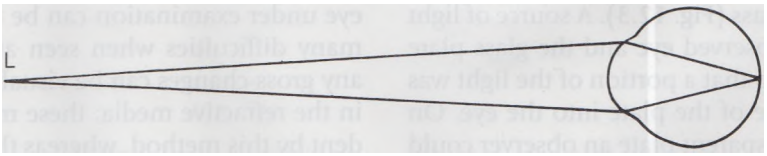


Fig. 12.1 The eye is accommodated for the light source L.

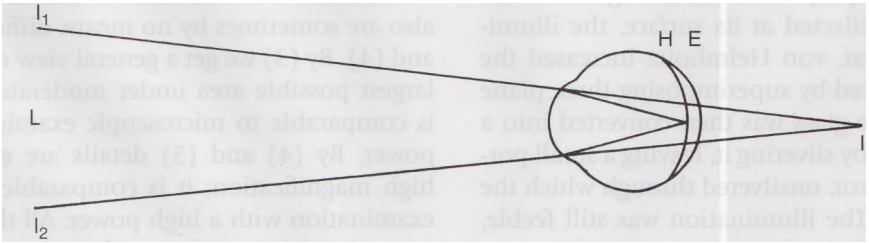
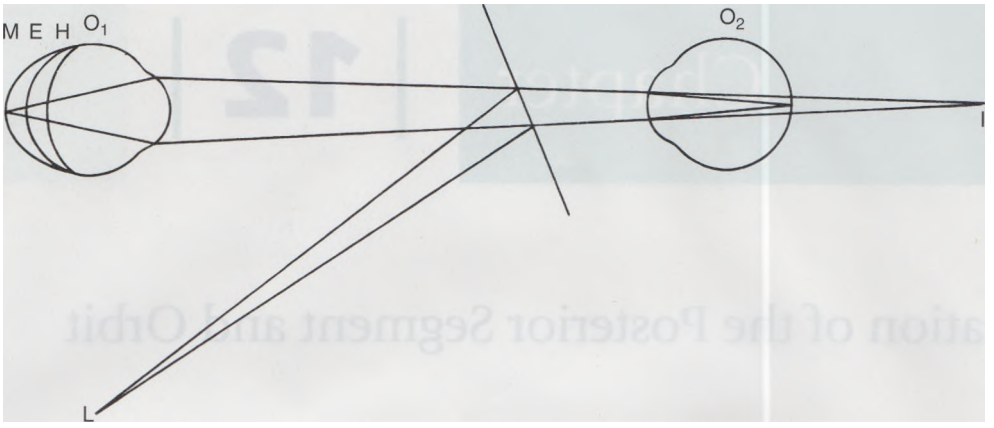


Fig. 12.2 The eye is not accommodated for the light source L. H, hypermetropia; E, emmetropia.



Fig, 12.3 Diagram of the von Helmholtz ophthalmoscope: $0_{1(}$ observed eye; 0_2, observer's eye; L, source of light; I, image of L formed by the plane mirror—immediate source of light; M E H, relative positions of the retina in myopia, emmetropia and hypermetropia, respectively, showing the relative size of the areas of retina illuminated in each case.

the fundus are divergent, as if coming from I. Therefore, an observing eye situated anywhere within the area I_x to I_2 of the cone of emergent rays will catch some of them, and the pupil of the observed eye will appear feebly illuminated. In these circumstances it is not necessary for the observing eye to occupy the exact position of the source of light, but only a spot in its immediate neighbourhood. On the same principle, the extremely hypermetropic retina pushed forwards by a tumour can be seen well by focal illumination.

The luminosity of albinos' eyes is due to light entering the eye, not only through the pupil but also through the iris and sclera, whereas only a small amount of light passes through the sclera in the normal eye. That this is the true explanation is shown by the fact that the pupil looks black if it is observed through a small hole in an opaque screen.

OPHTHALMOSCOPY

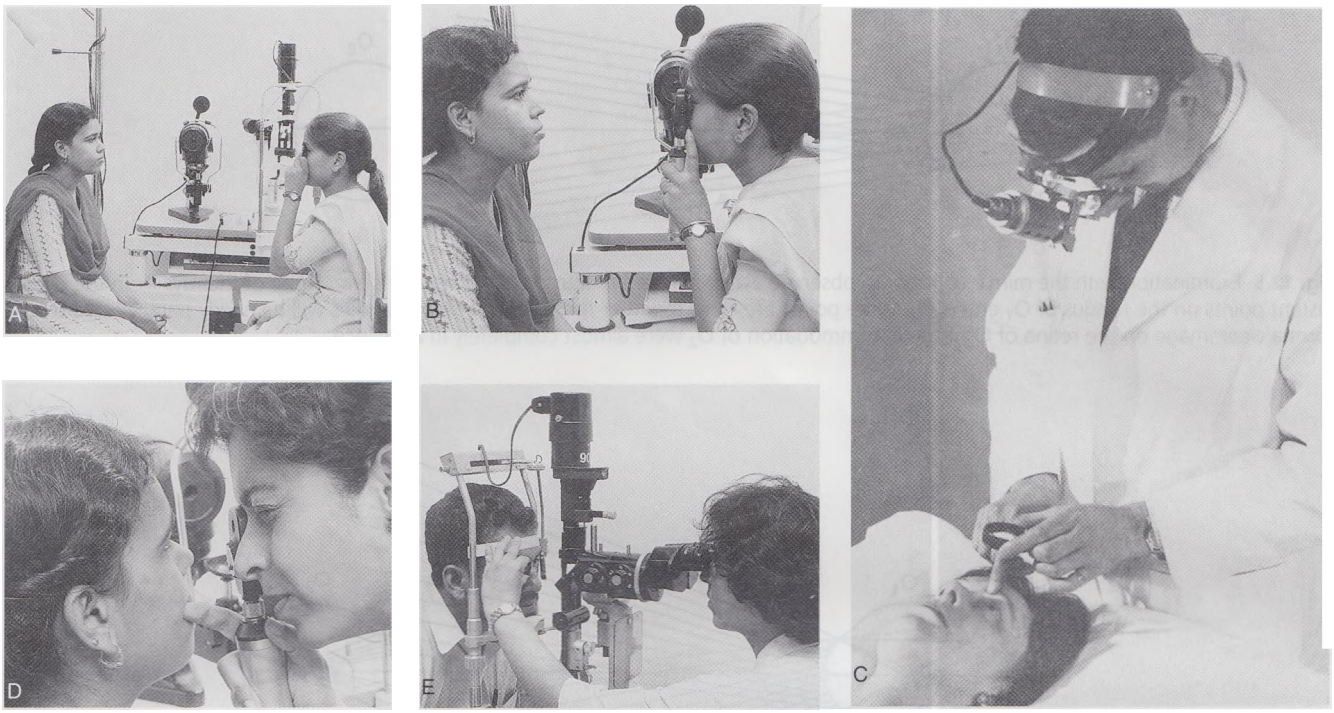
The original ophthalmoscope of von Helmholtz was merely a plane plate of glass (Fig. 12.3). A source of light was placed beside the observed eye and the glass plate obliquely in front of it, so that a portion of the light was reflected from the surface of the plate into the eye. On looking through the transparent plate an observer could now receive some of the rays from the fundus into his own eye, and thus obtain an image of the illuminated fundus. Since a small proportion of the light received upon the plate was reflected at its surface, the illumination was feeble. Next, von Helmholtz increased the amount of light reflected by superimposing three plane plates. The back of the glass was then converted into a more powerful mirror by silvering it, leaving a small portion, a hole in the mirror, unsilvered through which the observer might look. The illumination was still feeble, since the rays reflected by a plane mirror were divergent.

Reute (1852), therefore, introduced the perforated concave mirror, which is still generally used. The final modification was the addition of a battery of small lenses of various strengths, which could be brought into position behind the aperture. The many forms of ophthalmoscopes are merely various mechanical contrivances for doing this most conveniently.

The *routine of ophthalmoscopic examination* should be as follows (Fig. 12.4):

1. Preliminary examination with the plane mirror alone at a distance of about 1 m from the patient.
2. Examination with the mirror alone at a distance of about 22 cm from the patient or distant direct ophthalmoscopy.
3. Ophthalmoscopic examination by the direct method.
4. Slit-lamp biomicroscopy.
5. Ophthalmoscopic examination by the indirect method.

The following facts show the wisdom of this sequential procedure. By (1) the nature of the refraction of the eye under examination can be known; this will prevent many difficulties when seen at closer quarters. By (2) any gross changes can be visualized, especially opacities in the refractive media; these may at once be made evident by this method, whereas they may be very puzzling if first observed by (3) or (4). In addition, the details of any very hypermetropic part of the fundus, such as a detachment of the retina or a tumour can be seen; these also are sometimes by no means difficult to miss by (3) and (4). By (3) we get a general view of the fundus—the largest possible area under moderate magnification; it is comparable to microscopic examination with a low power. By (4) and (5) details are examined under a high magnification; it is comparable to a microscopic examination with a high power. All these examinations are easier if the pupils are dilated with a mydriatic.



Fig, 12.4 The different techniques of examination for assessing the clarity of the ocular media and posterior segment of the eye. (A) Preliminary examination at 1 m; (B) distant direct ophthalmoscopy; (C) direct ophthalmoscopy; (D) slit-lamp biomicroscopy with a +90 D lens; (E) indirect ophthalmoscopy (By courtesy of Hansell). All the tests are performed better with the room lights dimmed.

Ophthalmoscopic examination is carried out in a dark room. For *examination with the plane mirror alone* the observer sits facing the patient, about a metre away. The patient is asked to relax his accommodation by looking at a distant object, or a cycloplegic can be used. Light from the plane mirror is reflected into the eye, while the examiner looks through the sight-hole. When the light falls on the eye, a red reflex is noticed from the pupil. There ought to be no black spots in the pupillary area, but either a uniform red reflex or obscure details of the fundus. By tilting the mirror to-and-fro in various directions the examiner can obtain an approximate idea of the refraction of the eye. The observer now approaches the patient until his eye, still with the plane mirror, is about 20 cm from the eye under observation. He can now see the cornea and iris clearly, and can confirm any points, which were noted previously by external examination. An ophthalmoscope or the retinoscope can provide the same illumination.

Preliminary examination at 1 m: If the observed eye is emmetropic or has a low refractive error, the rays issuing from any point on the retina are parallel, and since the bundles of rays from two points on the retina diverge after leaving the eye, the observer cannot receive portions of both bundles simultaneously through his pupil (Fig. 12.5). He cannot, therefore, see two spots on the retina but can only focus one at a time, and thus sees only a general illumination. In the hypermetropic eye, however, the emerging rays are divergent, and the two bundles of rays from two points on the retina will form two divergent bundles (Fig. 12.6). These will appear to come from two points behind the eye where an imaginary erect image is formed. Since each bundle diverges, some of the peripheral rays of each will be received by the observer's pupil, so that a clear image of each point will be obtained and thus he will see the virtual image behind the patient's eye. In myopia, on the other hand, the rays coming from the two points will be convergent and will form a real, inverted image in front of the eye (Fig. 12.7). Continuing from this image the rays will diverge in two bundles, the peripheral parts of which will enter the observer's pupil. Thus a small inverted image of the fundus will be seen. If the observer now moves his head from side-to-side, the erect image in hypermetropia will appear to move in the same direction, and the inverted image in myopia in the opposite.

It therefore follows that in the preliminary examination with the plane mirror, if the fundus reflex is seen as a uniform red glow (the *red reflex),* the eye is emmetropic or approximately so; but if any details of the retinal structure are seen, a considerable degree of ametropia exists. If the picture thus presented appears to move in the same direction as the observer's head, the refraction is hypermetropic; if it moves in the opposite direction, it is myopic. This may be verified and a more accurate assessment of the refraction gained by retinoscopy.

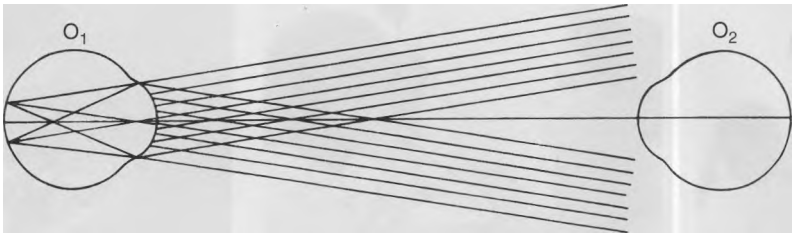


Fig. 12.5 Examination with the mirror at 1 m: 0,, observed eye, which is emmetropic; 0_2, observer's eye. None of the rays from the widely distant points on the fundus of 0, enters 0_2. If the points are close together the rays of the two bundles will be nearly parallel, and would form a clear image on the retina of 0_2 if the accommodation of 0_2 were almost completely in abeyance.

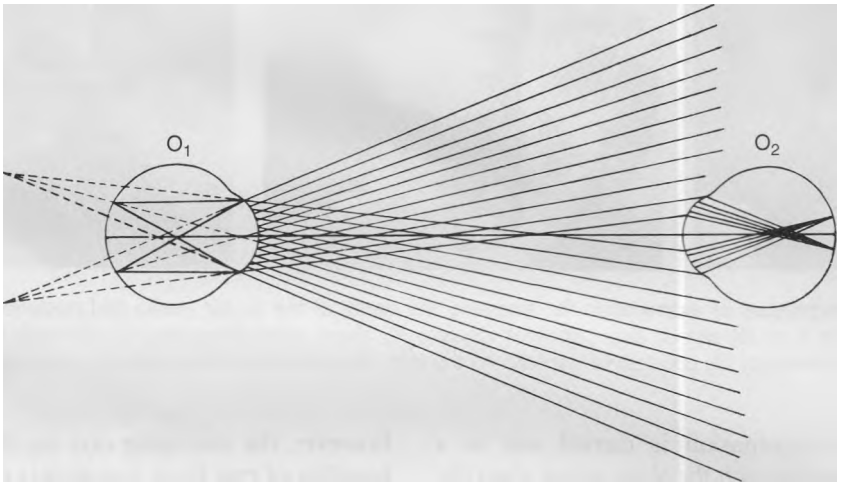


Fig. 12.6 Examination with the mirror at 1 m: $0_{1(}$ observed eye, which is hypermetropic; 0_2, observer's eye, emmetropic, but accommodated for the divergent rays from O,.

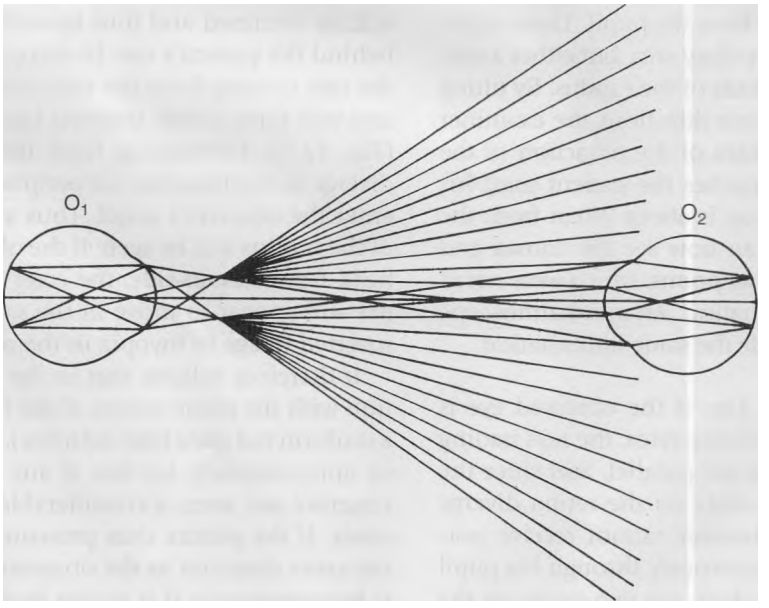


Fig. 12.7 Examination with the mirror at 1 m: 0,, observed eye, which is highly myopic; 0_2, observer's eye, emmetropic, but accommodated for the divergent rays from the far point of O,.

Examination at a convenient distance for near vision (22 cm): This may be performed using a plane mirror or an ophthalmoscope with the plane zero-powered lens in position. To examine the superficial parts of the eye more accurately the observer should be at a distance suitable for distinct unaided vision, i.e. about 22 cm. If he is hypermetropic or presbyopic he will naturally have to use a convex lens. The purposes of a preliminary examination in this manner are: (i) the recognition of opacities in the refractive media; (ii) the recognition of a detached retina or other structure not far behind the lens and (iii) the confirmation of results found by the external examination.

The diagnosis of opacities in the refractive media: If there is any opaque body in the course of the rays reflected from the fundus it will stop these rays and will therefore appear black. The whole field may be black, as when the lens is entirely opaque, or when there is blood in the vitreous. If small opacities are seen, their motility is determined by telling the patient to move his eye in different directions. A floating opacity will then continue to move after the eye is brought to rest, in which case it must be either in the aqueous or vitreous; in this case, the vitreous must be fluid. The exact position may be determined by observing its *parallactic displacement.*

In Fig. 12.8, if 4 is the centre of rotation of the eye, and if there are opacities at 1, 2, 3, 4, 5, then when the eye is rotated slightly, all the opacities except 4 will move; the movement being greater when the opacity is farther from the centre of rotation. Since all the movements will be referred to the edge of the pupil for comparison, to an observer situated at A, all the opacities will appear as a single spot in the centre of the pupillary reflex. If the observer shifts to position B, or if the eye is rotated in the opposite direction, opacity 2 will remain in the centre of the pupil, while 1 will appear to move towards one edge of the pupil, and 3, 4 and 5 towards the opposite edge, 5 being lost behind the iris.

Hence, it can be deduced that if the eye is moved slightly in a given direction, opacities in the pupillary plane will appear stationary. Those in front of that plane will move in the same direction, and those behind will appear to move in the opposite direction. The amplitude of apparent movement is a rough indication of their distance from the pupillary plane.

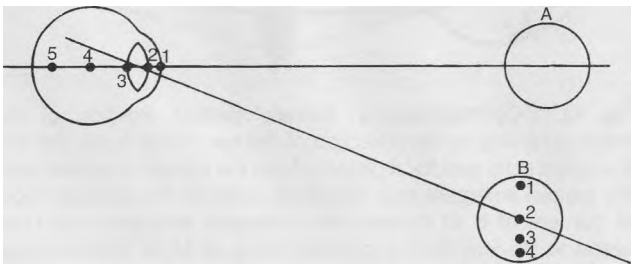


Fig. 12.8 Parallactic displacement.

The *corneal reflex,* the image of the mirror formed by the cornea, can also be used as a guide. It is a virtual image situated about 4 mm behind the anterior comeal surface, that is, a short distance behind the anterior surface of the lens (behind 2 in Fig. 12.8). The centre of curvature of the cornea is situated 8 mm behind its anterior surface (less than 1 mm behind 3 in Fig. 12.8). By this method of examination the corneal reflex will always cover the centre of curvature of the cornea, no matter what the position of the eye. Flence an opacity situated here will always be covered by the comeal reflex. Opacities in front of the corneal reflex move in the same direction with regard to the reflex as the eye moves, and opacities behind it move in the opposite direction to the movement of the eye.

This method of examination affords the surest means of discovering the edge of a *dislocated lens,* or the notch in the edge of the lens in congenital *coloboma of the lens.* When the edge of the lens crosses the pupillary area it is seen as an intensely black crescent, since the whole of the light reflected from the fundus which falls upon the extreme edge of the lens is totally reflected within the lens; none of it leaves the eye, so that none of it can enter the observer's eye.

The recognition of a detached retina or a tumour arising from the fundus: The optical conditions rendering such lesions visible have already been discussed, the retina being in the position of the fundus of a very hypermetropic eye. When light is thrown in by the mirror, a difference of colour in the reflex from different directions is noticed; red in some, grey or black in others. More minute investigation will reveal a whitish or greyish uneven surface upon which the retinal vessels are seen as black wavy lines, an important observation since the appearance of a detached retina by ophthalmoscopy may be puzzling to the beginner.

Confirmation of the results found by the external examination: By this method the results previously arrived at by external examination are not only confirmed, but also supplemented by important subsidiary information. Thus the limits of the opacities in the lens can be mapped much more accurately, since they now appear black on a red background. A black spot in the iris may allow a red reflex through it and thus appear as a hole. Similarly, a black patch at the ciliary margin of the iris may be a melanotic tumour of the ciliary body growing forwards and implicating the iris; or it may be a separation of the iris from its ciliary attachment (irido-dialysis). In the latter case it will be possible to obtain a reflex through it by the mirror, whereas in the former it will be opaque.

Superficial opacities, such as those in the cornea and near the anterior surface of the lens, can also be seen in

their natural colours at high magnification by approaching still nearer to the eye and using stronger convex lenses behind the mirror. Thus, if the eye is approached very closely and a +20 D lens placed behind the mirror, the opacities in the cornea are seen highly magnified, while those in the lens may be brought more clearly into focus with a slightly weaker lens.

Examination by indirect ophthalmoscopy: The binocular indirect ophthalmoscope is applicable to all refractive errors and, as its beam penetrates opacities in most media and there is a reduced image size, it is possible to obtain a wide view of the retina and its defects (Fig. 12.9). Binocular indirect ophthalmoscopy has the advantages of a large field of view, brighter illumination, and decreased distortion while examining the peripheral retina. Disadvantages of indirect ophthalmoscopy are that the image is inverted both vertically and laterally, a fact that needs to be remembered while drawing retinal diagrams and during surgery.

A wide convex lens is held between the thumb and forefinger of the left hand with the curved surface towards the examiner, and with the lens itself in a plane parallel to the plane of the iris of the patient. The strength of the lens may be +28 D, +20 D or +14 D, the weaker powered lenses giving images of increasing size, narrower fields of view and lesser stereopsis. The periphery of the retina may be brought into view by scleral depression and it is best seen with the patient recumbent. Drawings should be made on a retinal chart with accurate delineation of the vascular structure of the retina and careful assessment of its relationship to retinal holes or areas of degeneration *(see* Fig. 20.1).

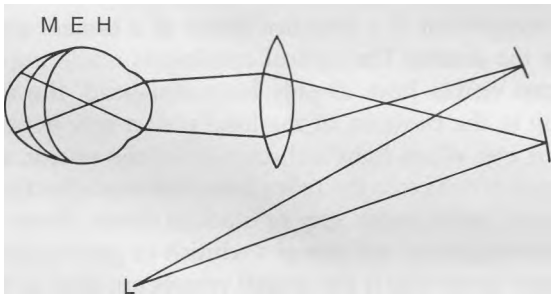


Fig. 12.9 Ophthalmoscopy: indirect method. Illumination of the fundus, showing the course of rays from the source of light to the mirror and through the eye; also the area of illumination.

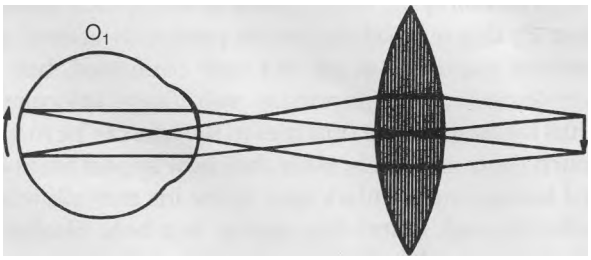


Fig. 12.10 Ophthalmoscopy: indirect method. Emergent rays from the fundus, showing the formation of the image. In the figure the lens is situated at the anterior focal plane of the eye; the rays which are parallel inside the eye, therefore, pass through the optical centre of the lens. The rays which pass through the nodal point of the eye are rendered convergent by the lens. The points where these two systems of rays cross give the position of the image, which is seen to be inverted.

Indirect ophthalmoscopy essentially makes the observed eye, irrespective of its refraction, highly myopic by placing a strong convex lens in front of it so that a real inverted image of the fundus is formed between the observer and the convex lens (Fig. 12.10). In all cases the image is magnified, the amount of magnification depending upon the refraction of the eye, the strength of the lens and its distance from the eye. With a lens of + 14 D, the fundus of an emmetropic eye is magnified about five times.

It will be seen that with the same lens the inverted image is formed at different distances beyond it, according to the refraction of the eye. If the lens is kept at a constant distance from the eye—for example, its own focal distance—the emmetropic image will be formed at the focal distance of the lens beyond it: the myopic will be nearer to the lens, the hypermetropic further from it (Fig. 12.11). Since in all cases the image is formed in the air between the lens and the observer's eye, the observer must not come too close to the patient (a natural impulse in order to see the aerial image clearly with the unaided eye). Once the head piece is comfortably adjusted on the observer's head, the two illuminated circles are observed on a surface, and the interpupillary distance between the prisms altered so that only one circle of light is seen. The lens is held between the thumb and forefinger of the left hand, and brought close to the eye, parallel to the plane of the iris. A good retinal glow is visualized and the lens is then gradually withdrawn from the eye till the retina comes into focus.

One of the difficulties in the indirect method is the reflexes formed by the eye and the surfaces of the lens.

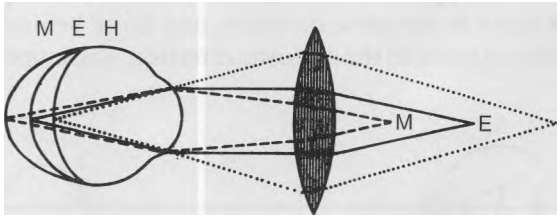


Fig. 12.11 Ophthalmoscopy: indirect method. Position of the image according to the refraction of the eye. In this figure the lens is situated at its own focal distance from the cornea. In emmetropia the parallel emergent rays, therefore, cross at the principal focus of the lens at E. In myopia the convergent emergent rays cross nearer to the lens than its principal focus, at M; in hypermetropia the divergent emergent rays cross further from the lens than its principal focus, at H.

The cornea forms a reflex of the illuminating light which, when seen through the convex lens, is magnified, so that it may cover the pupil and prevent anything behind from being seen. The surface of the lens towards the observer acts as another convex mirror and forms another reflex situated behind the lens. Similarly, the surface of the lens near the patient acts as a concave mirror and forms a reflex on the observer's side of the lens. These reflexes are troublesome, but they may be avoided by tilting the lens so that they move in opposite directions and a view is obtained between them. However, the tilting should not be overdone since the optical effect of astigmatism is produced and the fundus appears distorted.

Theoretically, to obtain the maximum field, the best place for the lens is at a distance of its own focal length from the patient's pupil; but this is the worst place for the corneal reflex. Since the latter is situated near the level of the iris, if the convex lens is at its focal distance from it, the rays from this image will be made parallel by the lens and the reflex will fill the whole area of the lens so that nothing else is seen. The best position, for practical purposes, is either nearer to or further from the eye than this, and the convenient distance is where the lens is at its focal distance from the anterior focus of the eye. Here, slight tilting of the lens, besides shifting the lens reflexes out of the way, will also move the corneal reflex and the image of the fundus in opposite directions, allowing an uninterrupted view.

Differences of level of two points near each other on the fundus are made very evident by parallactic displacement with the indirect method. Thus, in Fig. 12.12, if there are two points, a and b, at different levels in the fundus, e.g. on the edge of the disc and at the bottom of a glaucomatous cup, when the lens is shifted slightly so that its optical centre moves from O, to 0_2, the images of a and b will move from a_x to a_2 and bj to b_2.

Examination If}' direct ophthalmoscopy: Having obtained a good general view of the fundus, the observer again approaches the patient and proceeds to examine him by *direct ophthalmoscopy.* The direct ophthalmoscope is a portable, battery operated, self-illuminated hand-held instrument. It allows visualization of the posterior pole of the retina up to the equator. It projects light through a variably sized aperture. A series of lenses can be dialled in to allow the observer to focus the observed fundus (Fig. 12.13).

In the direct method the patient's eye is approached as closely as possible by the observer whose eye thus receives the emergent rays from the fundus directly.

If the patient is emmetropic (E, Fig. 12.14), the issuing rays will be parallel and will be brought to a focus on the retina of the observer. If the patient is hypermetropic,

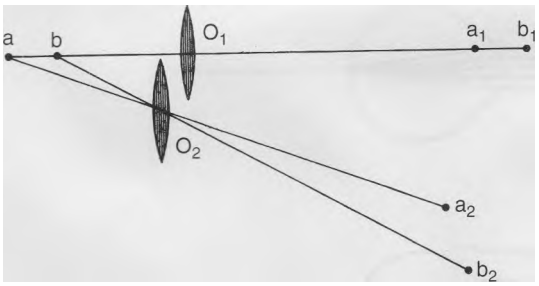


Fig. 12.12 Ophthalmoscopy: indirect method. Parallactic displacement.

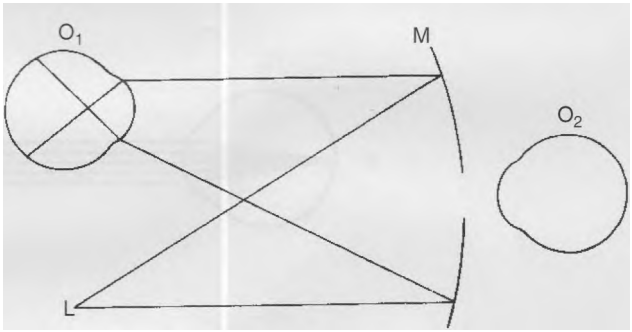


Fig. 12.13(A) Ophthalmoscopy: direct method. Illumination of the fundus, showing the course of rays from the source of light to the mirror and through the eye; also the area of illumination. Compare with Fig. 12.9.

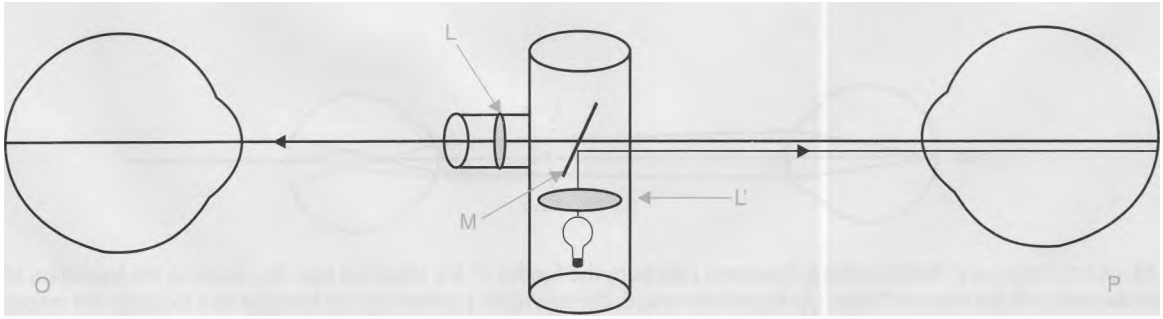


Fig. 12.13(B) Direct ophthalmoscopy. Light from a bulb is condensed by a lens, L', and reflected off a two-way mirror, M, into the patient's eye, P. The observer, O, views the image of the patient's illuminated retina by dialing in the requisite focusing lenses at L.

the emergent rays will diverge (H, Fig. 12.14) and consequently only be brought to a focus on the observer's retina on accommodation, or by the help of a convex lens. If the patient is myopic, they are convergent (M, Fig. 12.14) and must be made more divergent by the interposition of a concave lens if a similar focus is to be obtained. In emmetropia, therefore, the image of the retina is seen clearly without any lens in the ophthalmoscope; in ametropia, for the image to be clearly seen, a lens corresponding to the refractive error must be used. If, however, the eye is very highly myopic, its far point will be situated somewhere in space between the eye itself and the observer's ophthalmoscope so that it may be impossible to obtain a clear image with any correction; in such cases a view of the fundus may be possible if the patient's spectacles are left in place and the examination is made through them.

Much stress is generally laid upon the necessity and difficulty of relaxing one's accommodation in examination by the direct method. It is difficult to relax the accommodation entirely when the eye is apparently dose to the object looked at. The observer should try to think that a very distant object is being looked at, but even then, as soon as attention is directed to details of the picture, accommodation is almost certain. It is best for the beginner not to worry about this point: if the emmetropic fundus cannot be seen clearly, minus lenses should be used until it is.

The image by the direct method is always erect and is also more magnified than by the indirect method. In emmetropia the fundus is seen magnified about 15 times, somewhat less in hypermetropia and more in myopia.

The area of the fundus which can be seen by the direct method varies with the distance of the observer from the eye and with the refraction. It increases as the eye is approached, is greatest in hypermetropia, least in myopia and intermediate in emmetropia. Thus, the largest area, least magnified, is seen in hypermetropia, and the least area, most magnified, in myopia. In astigmatism the magnification is greatest in the more myopic meridian, and least in the more hypermetropic, so that there can be no clear image of the whole field. *Only lines perpendicular to the meridian which is corrected are seen clearly.*

If there is a difference in level between two points on the fundus, it is made manifest by the direct method and by parallactic displacement if the observer moves slightly to one side; an object further forward always moves in the opposite direction to the movement of the observer's head.

The difference in level can be accurately measured. Thus the bottom of a cupped disc will be relatively myopic to the edge so that a more concave lens will be required to see the vessels at the bottom of the cup clearly, while the top of an eminence, such as a swollen

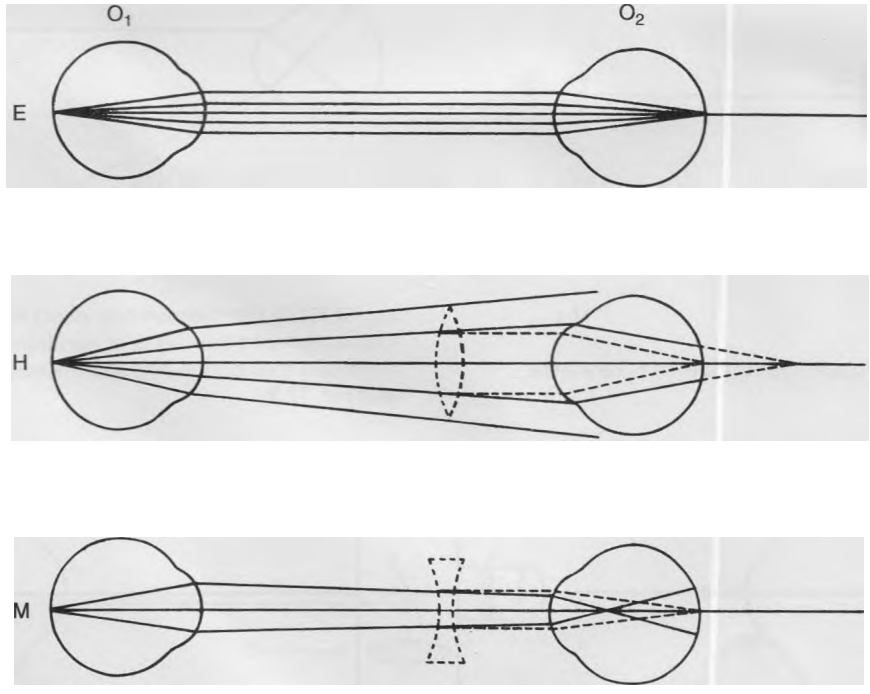


Fig. 12.14 Ophthalmoscopy: direct method. Emergent rays from the fundus of the observed eye, O,, showing the formation of the retinal image on the retina of the observer's eye, 0_2. In emmetropia, E, the emergent parallel rays are brought to a focus on the retina of 0_2 if the accommodation of this eye is absolutely at rest. In hypermetropia, H, the emergent divergent rays are brought to a focus on the retina of 0_2, either by means of accommodation or by placing a convex lens in front of 0_2. In myopia, M, the emergent convergent rays can only be brought to a focus on the retina of 0_2 by placing a concave lens in front of 0_2.

disc or a tumour, will require more convex lenses than are needed to see a blood vessel on a normal part of the retina near the disc clearly. It can be proved that *if the correcting lens is at the anterior focus of an emmetropic eye,* a difference of 3 D is equivalent to approximately 1 mm difference of level at the fundus. It is important to get as close as possible to the eye when measuring differences of level and to relax the accommodation, because only then are the conditions of accuracy fulfilled. In order to eliminate the effect of the observer's accommodation the lowest minus lens or the highest convex lens which allows clear vision must be chosen for the purposes of measurement.

In routine practice it is advisable to start ophthalmoscopy with the focusing lens of the direct ophthalmoscope kept at about +20 D, observe the retinal reflex and then decrease the power of the lenses gradually, as the observer moves closer to the patient. A gradual reduction of the power of the focusing lenses permits the visualization of each structure of the eye through from the cornea, backwards to the retina. An opacity in the vitreous provides the same optical conditions as the fundus of a hypermetropic eye. The appearance of opacities in the vitreous or lens will vary with their density and with the amount of light reflected from their surfaces; if they are very dense they will appear black against the background of the red reflex, but if they are semitransparent they will appear red or whitish according to the relative amounts of light transmitted from the fundus and reflected from their surface. A detached retina may, therefore, look red or white according to its degree of transparency, and if much light is reflected from the surface, details may be seen upon it.

Slit-lamp biomicroscopy: The slit-lamp cannot be used to explore the eye beyond the anterior parts of the vitreous because the beam of light is ordinarily brought to a focus in this region. If, however, the beam is made more divergent by eliminating the refractive influence of the corneal curvature by using a contact lens with a flat anterior face, or (more simply) by interposing a high power concave or convex lens in front of the cornea, the posterior part of the vitreous and the central area of the fundus can be examined by the binocular microscope in the focused beam of light (Fig. 12.15). The use of a powerful condensing lens produces a magnified image. Lenses for the examination of the fundus are of two types, contact and non-contact. Non-contact fundus lenses as used commonly are double aspheric, ranging in power from +60 D, +78 D to +90 D. The +60 D lens allows more magnification and is used for the examination of the macula and optic nerve head. These lenses form an aerial image that is inverted laterally and vertically. With these lenses large images are obtained, and because of their short focal length, fundus examination is possible on a slit-lamp.

The highly concave Hruby lens has a power of -55 D and can also be employed, but gives a low magnification and a small field (Fig. 12.16).

Such an examination is easier with full mydriasis but the disc can be visualized even through an undilated pupil. The slit-lamp provides bright, variable illumination and additional magnification. Fine changes in the posterior part of the vitreous and retina and at the optic disc can be readily studied binocularly under high magnification, areas of oedema are clearly outlined in the optical section, and difficult problems in diagnosis such as the difference between a cyst and a hole at the macula are clearly demonstrated. The examination provides a high quality, highly magnified and three-dimensional view of the optic disc and the posterior portion of the eye.

As in the binocular indirect examination, the condensing lens is held in front of the patient's eye. The convex lenses are initially held very close to the eye, between the thumb and forefinger, the hand being stabilized by



Fig. 12.15 Optics of a non-contact convex lens showing an inverted aerial image of the vitreous and retina.

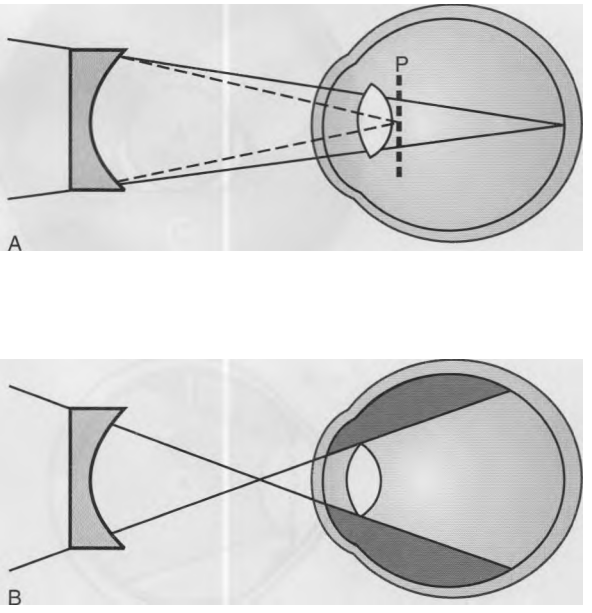


Fig. 12.16 Optics of the Hruby lens. (A) The image of the fundus appears in plane P; (B) a limited area of the fundus is seen.

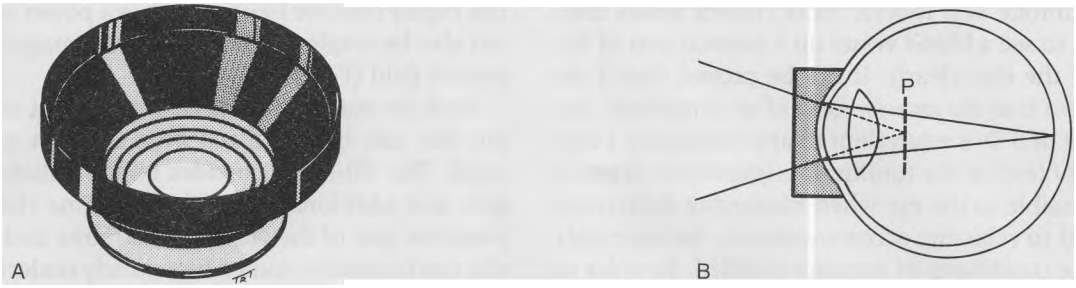


Fig. 12.17 (A) Posterior fundus contact lens; (B) posterior fundus contact lens with the image appearing in plane P.

the middle finger resting on the forehead bar of the slit-lamp. The slit-lamp is adjusted so that the illumination and observation arms are aligned and the magnification is initially 10 x. The illumination is kept low, the slit beam at a width of 2-3 mm, and the slit-lamp is withdrawn from the eye. Once the fundal glow is visualized the lens is drawn away from the eye till the posterior fundus comes into focus. Reflections that obscure visibility can be reduced by tilting the lens slightly. The basis of biomicroscopy of the vitreous body is the Tyndall effect. This is maximal with a high intensity of projected light, a good contrast between the observed structure and background, a large angle of separation between observer and illumination axes and when viewed by a dark-adapted eye. The patient's pupils must be widely dilated, so that the peripheral retina may be explored in combination with scleral depression.

Posterior fundus contact lenses nullify the power of the cornea. The posterior fundus can be directly visualized through such lenses. The image produced is virtual and erect, situated in the anterior vitreous cavity (Fig. 12.17A and B). Viewing the more peripheral retina requires the use of indirect contact lenses, which utilize angulated mirrors to bring the anterior retina into view. The Goldmann three-mirror contact lens has three mirrors placed in the cone, each with a different angle of inclination (B: 73°, C: 67°, D: 59°; Fig. 12.18). The central part of the contact lens allows a direct view of the posterior fundus (A). The peripheral fundus can be examined by each mirror, bringing into focus a different area (Fig. 12.18; 3). There are other lenses available for laser treatment of the retina, such as the panfundoscopic lens and the transequatorial lens.

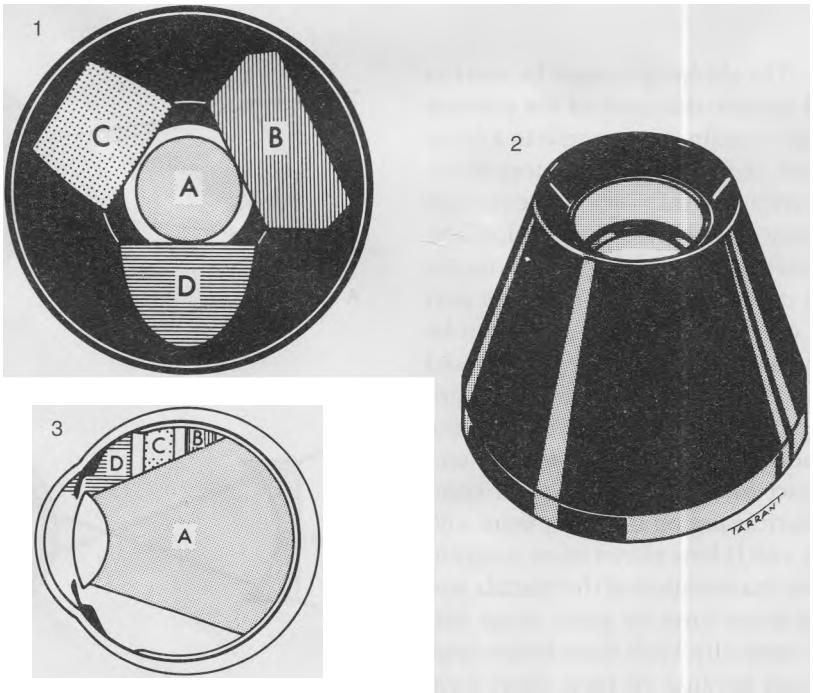


Fig. 12.18 Goldmann three-mirror contact lens and diagram of optical principles.

THE NORMAL FUNDUS

The appearance of the *fundus* is a uniform red, occasionally with a very delicate punctate stippling, especially towards the periphery. In very dark-complexioned people the fundus is a darker red and in fair-skinned individuals it appears lighter in colour. Normally the choroidal blood vessels cannot be seen as the retinal pigment epithelium blurs any details, but is not sufficient to prevent the colour of the blood manifesting itself. In people having a light pigmentation, the choroid and sometimes its larger vessels may be visible. Sometimes the pigment between the choroidal vessels is particularly dense, or the pigment is deficient in the retinal pigmentary epithelium, while the choroid is deeply pigmented; the choroidal vessels are then seen to be separated by deeply pigmented polygonal areas (*tigroid or tesselated fundus).* This appearance is often due to a condition called choroidal sclerosis and may be accompanied by a 'dry' age-related macular degeneration.

The *optic disc* is generally pale pink in colour, nearly circular in shape and about 1.5 mm in diameter. The edges are usually well defined, but may be irregular and, not uncommonly, especially in old people, a narrow white ring, the *scleral ring,* is visible around the pink disc. This is because the choroid and pigmentary epithelium of the retina do not extend up to the margin of the disc so that the sclera is seen through the retina. Sometimes there is a ring of black pigment

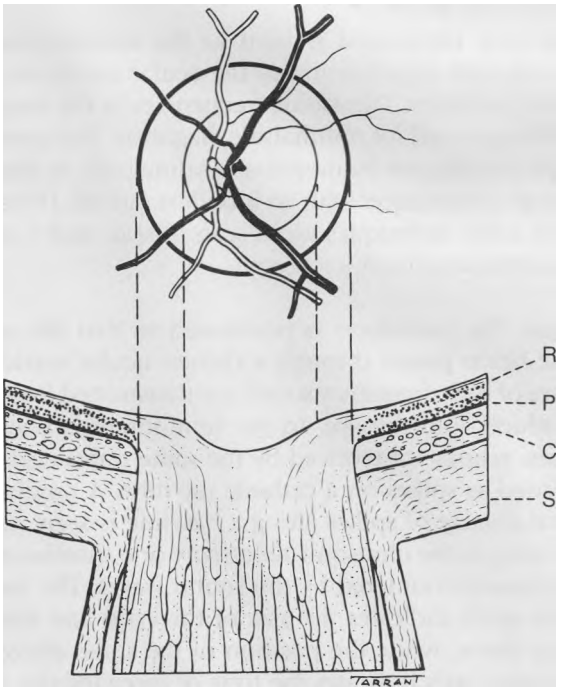


Fig. 12.19 Physiological cup: R, retina; P, pigmentary epithelium; C, choroid; S, sclera.

around the margin of the disc due to the heaping up of the retinal pigmentary epithelium. The disc itself is not uniformly pink throughout its extent. The central part of the optic disc is usually paler and may be quite white, and the temporal side is normally paler than the nasal. The central vessels emerge from a funnel-shaped depression, the *physiological cup.* This cup varies in different eyes. When deep, the central part may be seen to be speckled with grey spots representing the meshes of the lamina cribrosa through which the nerve fibres pass. The true nature of the physiological cup is best understood by comparing the ophthalmoscopic picture with a microscopic section vertically through the nerve head (Fig. 12.19). The colour of the disc is due to the white fibres of the lamina cribrosa seen through the vascularized nerve tissue. Where the nerve fibres are thinnest, in the centre, the white lamina shines through more brightly. The grey spots in the lamina, where they are seen, are due to the non-medullated nerve fibres reflecting less light than the white connective tissue fibres.

ANCILLARY INVESTIGATIONS

Fluorescein angiography

Fluorescein angiography of the fundus is based on the detection of fluorescent light emitted by a dye in circulation. This fluorescence is produced by irradiation of the dye with light of a wavelength within the absorption band of the fluorescein and blood mixture (420-490 nm). The emitted fluorescence (510-530 nm) is passed through a barrier filter to the film, with complete exclusion of the irradiating light.

Fluorescein is readily bound to the albumin in the blood stream. The blood-retinal barrier, by preventing dye leakage in the physiological state, facilitates the delineation of retinal vessels of all calibres. In the choroidal circulation, fluorescein passes freely across the endothelium of the capillaries to the extravascular spaces. A physiological barrier to the dye prevents the passage across Bruch's membrane and the intact retinal pigment epithelium.

When the dye enters the eye initially there is a choroidal blush and then the dye can be followed through the retinal arterioles, the capillary bed and into the veins, which are at first laminated due to a differential flow of blood. A late phase is usually recorded 5-30 minutes after injection (Fig. 12.20A-D).

Fluorescein angiograms reveal dissolution of the physiological barriers by the leakage of dye across the retinal vessel walls and Bruch's membrane and, having leaked, the dye may persist for longer than can be explained on physiological grounds. Retinal pigments

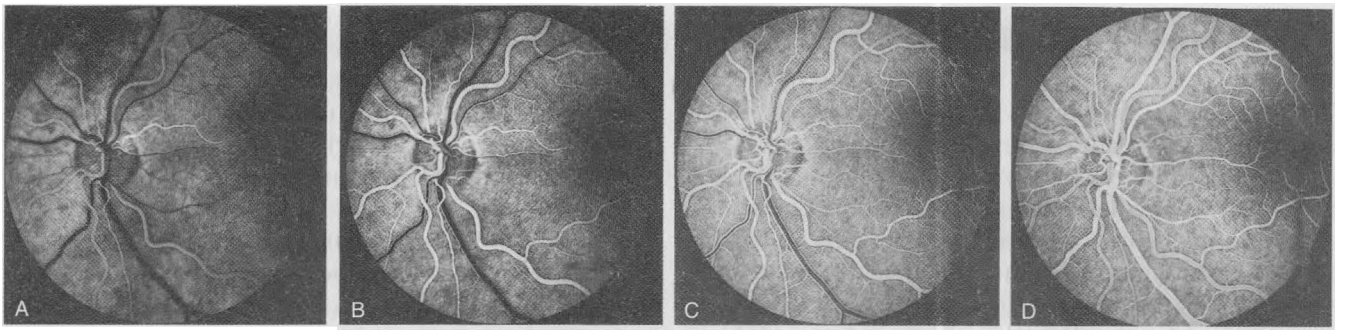


Fig. 12.20 (A) Early arteriolar phase showing choroidal blush and filling of a small cilioretinal vessel; (B) arterial phase; (C) arteriovenous phase showing laminar flow in the retinal veins; (D) Venous phase. (By courtesy of TJ Ffytche)

and red cells absorb fluorescent light and such tissues may therefore mask fluorescence in deeper structures. On the other hand, migration of pigment gives access to deeper fluorescence—a window effect.

Fluorescein angiography is particularly helpful in exposing the depth of pathological involvement in diabetic retinopathy and reveals neovascularization occurring in any area of the fundus. It gives a clear idea of the integrity of the vascular tree itself, and is also useful in the assessment of disorders of the fundus, including neoplasia and disorders of the optic nerve head such as papilloedema.

Fluorescein angiography is also helpful in the interpretation of neovascularization of the iris when leakage from the vessels of the iris may be the first sign of rubeosis.

Vitreous fluorophotometry allows measurement of fluorescein concentration in all parts of the vitreous chamber visible through the eye-piece of the slit-lamp. By this technique, minimal amounts of fluorescein in the range of 10^{-8}-10^{-9}g/ml may be detected in the vitreous. One of the early signs of diabetic involvement of the eye is an alteration in permeability of the blood-aqueous barrier allowing the passage of fluorescein into the vitreous chamber. A similar breakdown in the barrier occurs early in the course of retinitis pigmentosa and also in carriers of this disease.

Indocyanine green angiography

Indocyanine green stays within the choroidal circulation and is stimulated by a longer wavelength of light than fluorescein dye. This provides a better resolution of the choroidal vasculature, especially choroidal neovascular membranes (CNVM).

More precise and objective ways of assessing the retinal and optic nerve head morphology are available—scanning laser ophthalmoscopy, scanning laser polarimetry and optical coherence tomography (OCT) or scanning laser interferometry. These utilize the principle of a confocal system of pinholes and lenses, whereby precise visualization, layer by layer, is possible and any light reflected from above or below the plane of observation does not reach the imaging system. Three-dimensional morphometry is carried out by confocal scanning laser tomography, which calculates the area and volume of the neuroretinal rim and cup, steepness and depth of the cup, and height of the retinal nerve fibre layer, depending on an arbitrary reference plane. Laser scanning polarimetry measures the peripapillary nerve fibre layer thickness, by assessing the retardation of linearly polarized light passing through the retina. The principle of scanning laser interferometry provides a cross-section of the retina, because of the variances in reflectivity of different retinal layers. *Flowmetry*, with the help of the scanning laser ophthalmoscope, allows the flow through the retinal vessels to be measured.

Ultrasonography

Diagnostic ultrasound is used in the investigation of patients with opacification of the ocular media or with orbital problems. Ultrasonic frequencies in the range of 10 MHz are used for ophthalmic diagnosis. The sound is coupled to the eye by means of a saline bath or directly through a transducer with an inbuilt stand-off. Different 'pulse echo' techniques are A-scan, B-scan and C-scan, and ultrasound biomicroscopy.

A-scan: The transducer is positioned so that the ultrasonic beam passes through a chosen ocular meridian. Pulses of high-frequency sound are transmitted from the transducer into the eye. In the time intervals between pulses, echoes are received by the same transducer and recorded as spikes on a cathode ray tube. A unidimensional display of spikes along a baseline is seen, corresponding to the ultrasonic reflectivity or transmission of interfaces encountered by the sound waves. The height of the spike indicates the size of the echo and density of the tissue, while the position of the spike along the horizontal axis indicates the time of receiving the echo (Fig. 12.21). The amplitude of the retinoscleral spike is taken as a reference standard or normal and the height

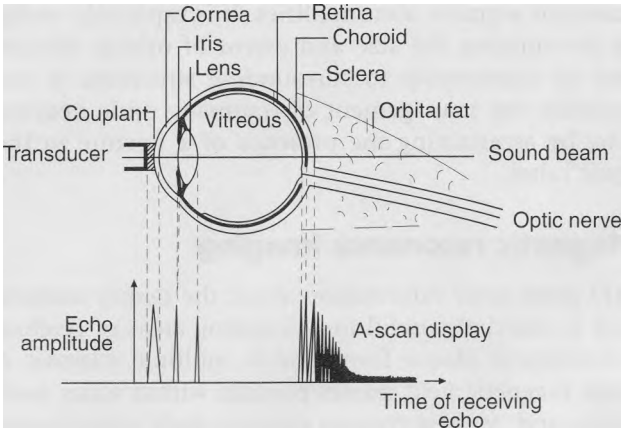


Fig. 12.21 A-scan technique. (By courtesy of Restori)

of the other spikes graded as being of small or moderate amplitude, providing a gross characterization of tissues. Supranormal spikes are evidence of calcification or a metallic foreign body. The linear distance between spikes allows the calculation of distances between interfaces, such as the depth of the anterior chamber or axial length. A-scans are used for biometry in intraocular lens power calculations and pachymetry in refractive laser procedures.

B-scan: Echoes are plotted as dots instead of spikes, and the brightness of the dot indicates the size of the received echo. The transducer is moved in an arc above the eye, and a whole series of intensity registrations are plotted. The resulting B-scan is comparable to a histological section through the eye and orbit. If the transducer is moved in the manner shown in Fig. 12.22, a 'linear' B-scan is produced. Such B-scans may be taken in the horizontal, sagittal or oblique planes (Fig. 12.23A and B). B-scan ultrasound provides a real-time, two-dimensional, grey-scale display ofthe eye and orbit, where

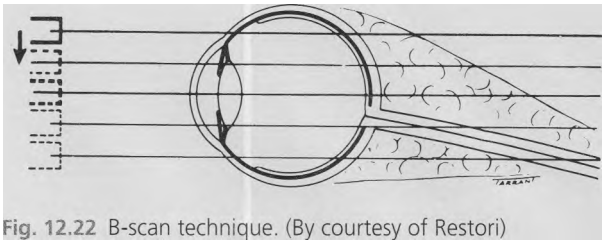


Fig. 12.22 B-scan technique. (By courtesy of Restori)

different echodensities are depicted in gradations of brightness. This is useful in delineating intraocular structures in eyes with opaque media, and in evaluating vitreoretinal and orbital mass lesions. Dynamic ultra-sound allows differentiation of detachments of the retina from those of the vitreous as well as identification of vascular abnormalities.

In general, ultrasonic techniques are complementary to computerized axial tomography (CAT) and magnetic resonance imaging (MRI).

Colour Doppler imaging is used to determine the blood flow in the large- and medium-sized vessels that supply the eye—the carotid and the ophthalmic vessels. Flow through the smaller orbital vessels such as the posterior ciliary artery can be visualized and measured, but is not routinely used.

Optical coherence tomography

OCT uses optical back scattering of light to image various tissues of the eye—the retina and optic nerve head and anterior segment, with a resolution of as low as 7 pim. It provides cross-sectional or 3D images of these tissues *in vivo,* similar to those of an ultrasound. Individual tissues can be identified, thickness measured and abnormalities identified, and compared over time.

In the retina it is used to diagnose macular oedema or traction, subretinal fluid, retinal pigment epithelial

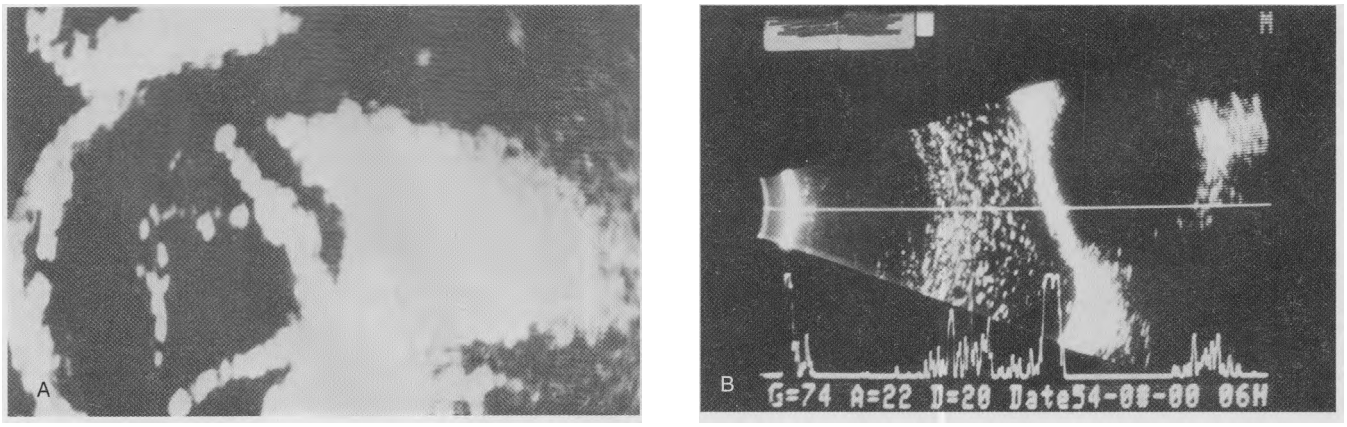


Fig. 12.23 (A) B-scan. Total retinal detachment with defined posterior hyaloid interface (By courtesy of Restori). (B) A- and B-scan. Large cystic lesion in the orbit deforming the posterior pole.

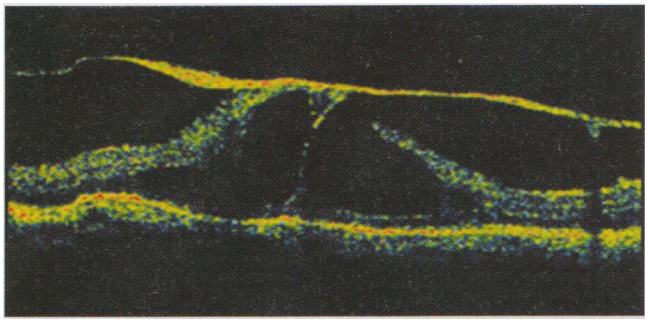


Fig. 12.24 Optical coherence tomography of macular oedema.

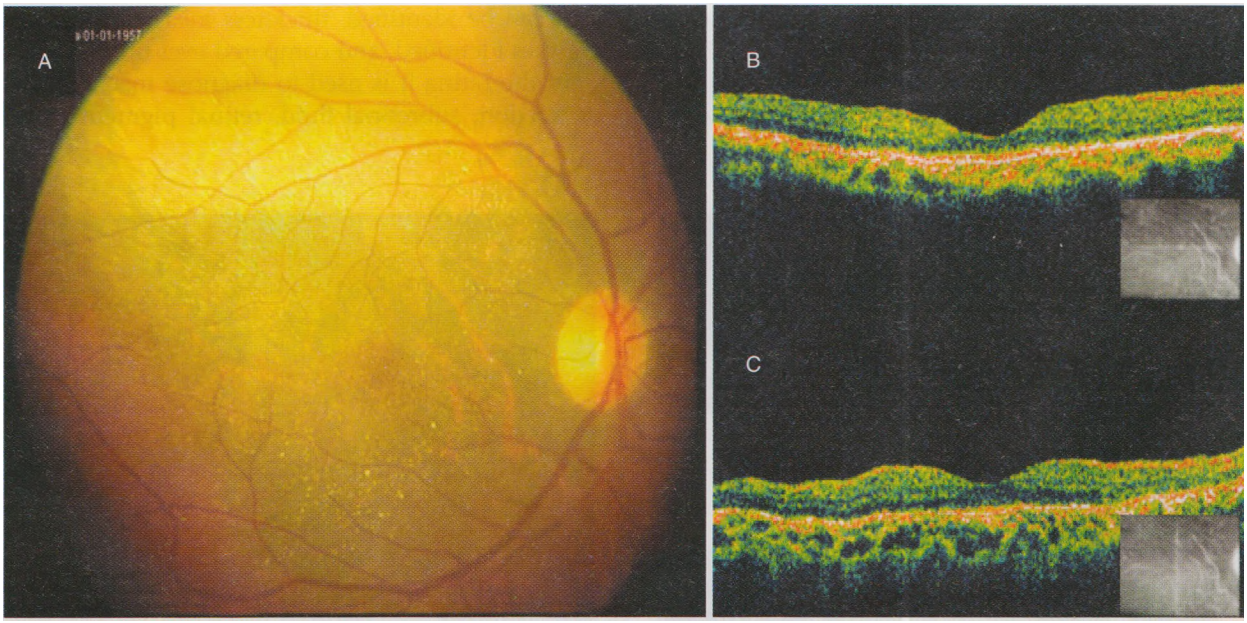
irregularity, monitor therapy over time (Figs 12.24 and 12.25). In the anterior segment it allows visualization of the anterior chamber angle, and all structures anterior to the pigment epithelium.

Computerized axial tomography

CAT scanning outlines the bones and orbital apex more fully than ultrasound, but has been less successful in tissue diagnosis. In this technique ionizing radiation is used to form images which are then formatted by computer to form multiple planar images. These can be axial or coronal and can be further formatted to sagittal images. Ophthalmic disorders are best detected on an orbital scan having the thinnest cuts. It can identify very small metallic foreign bodies in the eye or in the orbit. In the presence of media opacities it helps to identify posterior segment abnormalities. It is especially useful in determining the size and extent of orbital disease, and its relationship to surrounding structures. It can facilitate the management of traumatic optic neuropathy by ascertaining the presence of a fracture in the optic canal.

Magnetic resonance imaging

MRI gives more information about the tissues scanned and is especially useful in delineating areas of cerebral infarction or plaque formation in multiple sclerosis. A large magnetic field excites protons within water molecules and, as these protons return to their normal state, energy is given off. This is detected and reconstructed by computer into an image that can be axial, coronal or sagittal. T1 -weighted images provide details of intraorbital structures such as the extraocular muscles and optic nerve, and can be recognized by a high signal intensity or brightness from fat. In T2-weighted images there is a high signal intensity from the vitreous which appears bright, and intraocular details are obscured. This is utilized primarily for soft tissue delineation in the orbit and central nervous system. Arteriovenous malformations are well defined by magnetic resonance angiography. An orbital surface coil is ideal for orbital studies and a head coil if pathological conditions of the central nervous system are suspected. It is useful in delineating areas of cerebral infarction or plaque formation in multiple sclerosis. It is contraindicated in the presence of magnetic foreign bodies.



Fig, 12.25 Ocular coherence tomography of the macula.

SUMMARY

The posterior segment of the eye includes structures behind the lens, i.e. the vitreous, the posterior part of the ciliary body and retina. These structures can be directly viewed using different instruments such as the slit lamp combined with the aid of various lenses, namely a posterior pole viewing contact lens, a strong concave Hruby lens of -55 D or strong convex lenses of +78 and +90 D. Other methods of examination include use of a direct ophthalmoscope for a magnified monocular view and indirect ophthalmoscope for a wider binocular stereoscopic view.

Structures that are not easily visible by direct observation can be studied by fluorescein angiography, indocyanine angiography, ultrasonography, OCT, scanning laser ophthalmoscopy, radiological investigations and ophthalmodynamometry.

SUGGESTED READING

1. Lightman S, McCluskey P. On behalf of the International Council of Ophthalmology 2009. *Ophthalmology handbook for medical students learning ophthalmology.* Compiled by The Task Force on Undergraduate Teaching in Ophthalmology of the International Council of Ophthalmology and based on their curriculum 2009. Retreived August 10, 2010, from http://archive.icoph.org/pdf/ICOMedicalStudentEnglish .pdf.
2. Videos for clinical examination of the eye. Eye Exam 3/8. Mar, 2007. www.youtube.com, uploaded by solidaditorebelde.

13

Ocular Therapeutics

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There is a wide range of medications available for the treatment of ocular diseases.

ROUTES OF ADMINISTRATION

The routes by which therapeutic substances may be introduced into the eye are:

- instillation into the conjunctival sac;
- subconjunctival injection;
- peribulbar injection;
- systemic administration;
- direct injection into the globe itself—into the anterior chamber, intracameral or intravitreal.

The main barriers to transfer of medication into the eye are the corneal epithelium, and the blood-retinal and blood-aqueous barriers. Severe inflammation causes a breakdown of the latter two.

Instillation: In the form of drops, ointments or ocuserts, topically instilled drugs enter the eye largely through the cornea, and the ease with which solutes instilled into the conjunctival sac permeate into the aqueous is measured by their concentration in the aqueous humour. Different layers of the cornea have selective permeability characteristics. The epithelium is more permeable to fat- or lipid-soluble substances and the stroma to water-soluble compounds. The cornea offers considerable resistance to the passage of electrolytes largely due to the action of the epithelium and, to a lesser extent, of the endothelium, while the passage of large colloidal molecules is barred. The corneal stroma, like the sclera, is permeable to all water-soluble substances. In general terms, the passage of drugs through the epithelium is determined by factors controlling the penetration of drugs into cells, the most important of which are fat solubility, a molecular weight below 500 and the degree of dissociation of the electrolytes. Drug absorption is also regulated by the duration of contact of the drug with the corneal epithelium. Bioavailability of a drug in the eye is enhanced by the use of viscous vehicles such as hydroxypropylmethylcellulose, polyvinyl alcohol, polyvinyl pyrrolidone and hyaluronic acid. Drugs may be incorporated into carriers such as water-soluble hydrophilic polymer inserts, collagen shields, water-soluble vinyl alcohol film inserts, liposomes and microparticulates which can remain in contact with the epithelium for many hours, days or weeks.

Since the epithelium forms the main barrier, permeability is greatly increased if the epithelium is damaged or abraded or if its vitality is impaired by a local anaesthetic. This is well demonstrated by fluorescein staining of a corneal abrasion or an ulcer; abraded tissue quickly takes up the stain.

Subconjunctival injections: These enable a wider range of substances to be introduced into the eye, as the sclera allows the free and indiscriminate transit of molecules of considerable size. Thus, antibiotics which do not penetrate the cornea enter the eye freely by this route. This is useful when high intraocular concentrations of antibiotics or steroids are required as in acute anterior segment infections and inflammations.

Peribulbarjsub-Tenon injections: Both anterior sub-Tenon and posterior peribulbar/retrobulbar injections also use the scleral route for access into the eye. A short, curved needle with its bevel towards the globe is passed through a conjunctival incision and medication injected close to the inflamed tissue. These injections are used in the treatment of intermediate and posterior inflammations. Depots of crystalline suspensions of corticosteroids lead to high intraocular levels of steroids without systemic side effects.

Systemic administration: Inflammations or infections involving the posterior retina, optic nerve or orbit that cannot be reached by local applications require systemic therapy. This is also necessary if a disease spreads outside the eye. The efficacy of drugs given orally or as injections has its obvious limitations because of the impermeable blood-aqueous barrier. Large-sized molecules (such as penicillin) are not allowed to pass and when the molecular size is at the borderline, lipid-solubility is again the most important determining factor. Among the common antibiotic drugs, chloramphenicol, which is lipid-soluble, enters the eye easily.

Direct injection into the globe: Drugs are injected either into the anterior chamber or the vitreous. It is employed, for example, to flood the ocular tissues with antibiotics in acute endophthalmitis. The half-life of drugs in the aqueous is only a few hours, but effective concentrations of antibiotics may last for 1-4 days when injected into the vitreous. Vitreous implants have been used to deliver ganciclovir in the treatment of cytomegalovirus (CMV) retinitis and fluocinolone for chronic uveitis.

CHEMOTHERAPY IN INFECTIVE CONDITIONS

Antimicrobials

Among the antimicrobial drugs many are bacteriostatic, but some are bactericidal, acting by competing for the raw materials necessary for the existence of the organisms. As soon as the influence of the drug is withdrawn, the remaining organisms may resume growth and multiply, so the rationale of treatment is to keep the drug continuously in contact with the infected tissue until the infection is overcome. Since these drugs are rapidly excreted from the body or diffuse from any site of local application, repeated or continuous administration during this crucial period is necessary.

The essential value of all these drugs lies in the treatment of acute infections; in chronic infections they are relatively ineffective or a relapse follows their withdrawal.

The antibiotics are a class of substances derived from fungi or other bacteria or are synthetic. Their action depends on the inhibitory effect which one organism exerts on another. These are effective against bacteria. Other antimicrobial agents are effective against spirochaetes, rickettsiae, fungi and viruses. Antibiotics may be bacteriostatic or bactericidal. In general, effectivity against gram-positive organisms is seen with penicillin G, erythromycin, oxacillin and vancomycin, while neomycin, polymyxin B, azlocillin and streptomycin are largely effective against gram-negative organisms. The 'broad-spectrum' antibiotics—gentamicin, amikacin, ampicillin, cephalosporin, tobramycin, chloramphenicol, tetracycline, fluoroquinolones and others—are clinically effective against both gram-positive and gram-negative organisms as well as rickettsiae, the chlamydia, certain spirochaetes and protozoa (Table 13.1).

Table 13.2 lists some commonly used antibacterial medications, their dosages and routes of administration.

Penicillins

All penicillins have a bactericidal effect, but have a short half-life. Differences in antibacterial activity, absorption and resistance to penicillinase depend on alteration of the side-chains attached to the amino group. They are excreted mainly via the kidney and appear in the urine in active forms; a small fraction is excreted via the biliary tract.

Penicillins in general act by interfering with cell wall synthesis. Most of them have a rather narrow antibacterial spectrum, being chiefly confined to cocci and gram-positive organisms. They diffuse readily into tissue fluids but not into the eye. When given systemically some have to be injected intramuscularly because they are destroyed by the acidic gastric juice, others can be given by mouth. As patients are liable to develop hypersensitivity to penicillin, it is wise to enquire about this before starting a course of treatment.

Immediate reactions such as urticaria and anaphylactic shock are probably associated with hypersensitivity to the 6-aminopenicillanic acid nucleus. Delayed reactions may be due to hypersensitivity to protein residues occasionally present in penicillin preparations derived from the fermentation process.

Table 13.1 Spectrum of action and systemic dosages of commonly used antibiotics

Drugs	Spectrum	Dose
Penicillin derivatives		
Cloxacillin	Gram-positive organisms, penicillinase-producing	50–100 mg/kg/day oral/i.v. 6 hourly
Ampicillin	Gram-positive organisms, *H. influenzae, E. coll, Proteus, Salmonella, Shigella*	50–100mg/kg/day oral/i.v. 6hourly
Amoxycillin	Gram-positive organisms	25–50 mg/kg/day oral 8 hourly
Vancomycin	*H. influenzae, E. coli, Proteus, Salmonella*	
Cephalosporins		
Cephalexin	Gram-positive organisms, penicillinase-producing staphylococci, C. *diphtheriae,* Clostridia, *Actinomyces, E. coli, Klebsiella, Shigella, Salmonella, Proteus, H. influenzae*	25–50 mg/kg/day oral 6 hourly
Cephazolin	Gram-positive organisms, *E. coli, Proteus, H. influenzae*	25–50 mg/kg/day i.m./i.v. 8–12 hourly
Cefaclor	Gram-positive organisms, *E. coli, Proteus, H. influenzae*	25–50mg/kg/day oral 8–12 hourly
Cefuroxime	Gram-positive and -negative organisms, penicillinase-producing *N. gonorrhoeae, ampicillin*-resistant *H. Influenzae*	30–100mg/kg/day i.m./i.v. 8–12 hourly
Cefotaxime	Aerobic gram-negative organisms	100–150mg/kg/day i.m./i.v. 8–12 hourly
Ceftriaxone	Aerobic gram-negative organisms	80–150 mg/kg/day i.v. 8–12 hourly
Cefoperazone	Gram-positive organisms. *Pseudomonas, Salmonella, Bacteroides fragilis*	50–200 mg/kg/day i.m. 8–12 hourly
Ceftazidime	Aerobic gram-negative organisms, *Pseudomonas*	50–100 mg/kg/day i.v. 8–12 hourly
Ceftizoxime	Aerobic gram-negative organisms	30–60 mg/kg/day i.v./i.m. 8–12 hourly
Aminoglycosides		
Gentamicin	Aerobic gram-negative organisms. *Pseudomonas, Proteus, E. coli, Klebsiella*	4–8mg/kg/day i.m./i.v. 8–12 hourly
Amikacin	Aerobic gram-negative organisms, gentamicin-resistant organisms	15–20mg/kg/day i.m./i.v. 8–12 hourly
Tobramycin	Aerobic gram-negative organisms, *Proteus, Pseudomonas*	6–7.5mg/kg/day i.m./i.v. 8–12 hourly
Tetracycline and its derivatives		
Doxycycline	Gram-positive and gram-negative organisms, spirochaetes, rickettsiae, chlamydiae, *Mycoplasma, Actinomyces, Entamoeba histolytica*	1.5–2mg/kg/day oral 12–24hourly
Tetracycline	Gram-positive organisms	50mg/kg/day oral 6 hourly
Macrolides		
Azithromycin	Gram-positive organisms, *Chlamydia, Toxoplasma gondii*	20–30 mg/kg single oral dose
Combination drugs		
Co-trimoxazole	(400 mg sulphamethoxazole + 80 mg trimethoprim) Gram-positive and gram-negative organisms	6 mg of trimethoprim equivalent/kg/day oral 12 hourly
Fluoroquinolones		
Ciprofloxacin	*Actinomyces, Nocardia spp., Toxoplasma* spp., Aerobic gram-positive organisms	15–20 mg/kg/day oral 12 hourly 7–10 mg/kg/day i.v. 12 hourly
Norfloxacin	Aerobic gram-positive organisms	10 mg/kg/day oral 12 hourly
Ofloxacin	Gram-positive and gram-negative organisms	200–400 mg oral 12 hourly
Gatifloxacin	Gram-positive and gram-negative organisms	200–400 mg once daily
Polyenes		
Amphotericin B	*Candida,* systemic fungal infections	1 mg/kg/day i.v. infusion over 6 hours (to be prepared in dextrose)

Table 13.2 Antibacterial ocular medications: dosages and routes of administration

Antibiotic	Topical	Subconjunctival	Intravitreal
Cephazolin/Ceftazidime	5%	100 mg	2.25 mg/0.1 ml
Ceftriaxone	10%	100 mg	3.0mg
Penicillin G	1 00 000 units/ml	0.5 million units	1000–5000 IU
Ticarcillin	0.6%	—■	—
Ciprofloxacin	0.3%	—	0.1 mg
Ofloxacin	0.3%	—	0.1 mg
Moxifloxacin	0.5%	—	400 ^g
Gatifloxacin	0.3%	—	400 ^g
Polymyxin B	50 000 units/ml	10–25 mg	—
Vancomycin	2.5–5%	25mg	1 mg/0.1 ml
Tobramycin	1–1.4%	20–40 mg	0.2 mg/0.1 ml
Gentamicin	0.3–1.4%	20–40 mg	0.1 mg/0.1 ml
Amikacin	1–2.5%	25–50 mg	0.2–0.4 mg/0.08 ml
Chloramphenicol	0.50%	100 mg	—

There are three main groups of penicillins:

1. *Penicillins effective against coccal infections and gram-positive bacilli:* Benzyl penicillin is not acidstable and can therefore only be given parenterally. Acid-fast penicillins are penicillin V and sodium oxacillin.
2. *Penicillinase-resistant penicillins* consist of cloxacillin sodium and flucloxacillin sodium. Their advantage lies in their activity against penicillin-resistant staphylococci.
3. *Broad-spectrum penicillins* such as ampicillin and amoxycillin are absorbed well orally and can also be administered parenterally. They are effective against most cocci other than penicillinase-producing staphylococci, *Neisseria* and partly *Escherichia coli.* Their intraocular penetration is good. Carbenicillin sodium, ticarcillin and azlocillin are given parenterally and act against *Pseudomonas aeruginosa.*

Penicillins show a synergistic action with antibiotics of the aminoglycoside group. In deep-seated inflammations of the orbit or lids, they are administered parenterally. In superficial inflammations of the conjunctiva and cornea drops or ointment are administered locally.

Cloxacillin and flucloxacillin: These penicillins are not affected by staphylococcal penicillinase and are therefore used for treating staphylococcal infections which are resistant to other penicillins. *Flucloxacillin* has the same activity against penicillin-resistant staphylococci as cloxacillin, but levels of flucloxacillin in the blood after oral administration are nearly twice as high as after an equivalent dose of cloxacillin. This is because flucloxacillin is better absorbed from the gastrointestinal tract and is also excreted more slowly from the body. Serum levels following intramuscular or intravenous injections of flucloxacillin are also higher than those of cloxacillin. The dose is 250-500 mg 6 hourly.

Carbenicillin is resistant to the penicillinase produced by some strains of *Proteus, Pseudomonas* and coliform organisms. The drug is ineffective orally.

Ampicillin is a broad-spectrum penicillinase sensitive penicillin which is acid-resistant and is usually administered orally. It is not as effective as benzyl penicillin and should be used for organisms which are resistant to benzyl penicillin but do not produce penicillinase.

Amoxycillin: This penicillin has an antibacterial activity identical to that of ampicillin but its main advantage is that it is well absorbed after oral administration, producing serum levels about twice as high as those after an equivalent dose of oral ampicillin. Food in the stomach has little effect on amoxycillin absorption from the small bowel. The adult dose is 250-500 mg every 8 hours.

For gram-positive infections moxifloxacin 0.5% is slightly more efficacious than gatifloxacin 0.3%, but against gram-negative and atypical bacteria gatifloxacin is more effective. Moxifloxacin, in a 0.5% solution, achieves higher intraocular concentrations than gatifloxacin in a 0.3% solution; however, neither moxifloxacin drops nor gatifloxacin drops effectively penetrate the vitreous. Oral gatifloxacin has been shown to have extremely high levels in the vitreous.

Cephalosporins

These drugs have a structure and mode of action similar to penicillin and are bactericidal. They are relatively resistant to staphylococcal penicillinase. Patients already allergic to penicillin may develop an allergy. When cephalosporins are used extensively, strains of staphylococci resistant to cloxacillin as well as the cephalosporins

emerge. This limits their use to special situations. The intraocular penetration of cephalosporins is not very good. The main adverse effect of cephalosporins is nephrotoxicity.

The first generation of cephalosporins, such as cephazolin and cephalexin, were highly effective against gram-positive cocci, but moderately so for some gram-negative enterobacilli. The second generation of cephalosporins, such as cefuroxime and cefaclor, had a wider gram-negative spectrum. Some of the third-generation cephalosporins, e.g. ceftazidime and cefotaxime, are particularly effective against gram-negative organisms.

Cephazolin is suitable for either intramuscular or intravenous administration. The usual adult dose is 0.5 g intramuscularly 8 hourly.

Cephradine can be given orally, intramuscularly or intravenously. The dose is 0.5-1.0g every 6 hours. It is more stable than cephazolin to the beta-lactamase produced by *Staphylococcus aureus* and to the betalactamases of some gram-negative bacilli.

Ceftazidime acts against many gram-positive and gram-negative organisms, especially *Pseudomonas.* In adults, a dose of l-2g intramuscularly or intravenously is given every 8-12 hours. Retinotoxicity is one of the adverse effects.

Cefuroxime and cefotaxime are available only as injectable preparations.

Aminoglycosides

This group includes streptomycin, soframycin, neomycin, gentamicin, sisomycin, netilmycin, tobramycin and amikacin, which are all bactericidal. Though they have a broad spectrum of activity against many gram-negative organisms and gram-positive staphylococci, they provoke allergy and bacterial resistance. All these agents are toxic to the eighth nerve and the kidney, and interfere with neuromuscular conduction, causing serious paralysis in patients with myasthenia gravis or those receiving neuromuscular blocking agents. Intravitreal injections are retinotoxic and may cause macular infarction.

Streptomycin: This bactericidal drug is used in the treatment of *Mycobacterium tuberculosis* infections but the organism rapidly develops resistance. Thus, the drug should be used only after confirmation of *in vitro* susceptibility and in combination with a second drug to prevent resistance developing during treatment.

Soframycin is highly effective against gram-positive cocci and gram-negative bacilli including *Ps. pyocyanea.* It is not available for systemic use and can only be administered topically as drops or ointments.

Gentamicin: This drug may be used parenterally for the treatment of serious infections by gram-positive and gram-negative organisms. As the margin between toxicity and efficacy is narrow, it should be reserved for infections resistant to other antibiotics. Because it is nephrotoxic and ototoxic and secreted through the kidneys, the dose must be decreased in patients with renal disease. It is also retinotoxic. Gentamicin is effective against an exceptionally wide range of bacteria which includes penicillin-resistant strains of staphylococci and *Ps. pyocyanea. Pseudomonas* strains show an increasing incidence of resistance to gentamicin, therefore amikacin is recommended for treating intraocular infections. Bactericidal concentrations are found in the aqueous following topical administration of 0.3-2% drops, or 20-40 mg subconjunctivally. As it may occasionally cause conjunctival necrosis, the sub-Tenon route is recommended.

Neomycin: This has similar properties to gentamicin but is too toxic for parenteral use. It can be used topically, especially in combination with another antibiotic as eye drops or ointment, but often causes contact allergy.

Sisomycin and *netilmycin* are similar to gentamicin, but are more effective against gram-negative organisms.

Tobramycin is more effective than gentamicin against *Pseudomonas,* but less for other gram-negative bacteria such as the *Enterobacteriaceae.* Fortified drops enhance bioavailability and it can also be given sub-conjunctivally or intravitreally.

Amikacin acts against many gram-positive and gram-negative organisms. It is less retinotoxic than gentamicin, but is more retinotoxic than ceftazidime. For the treatment of endophthalmitis, 0.4 mg amikacin is injected intravitreally along with vancomycin, which acts synergistically.

Tetracyclines

Tetracyclines such as tetracycline, chlortetracycline and oxytetracycline are broad-spectrum antibiotics with considerable bacteriostatic action against both gram-positive and gram-negative organisms as well as some fungi, rickettsiae and the chlamydiae; the last group includes the infective agent of trachoma. Many bacteria have now developed resistance to these drugs. Their ability to penetrate the ocular tissues either from the conjunctival sac or after systemic administration is small. They are administered essentially in the form of drops or ointment for superficial ocular infections such as trachoma. They may occasionally be used orally in acne rosacea and chronic staphylococcal infection of the lids and conjunctiva. Doxycycline and minocycline provide better aqueous concentrations. They get deposited in growing bones and teeth and hence are not to be used in children and pregnant or lactating mothers.

The macrolides and the lincomycin group

Erythromycin, azithromycin, lincomycin and clindamycin are relatively narrow-spectrum bacteriostatic agents used for treating gram-positive infections and those due

to *Chlamydia* and *Toxoplasma gondii.* They may be given orally (but there is a tendency to cause diarrhoea), or parenterally, when there is a possibility of damage to the liver or fever due to the drug.

Azithromycin is long acting and is used as a single stat dose of 500-1500 mg (20-30 mg/kg) in the treatment of trachoma, toxoplasmosis and Lyme disease.

Glycopeptides

Vancomycin is a bactericidal antibiotic very effective against nearly all gram-positive organisms as well as against methicillin-resistant *Staphylococcus aureus* and *Staphylococcus epidermidis.* A dose of lmg in 0.1ml is given intravitreally for endophthalmitis.

It is the drug of choice in endophthalmitis together with amikacin or ceftazidime. It is toxic if used topically or subconjunctivally.

Fluoroquinolones

These bactericidal drugs are derivatives of nalidixic acid and have a broad spectrum of activity. Ciprofloxacin, norfloxacin, ofloxacin and lomefloxacin are used topically and have prolonged bactericidal concentrations in the tear film. Because these drugs get deposited in the growing cartilage, they are not routinely recommended for treating children below 12 years of age.

Other antibiotics

Chloramphenicol: This bacteriostatic antibiotic is effective against bacteria, spirochaetes, rickettsiae, chlamydiae and mycoplasmas. The molecule is small and lipid soluble so that on systemic administration it enters the eye in therapeutic concentrations. However, its effects on intraocular inflammations are usually not dramatic. It has the widest spectrum for superficial ocular infections and does not commonly cause resistance to develop. Of all topical antibiotics, it is the least toxic to the corneal epithelium. Topical administration may rarely lead to blood dyscrasias.

Polymyxins are potent antibiotics against gram-negative bacteria. They are often used topically in combination with neomycin, bacitracin and gramicidin for superficial eye infections. They are useful against extra- or intraocular infections of *Ps. pyocyanea,* administered as drops in the former or as subconjunctival injections in the latter.

Sulphonamides

This group of drugs has a bacteriostatic effect on most gram-positive bacteria and chlamydia. They are used in the treatment of toxoplasmosis in combination with pyrimethamine or trimethoprim. Topical 10-30% sulphacetamide is used in the treatment of trachoma.

Antiviral agents

Antiviral drugs used to treat herpesvirus infections are usually pyrimidine and purine derivatives.

Pyrimidine derivatives

A non-selective virustatic drug, 5-iodo-2-deoxyuridine (IDU) inhibits the synthesis of DNA and, on topical application, prevents the replication of the herpesvirus. Eighty-five per cent of initial dendritic ulcers treated with 0.1% IDU drops every 1-2 hours and 0.5% ointment at night are cured within 2 weeks, but some toxicity may be apparent. However, it does not cure stromal keratitis or prevent recurrences. When corticosteroids are used to suppress the host response that leads to destructive stromal disease along with IDU, the antiviral effect of the combination may be insufficient to prevent permanent vascularization and scarring of the cornea. Commonly seen toxic reactions are superficial punctuate keratitis, follicular conjunctivitis and punctal occlusion.

Trifluorothymidine (F_3T) used as 1% drops five times a day results in the healing of 90% of herpetic ulcers in 2 weeks. This drug is soluble and more effective than others in the prevention of complications produced by corticosteroids. Only a few strains of herpes simplex virus are resistant to F_3T.

Purine derivatives

Adenine arabinoside, another virustatic antiviral substance, has no activity against stromal disease and produces the same forms of toxicity as IDU. It acts by blocking the synthesis of nucleic acids. It can be given clinically only in the form of a 3% ointment five times a day.

Acyclovir is a selective, virustatic drug, which is activated largely in virus-infected cells. It is of proven value in the treatment of acute cases of the common herpesvirus infections such as herpes simplex keratitis and herpes zoster. It is used as 3% ointment five times a day till all activity subsides and is less toxic than the other antiviral drugs. Systemic administration is required in some forms of ocular herpes infections such as recurrent herpes simplex keratitis, herpes simplex iridocyclitis, and acute herpes zoster ophthalmicus. Oral acyclovir 400 mg five times a day for 5-7 days is used for acute herpes simplex infections and 200 mg twice daily for 6 months to 1 year if used prophylactically against recurrent disease. Oral acyclovir in a dose of 800 mg five times a day for 7-10 days is administered within 72 hours of an acute attack of herpes zoster ophthalmicus to decrease the incidence of neuralgia in herpes zoster and reduce the likelihood and severity of complications such as uveitis. It is also effective against the Epstein-Barr virus and cytomegalovirus (CMV). The intraocular penetration after oral

and intravenous administration is good and it can thus be administered for the treatment of keratouveitis and acute retinal necrosis.

Ganciclovir is a derivative of the antiviral nucleoside, acyclovir. It has good antiviral activity against herpes simplex viruses 1 and 2, Epstein-Barr virus, and is at least 10-100 times more potent an inhibitor of CMV replication *in vitro* than acyclovir. It is administered intravenously in a dose of 3.5-5 mg/kg twice daily for 10-20 days and then 5 mg/kg is given 6 hourly. An oral maintenance dose of 1 g is given thrice daily with meals. Intravitreal injection or an ocular implant containing 5-6 mg of ganciclovir can be inserted into the vitreous. The implant releases the drug such that a level of 4 lxg/ml of the active drug is maintained for up to 8 months.

The newer antivirals, valacyclovir (1000 mg three times daily for adults) and famcyclovir (500 mg three times daily for adults), are at least as effective as acyclovir.

Other antiviral agents

Foscarnet inhibits the replication of all human herpes and retroviruses. It is nephrotoxic and is used only for severe CMV infection or acyclovir-resistant herpetic disease among HIV-positive individuals.

Zidovudine inhibits the virus-induced reverse transcriptase which is essential for virus replication in the infective process. This drug is used extensively in the treatment of HIV-infected individuals. It is effective for CMV retinitis in doses of 100-200 mg five times a day. Prophylactic zidovudine therapy should be initiated as soon as possible after the diagnosis of AIDS.

Table 13.3 lists some commonly used antiviral drugs and their dosage for ocular administration.

Antifungal agents

Polyene antibiotics

Amphotericin B is the most effective antibiotic in the treatment of systemic fungal infections. It is used in the therapy of keratomycosis, metastatic and exogenous endophthalmitis, and is effective against both yeast and filamentous fungi. It is used topically as 0.1-0.25% drops or a 2.5% ointment. It can be given in a dose of 5-10 p.g intravitreally and incremental doses are given i.v. in distilled water or 5% dextrose up to a total dose of 3-4 g. Prolonged use may cause kidney, bone marrow or CNS toxicity.

Nystatin is used against certain fungal infections, Particularly *Candida albicans.* It is not absorbed by mouth and is applied topically as a suspension (1 00 OOOunits/g).

Natamycin is used topically in the treatment of superficial filamentous fungi and *Candida albicans* infections as it does not penetrate the cornea. A 5% suspension is applied every hour and then tapered off as the infection subsides.

Imidazoles

These drugs have a complex mechanism of action causing changes in the permeability of fungal cell membranes by blocking the production of ergosterol. They are less toxic than the polyenes and are also effective against bacteria and *Acanthamoeba.*

Miconazole is effective against yeast and filamentous fungi and is used topically as 1% drops hourly or as a 2% ointment given 6 hourly. In high concentrations miconazole is fungicidal.

Ketoconazole is active against *Candida,* but not as much against *Aspergillus.* In cases of fungal endophthalmitis, adnexal or severe comeal infections, it can be given orally in a dose of 200-800 mg daily for 7 days and up to several months, depending upon the healing response. Its adverse effects include liver toxicity. Subconjunctival and intravitreal injections may also be given.

Triazoles

Fluconazole is particularly effective against *Candida* and *Cryptococcus.* Oral absorption is good, with effective corneal and anterior chamber concentrations at 100-200 mg 6 hourly. A topical solution of 0.2% is used.

Itraconazole: This drug is similar to ketoconazole and is well tolerated orally in a dose of 100-400 mg daily. A 1% solution may be used topically.

Fluconazole has the lowest overall incidence of adverse effects and has emerged as a preferred oral drug for candidiasis. It also has the highest activity against *Cryptococcus,* but otherwise has a narrower antifungal spectrum than the other azoles. Ketoconazole has the highest incidence of adverse effects, which limits its usefulness. Itraconazole and voriconazole have activity against *Aspergillus,* which normally must be treated with amphotericin B. Terbinafine is indicated for fungal infections of the skin and nails.

Commonly used antifungal agents, their dosages and routes of ocular administration are detailed in Table 13.4.

Table 13.3 Antiviral ocular medications

Medication	Concentration
5-iodo-2-deoxyuridine (IDU)	0.1% drops/0.5% ointment
Trifluorothymidine	1 % drops
Adenine arabinoside	3% ointment
Acyclovir	3% ointment

Table 13.4 Antifungal medications

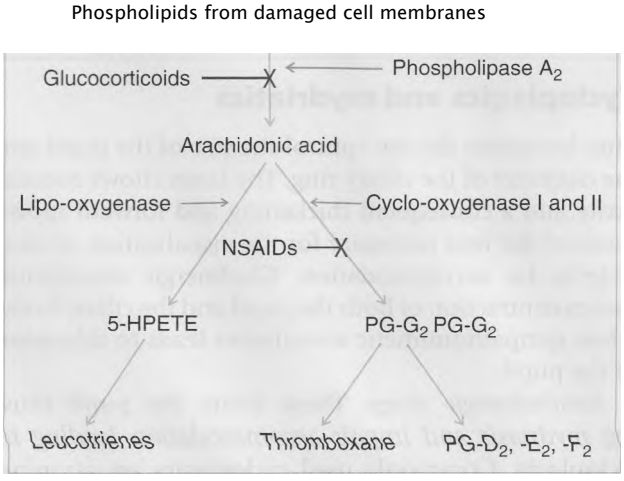
Drug	Topical	Subconjunctival	Intravitreal
Amphotericin B	1–10mg/ml drops, 2.5% ointment	0.37 mg	5–10 jj,g
Natamycin	5% suspension		25 (xg
Miconazole	1 % drops, 2% ointment		
Ketoconazole	1–5%		0.5 mg
Fluconazole	0.2–2%		0.1 mg
Flucytosine	1%		
Voriconazole	1–2%		100 n,g

ANTI-INFLAMMATORY THERAPY

Corticosteroids

Corticosteroids are very effective for treating inflammations and immune-related ocular diseases. Unfortunately, they also produce substantial local and systemic side effects. They act by suppressing the formation of arachidonic acid and other inflammatory mediators by the induction of phospholipase A_2 inhibitory proteins, called lipocortins. Lysosomal membranes are stabilized and the production of lymphokines and prostaglandins is decreased (Flowchart 13.1). Prolonged use of corticosteroids may lead to the formation of posterior subcapsular opacities in the lens and is known to cause glaucoma in genetically susceptible persons.

The general clinical effect of these drugs is a temporary blockage of the exudative phases of inflammation and an inhibition of fibroblast formation during tissue repair, whether the cause of the disease is bacterial, anaphylactic, allergic or traumatic. In acute inflammations,



Flowchart 13.1 The inflammatory cascade and anti-inflammatory therapy. PG, prostaglandins; 5-HPETE, 5-hydroxyper oxyeicosatetraenoic acid.

capillary permeability is decreased and cellular exudation reduced, while in the stage of healing, the formation of granulation tissue, new vessels and fibrosis is diminished. It is of the utmost importance to remember that corticosteroids do not affect the cause of any disease but merely provide tissues with a temporary protection against an irritant—organismal or otherwise. The tissue cells are hence protected from inflammatory injury and are able to function normally in an environment which has become grossly abnormal. This effect is limited to the blocking of the pathological evidences of inflammation as long as the administration of the drug is continued. The disease resumes its natural course once the drug is withdrawn. Therefore, it follows that corticosteroids primarily control acute disease and are completely ineffective in the removal of structural damage caused by old or long-standing inflammation, nor are they of any value in the treatment of degenerative conditions.

Topical therapy avoids the numerous systemic side effects of corticosteroids, such as immunosuppression, osteoporosis, hyperglycaemia, hypertension and gastrointestinal ulceration. A solution of 1% prednisolone acetate has the greatest anti-inflammatory action, followed by 0.1% fluorometholone acetate, 0.1% dexamethasone acetate and 0.1% betamethasone. Fluoromethalone 0.1%, 1% medrysone (medroxyprogesterone) and a 1% suspension of rimexolone are less likely to cause a rise in intraocular pressure. Loteprednol is a 'soft' steroid has no effect on the intraocular pressure or systemic side effects as it binds to the glucocorticoid receptor and the remainder is rapidly metabolized to an inactive metabolite in the eye. Corticosteroids are used as drops every 6 hours or more frequently, depending on the degree of inflammation. Administration of an ointment at night is particularly useful as the medication is equally well absorbed into the eye and has a longer duration of action. Local therapy by corticosteroids has been found to be beneficial in phlyctenular and rosacea keratitis, spring catarrh, episcleritis, some forms of deep keratitis (including zoster and certain stages of other viral diseases) and the acute and subacute phases of iridocyclitis.

ev&\ \v, Awd cctV&va vafes&w towdVvioRs, Vi-

Frequent instillation of drops is as effective as subconjunctival injections. Periocular injections of corticosteroids, such as 40 mg triamcinolone acetonide, are indicated for chronic intermediate uveitis and other posterior segment diseases. Proliferative retinal changes after endophthalmitis are prevented by using 1 mg dexamethasone injections intravitreally, under cover of appropriate antibiotics.

Steroids can down-regulate inflammatory stimuli by modulating the response of the vascular endothelial growth factor (VEGF) gene, whose antigens are present on human retinal pigment epithelium (RPE). They thus may play a role in regulating edema. Triamcinolone acetonide in an intravitreal dose of 1/2/4 mg has been evaluated in the treatment of retinal diseases such as diabetic retinopathy, exudative age related macular degeneration, cystoid macular edema, venous occlusion, Eales' disease etc. In the setting of macular degeneration, neovascularization disrupts the blood-brain barrier function of the RPE, and it has been shown that Triamcinolone acetonide can induce RPE proliferation and stabilization.

Oral prednisolone in a dose of 50-150 mg (1-2 mg/kg), daily or on alternate days, is used to treat inflammations of the orbit, panuveitis, postoperative inflammation and systemic diseases causing ocular problems. Alternate-day therapy reduces the suppression of normal adrenal function. High doses of methylprednisolone intravenously are given in 'pulses' to treat optic neuropathies.

Non-steroidal anti-inflammatory drugs (NSAIDs)

These drugs are now replacing steroids in less severe or more chronic inflammations. They act by inhibiting the cyclooxygenase pathway for prostaglandin formation (Flowchart 13.1). Topical NSAIDs are used for the management of anterior segment inflammation and the prophylaxis of cystoid macular oedema. Systemic supplementation is required for diseases involving the retina and uvea.

Indomethacin 0.5-1% drops given four times every 15 minutes, 1 hour before extracapsular cataract surgery along with mydriatic-cycloplegics are used for preventing intraoperative miosis, and 6 hourly in the management of postoperative inflammation.

Flurbiprofen 0.03% has good corneal penetration, and is useful in preventing intraoperative miosis when given four to six times prior to surgery.

Ketorolac as 0.5% drops is effective in the treatment of allergic conjunctivitis—a marked decrease in itching has been reported by patients.

Diclofenac 0.1% drops are used 6 hourly postoperatively and in the treatment of uveitis to prevent the occurrence of cystoid macular oedema.

THERAPY FOR OCULAR ALLERGIES

Antihistamines

Antihistamines show a competitive antagonism to histamine at the receptor site (II, and H_2 receptors). Antihistamine eye drops are commonly combined with vasoconstrictors to take care of both the congestion and symptoms of itching. They are used for vernal keratoconjunctivitis, giant papillary conjunctivitis and other forms of allergic conjunctivitis. Antazoline and chlorpheniramine are administered topically four times a day. 11, receptor antagonists are emedastine used four times a day, and azelastine used once or twice a day. In severe cases, loratadine, cetrizine and astemizole can be used systemically.

Mast cell stabilizers

These drugs stabilize the membranes of mast cells, preventing the release of histamine. They can also have an antihistaminic action.

Cromolyn sodium given as 2-4% drops 6 hourly is used prophylactically in chronic allergies such as vernal catarrh and giant papillary conjunctivitis. A 2% ointment can be used at night. The onset of its mast cell stabilizing effect takes 3-4 weeks.

Ketotifen drops are instilled thrice a day. This drug is also a mast cell stabilizer but has the advantage of a quicker onset of action.

Lodoxamide is much more potent than cromolyn sodium and 0.1% drops are used thrice a day.

Olopatadine has both a mast cell stabilizing effect and an antihistaminic action. It is administered as 0.1% drops 12 hourly.

DRUGS AFFECTING THE PUPIL AND ACCOMMODATION

Cycloplegics and mydriatics

Muscles within the eye control the size of the pupil and the diameter of the ciliary ring. The latter allows zonular laxity and a consequent thickening and forward movement of the lens necessary for the visualization of near objects, i.e. accommodation. Cholinergic stimulation causes contraction of both the pupil and the ciliary body, while sympathomimetic stimulation leads to dilatation of the pupil.

Anticholinergic drugs: These dilate the pupil causing mydriasis and impair accommodation leading to cycloplegia. Commonly used cycloplegics are atropine 1%, homatropine 2%, cyclopentolate 1% and tropicamide 0.5%. They are used in determining the correct refraction of an eye, especially in children, as well as in

adults who are hypermetropic or those undergoing laser refractive surgery. Cycloplegics relax the ciliary spasm seen with anterior uveitis.

Atropine is the most potent and has the longest duration of action, retaining its activity for 7 days or more. Atropine 1% eye ointment is used for refraction and fundus examination in children, especially those with darkly pigmented irises and those less than 5 years of age. The ointment is instilled twice a day for three days before examination. Systemic absorption may occasionally lead to facial flushing hence ointment is preferred over drops in young children. Atropine 1% drops or ointment may also be used as 'penalization' therapy in the better eye, in patients with amblyopia. Contact dermatitis occurs relatively frequently when atropine is used for prolonged periods. Homatropine 2% drops are less potent and used in the treatment of uveitis and for refraction in children. Its effect lasts for 4-5 days.

Cyclopentolate has a shorter duration of action, lasting up to 24 hours. Cyclopentolate 1% drops three times 5 minutes apart are used for refraction and fundus examination in children.

Tropicamide 0.5%, 1% drops three times 5 minutes apart are short-acting. Though effective for up to 3 hours, the maximum cycloplegic effect appears 30 minutes after the last drop and lasts for only 10-15 minutes, so proper timing of refraction is crucial.

Side effects of cycloplegics are blurred vision and photophobia. Driving immediately after dilatation or cycloplegia is not recommended. In patients above 60 years of age having hypermetropia and a shallow anterior chamber, mydriasis may precipitate acute angle-closure glaucoma.

Sympathomimetics

These dilate the pupil and are used prior to fundus examination or retinal laser procedures. They are used in combination with cycloplegics in the preoperative preparation of patients undergoing cataract surgery. Phenylephrine 5-10%, a selective alpha-1 agonist, is commonly used. Side effects include stinging on application, and a rise of blood pressure in predisposed individuals.

MEDICAL THERAPY FOR GLAUCOMA

At present, the treatment of glaucoma is aimed at lowering the intraocular pressure to levels that permit the normal functioning of the optic nerve. This is achieved by suppressing the production of aqueous or by increasing the outflow of aqueous through the trabecular meshwork or the uveoscleral pathway. Medications directed towards preventing neural cell loss are presently under investigation, e.g. memantine and brimonidine (Table 13.5).

Parasympathomimetics

Cholinergic agents help to improve the trabecular outflow of aqueous. Longitudinal fibres of the ciliary muscle are attached to the scleral spur and contraction of these fibres exerts a pull on the trabecular meshwork increasing the size of the pores. In eyes having a narrow angle recess or angle-closure glaucoma, constriction of the pupil pulls the peripheral iris away from the angle structures, opening a functionally closed angle. Pilocarpine has been used in the treatment of glaucoma for over a century. It is commonly used as 2-4% drops 6-8 hourly. Its therapeutic effect begins in half an hour, with a peak action at 2 hours. Pilocarpine 4% in a high-viscosity acrylic gel is effective for 18-24 hours. Controlled delivery of pilocarpine is available through ocuserts that release pilocarpine at 20 (jug or 40 (jig/hour for a week. Pilocarpine causes an 18-25% fall in intraocular pressure, but its use is limited by the occurrence of miosis, browache and accommodative spasm. In patients with dark-coloured irises, these side effects are less troublesome.

Sympathomimetics

Non-selective alpha- and beta-agonists

Epinephrine 1% (adrenaline) given twice daily lowers intraocular pressure by increasing the rate of aqueous outflow. The fall in intraocular pressure can be seen in an hour, but is maximal at 4 hours. The use of epinephrine causes local complications such as stinging, reactive hyperaemia, adrenochrome deposits and cystoid macular oedema in aphakic eyes. It is contraindicated in patients with narrow anterior chamber angles due to the mydriasis it produces, and should be used with care in patients with systemic hypertension, thyrotoxicosis and diabetes.

Dipivefrine 0.1% is a pro-drug that is more lipid soluble and is converted to epinephrine once inside the eye. This decreases the incidence of local and systemic side effects.

Alpha-agonists

Alpha-agonists reduce the production of aqueous humour and increase aqueous outflow.

Clonidine produces a fall in intraocular pressure by decreasing aqueous secretion and also, to a lesser extent, by increasing trabecular and uveoscleral outflow. It is used as 0.06 or 0.125% drops 6-8 hourly, which is equivalent in action to 2% pilocarpine. Conjunctival blanching, sedation, dryness of the mouth and a fall in systemic blood pressure are the known side effects with this drug. It is commercially available only in Europe.

Apmclonidine has mixed alpha-1 and alpha-2 stimulatory activity. The maximum fall in intraocular pressure is seen in 2 hours and its effect lasts for 12 hours. It is commonly used as 0.25-1% drops for the prophylaxis

Table 13.5 Topical medications for glaucoma

Pharmacological group	Name of drug	Ocular side-effects	Systemic side-effects	Contraindications
Parasympathomimetics	Pilocarpine 2-4%	Fluctuating and blurred vision, miosis, browache, accommodative spasm	Increased sweating and salivation, urinary frequency, diarrhoea, bronchospasm	Uveitis
Adrenergic antagonists				
Non-selective beta-blockers (p-1 and p-2)	Timolol 0.25-0.5%	Stinging, local anaesthesia	Bronchospasm, bradycardia, decreased cardiac output, hypotension, depression, impotence, altered lipid profile	Asthma, chronic obstructive pulmonary disease, congestive heart failure, sinus bradycardia, atrioventricular blocks
Selective beta-blockers (P-1)	Betaxolol 0.25-0.5%	Stinging, local anaesthesia	Less pulmonary side-effects	Sinus bradycardia, atrioventricular blocks
Sympathomimetics				
Non-selective (a-1, a-2, P-1, P-2)	Dipivefrine 0.1%	Follicular conjunctivitis, rebound congestion, macular oedema in aphakes	Increase in blood pressure, arrhythmias	Angle-closure glaucoma, cardiovascular disease
Selective (a-2)	Brimonidine	Conjunctival blanching, ocular allergy	Drowsiness, fatigue, blood pressure changes	Use of MAO inhibitors, Parkinson disease, hypertensive crisis
(a-1 and a-2)	Apraclonidine	Allergies, fluctuation in visual acuity	Headache, drowsiness, fatigue	As above, but fewer
Carbonic anhydrase inhibitors	Dorzolamide 2% Brinzolamide	Punctate keratitis, ocular allergies	Bitter taste, headache, asthenia, renal calculi	Hypersensitivity to sulphonamides, eye injury
Prostaglandins and hypotensive lipids	Latanoprost 0.005% Bimatoprost 0.03% Travoprost 0.004%	Iris pigmentation, punctate keratitis	Headache, symptoms of upper respiratory tract infection	Ocular infection or inflammation

of spikes of raised intraocular pressure after laser or surgical procedures and in other short-term increases in intraocular pressure. An ocular allergic reaction is very common, as are conjunctival blanching and follicular conjunctivitis. Systemic side effects are dry mouth, fatigue and drowsiness.

Brimonidine has a significantly higher relative selectivity for the alpha-2 receptors, hence cardiovascular and pulmonary effects are minimized. It appears to work largely by increasing the uveoscleral outflow and reducing aqueous inflow. A fall in intraocular pressure of 20-25% is seen when it is given as 0.2% drops twice or thrice a day. Contact allergy is recorded in about 15% of patients and systemic side effects are similar to those of apraclonidine.

Adrenergic antagonists

Beta-blockers

Beta-blockers decrease the rate at which the aqueous is produced. The non-specific beta-1 and beta-2 receptor blockers, e.g. timolol, levobunolol, carteolol and metipranolol, appear to have a slightly greater pressure-lowering effect than the specific beta-1 receptor blocker betaxolol, but the latter is safer in patients with pulmonary disease such as asthma or emphysema, and may have less of an effect on blood pressure. Initial control of intraocular pressure with these drugs is very good, but with tachyphylaxis this decreases in a few months to a 25% reduction in intraocular pressure. It must be remembered that oral beta-blockers are commonly used for hypertension and angina and, in these situations, also lower intraocular pressure. Common side effects are a dry eye, bradycardia, bronchial spasms, depression and fatigue. These drugs are contraindicated in patients with asthma or chronic bronchitis, atrioventricular blocks and cardiac failure.

Timolol maleate 0.25-0.5% drops are given twice a day while gel preparations are available for use once daily.

Levobunolol 0.25-0.5% drops have a similar efficacy but a longer half-life than timolol.

Betaxolol is the only beta-1 specific betablocker and has fewer pulmonary side effects. It is believed to increase the perfusion of the optic nerve head. It is slightly less effective than both timolol and levobunolol when used as 0.25-0.5% drops.

Carteolol has intrinsic sympathomimetic activity and causes less bradycardia. It is well tolerated locally, but its efficacy as 1-2% drops is less than that of other beta-blockers.

Prostaglandin analogues and hypotensive lipids

Prostaglandin analogues lower intraocular pressure by stimulating a prostanoid receptor in the ciliary muscle. This causes the release of matrix metalloproteinases and increases the uveoscleral outflow. They are additive with all other agents.

Latanoprost is a pro-drug and is activated during its passage through the cornea. When used in a concentration of 0.005% once a day, it lowers the intraocular pressure by 25-30%. This is equivalent to the effect produced by timolol, with which latanoprost shows a further additive effect. Latanoprost can also lower the intraocular pressure to a moderate extent in normotensive eyes. Common side effects are conjunctival hyperaemia, superficial punctate keratopathy and pigmentation of the iris. Tachyphylaxis has not been reported.

Unoprostone 0.12%, another prostaglandin derivative, is less effective than latanoprost.

Newer drugs with similar properties are *bimatoprost* and *travoprost.*

Carbonic anhydrase inhibitors

Carbonic anhydrase inhibitors block the action of carbonic anhydrase and reduce the production of aqueous in the eye.

Acetazolamide reduces the production of aqueous by 30-40% and substantially lowers the intraocular pressure. It is commonly used for controlling very high intraocular pressures in acute angle-closure glaucoma and secondary glaucomas. Tablets of 250 mg administered 6 hourly have a maximal effect in 2 hours and lasts for 4-6 hours. Sustained-release preparations of 500 mg act for up to 18 hours. Acetazolamide 500 mg administered intravenously lowers the intraocular pressure within 20 minutes. Patients commonly complain of altered taste, loss of appetite, paraesthesias of the hands and feet, depression and transient myopia. Systemically, carbonic anhydrase inhibitors are known to produce metabolic acidosis, renal stones and, rarely, blood dyscrasias.

Methazolamide, though not as effective, is less likely to cause renal stones and acidosis as compared to acetazolamide.

Dorzolamide 2% is the first topical carbonic anhydrase inhibitor. It is used twice or thrice daily and causes a fall in intraocular pressure of 13-24% in the long term. Patients complain of a bitter taste and common allergic reactions. There is a possible decomposition of the corneal endothelium in predisposed individuals. Systemic side effects of topical carbonic anhydrase inhibitors are uncommon.

A newer topical carbonic anhydrase inhibitor is *brinzolamide* 1%.

Hyperosmotic agents and hypotensive lipids

Hyperosmotic agents increase the osmolality of the serum causing water to leave the vitreous cavity, thereby lowering the intraocular pressure, reducing the vitreous volume and deepening the anterior chamber. An ideal hyperosmotic agent should be rapidly absorbed and distributed, and have a high molecular weight so that it does not enter the eye.

Mannitol 5-25% is given intravenously at a dose of l-2g/kg. It is well tolerated, but should be given with caution in uncontrolled hypertensives, those with pulmonary oedema and cardiac or renal failure. Urinary retention may occur in patients with prostatic hypertrophy.

Glycerol 0.6g/ml is administered up to a maximum dose of l-1.5g/kg twice or thrice daily. It is sickeningly sweet and induces nausea and vomiting but can be taken mixed with lemon juice. It is less suitable for diabetics.

MEDICAL THERAPY FOR DRY EYE

Ageing causes a gradual decrease in the secretions from the various glands of the eye and ultimately affects the stability of the tear film which is important for clear vision and comfort of the eye. Diseases affecting the conjunctiva, such as trachoma, benign pemphigoid, vernal catarrh, or those affecting the secretion of the lacrimal glands such as Sjogren syndrome can also cause a 'dry eye'. A dry eye is an irritated eye. There are many tear substitutes available, which largely replace the aqueous component of tears. They should contain electrolytes, be viscous, have an alkaline pH and should remain in contact with the cornea. The available substitutes commonly contain hydroxypropylmethylcellulose, hydroxyethylcellulose, polyvinyl alcohol, carboxymethylcellulose, hyaluronic acid and chondroitin sulphate. Polyvinylpyrrolidone 0.03% drops have a mucomimetic action. It is worth remembering that preservatives in standard commercial preparations can themselves be epitheliotoxic to the cornea and conjunctiva if the medication is used very frequently. Benzalkonium chloride is the most epitheliotoxic among the preservatives, and povidone and chlorobutanol are better tolerated and, therefore, superior. Preservative-free drops are an even better alternative. Some newer preservatives such as sodium perborate and purite disintegrate into harmless molecules on contact with the eye and exposure to light. Slow release of tear supplements by a conjunctival insert is useful in patients who find it difficult to apply drops frequently. For such patients, preservative- and lanolin-free ointments are used at night.

Dry eye is associated with chronic inflammation of the ocular surface and both entities interchangeably have both a cause and effect relationship in general and this particularly may be more marked in chronic connective

Table 13.6 Composition of commonly used irrigating solutions

Ingredients in mEqs	Ringer lactate	Normal aqueous	Normal vitreous	Balance salt solution (BSS)	BSS plus
Sodium	131	162.9	144	155.7	160
Potassium	5	2.2–3.9	5.5	10.1	5
Calcium	4	1.8	1.6	3.3	1
Magnesium		1.1	1.3	1.5	1
Chloride	111	131.6	177	128.9	130
Bicarbonate		20.15	15		25
Phosphate		0.62	0.4		3
Lactate	29	2.5	7.8		
Glucose		2.7–3.7	3.4		5
Glutathione		0.0019			0.3
Ascorbate		1.06	2		
Citrate				5.8	
Acetate				28.6	
Ph	6.25	7.38		7.6	7.4
Osmolarity (mOsm)	270	304		298	305

tissue or autoimmune disorder such as rheumatoid arthritis or Sjogren's syndrome. In such situations known to be associated with dysfunctional tear syndrome, activation of T cells and increased levels of inflammatory markers can be controlled by local immunomodulating agents such as typical cyclosporin 0.05% eye drops administered twice daily for 3-6 months or even longer which can be useful for controlling the signs and symptoms and easing the discomfort.

PHARMACOLOGICAL AGENTS USED IN INTRAOCULAR SURGERY

Irrigating solution

These are physiological solutions with different electrolytes and varying composition which are used to irrigate the eye and maintain the intraocular pressure during surgery. They also provide a fluid infusion to facilitate flow and aspiration of the lens and reconstitute the aqueous humour in the anterior chamber at the end of surgery. The fluids used have different combinations of salts and electrolytes to match the physiological composition of the aqueous and protect the delicate intraocular structures particularly the metabolically active corneal endothelium. Additives to the infusion fluid include preservative-free antibiotics and adrenaline (0.3 ml of 1:1000 adrenaline in 500 ml) in routine cases. The former have a prophylactic role and the latter help to maintain adequate pupil dilatation. Use of adrenaline is contraindicated in hypertensive patients and those with ischaemic heart disease. In young children preservative-free low molecular weight heparin can be added to the irrigating fluid in a dose of 10 IU per ml to prevent postoperative severe fibrinous inflammatory membrane formation. Table 13.6 shows the composition of commonly used irrigating solutions.

Viscoelastics or viscosurgical devices

Viscous inert non-toxic fluids that assist the surgeon in different intraocular surgeries are known as viscoelastics or viscosurgical devices. Depending on their physicochemical properties they may be used to maintain spaces within the eye, for manipulating tissues, isolating compartments of the eye, in times of intraoperative complications or as protection for delicate structures such as the corneal endothelium. They can be classified as either cohesive or dispersive. Cohesive viscoelastic molecules adhere to each other and are useful as spacers and for tissue manipulation, and are easy to remove. They are best used for capsulorhexis and placement of intraocular lenses. Dispersive viscoelastics coat ocular surfaces, remaining in position during irrigation, and are utilized especially for protecting the corneal endothelium in phacoemulsification.

Sodium hyaluronate 1% is a cohesive viscoelastic, which is characterized by a high molecular weight, high pseudoplasticity and high surface tension. It provides excellent space maintenance, facilitates intraocular lens implantation, and is easily removed. A combination of 4% *chondroitin sulphate* and 3% *sodium hyaluronate* is a highly retentive, dispersive viscoelastic. It is characterized by a low molecular weight, low pseudoplasticity and low surface tension. It provides good maintenance of space and excellent tissue protection.

Table 13.7 Different ocular viscosurgical devices (OVDs) used during cataract surgery

Composition	Commercially available	Main properties	Indications for use
Hydroxypropyl-methylcellulose 3%	Visilon, Moisol, Adatocel, Ocu-coat, etc.	Viscoelastic	Extracapsular cataract surgery, conventional and manual SICS and phacoemulsification
Sodium hyaluronate 1 %	Healon, Amvisc	Viscoelastic and cohesive	Especially if shallow anterior chamber, small pupil, mature white cataract or in children
Sodium hyaluronate 1.4%	Healon G.V.	Cohesive	Especially if shallow anterior chamber, small pupil, mature white cataract, hard nucleus or in children
Sodium hyaluronate 2.4%	Healon 5	Viscoadaptive	Phacoemulsification of hard cataract and cases with small pupil
Sodium hyaluronate 3% and chondroitin sodium sulphate 4%	Viscoat	Viscoelastic with a high coating ability	Especially in cases with compromised corneal endothelial function

Hypermellose 2% is less viscous than sodium hyaluronate and is used to coat intraocular lenses and instruments during cataract extraction and intraocular lens insertion. Table 13.7 gives composition and properties of different ocular viscosurgical devices.

ANTIMITOTIC AGENTS OR ANTIMETABOLITES

Antimetabolites are specifically antitumour drugs, but some of them have been used to decrease the fibroblastic response in different ocular surgeries.

5-Fluorouracil (5-FU): Failure of glaucoma filtering surgery is commonly due to excessive scarring in the postoperative period. 5-FU is a pyrimidine antagonist that interferes with nucleic acid synthesis. In a concentration of 50 mg/ml it can be placed under the conjunctiva peroperatively or administered as subconjunctival injections of 5 mg/ml daily or on alternate days, up to a total dose of 50 mg. Subconjunctival usage sometimes results in a keratopathy which is painful and difficult to treat. This may be prevented by ensuring that none of the 5-FU solution is allowed to leak into the palpebral sac. It has also been used in the treatment of proliferative vitreoretinopathy.

Mitomycin C (MMC) is an alkylating agent derived from *Streptomyces caespitosus.* It leads to a crosslinking of DNA as well as an inhibition of RNA and protein synthesis. Topical drops of 0.2-0.4 mg/ml of MMC have been used daily after pterygium surgery to reduce scarring and recurrences. There are reports of scleral ulceration and iridocyclitis following such applications. In glaucoma surgery at high risk of failure, a sponge soaked in 0.2-0.4 mg/ml of MMC is placed subconjunctivally or between the two scleral layers during surgery for a duration of 1-3 minutes.

Dyes

Dyes like trypan blue (0.06%), indocyanine green and sodium fluorescein are sometimes used to stain the anterior capsule to enhance its visualisation and facilitate performing the anterior capsulotomy. They are particularly useful in cases with dense cataracts and absence of any fundal glow, which normally permits visualization of the anterior capsule by retroillumination.

Anti-VEGF agents

Retinal ischaemia commonly occurs in retinal diseases such as diabetic retinopathy and retinal venous occlusions, leading to the subsequent development of neovascularization on the disc, NVD, or elsewhere in the retina, NVE, together with macular edema. Development of new vessels is also a feature in age related macular degeneration (neovascular form) and retinopathy of prematurity.

Photocoagulation—as per protocol, remains the standard treatment of choice, but has frequent adverse effects. Adjunctive modes of inhibiting vascular endothelial growth factor allow greater success in controlling the neovascularization. Pro-angiogenic factors are released in response to an ischaemic environment within the eye, the principal factor regulating angiogenesis and macular edema is vascular endothelial growth factor, VEGF. Adjunctive modes of inhibiting vascular endothelial growth factor allow greater success in controlling the neovascularization. Several anti-VEGF agents, such as Pegaptanib (Macugen), Bevacizumab (Avastin) and Ranibizumab (Lucentis), have been developed and are now being successfully used in pharmacotherapy of conditions like neovascular age related macular degeneration and diabetic retinopathy.

SUMMARY

Medications used to treat various eye conditions can be delivered by local application (ointments); topical instillation (eye drops); subconjunctival, subtenons, parabulbar, peribulbar, retrobulbar, intracameral or intravitreal injections; systemic administration by oral or intravenous route; and implantation of ocuserts or intraocular inserts for slow release of the medication for sustained prolonged duration of action.

There are a wide variety of medications used to treat various conditions and the choice of agent is determined by the dictum choose the most effective, least toxic, best tolerated drug in the right dose and frequency, for the shortest duration necessary, to achieve maximum efficacy and best compliance.

SUGGESTED READING

1. Onofrey BE, Skorin L, Holdemen NR (eds). *Ocular Therapeutics Handbook: A Clinical Manual.* Philadelphia: Lippincott-Raven, 1998.

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Chapter 14

Diseases of the Conjunctiva

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ANATOMY AND PHYSIOLOGY

Anatomically the conjunctiva is a thin mucous membrane lining the surface of the eye and eyelids and is divided into two portions, *palpebral* and *bulbar.* The folds or cul-de-sacs uniting the palpebral and bulbar portions are the *fornices* (Fig. 14.1). The palpebral conjunctiva is said to commence at the anterior margin of the edge of the lid, but from this point to the posterior margin of the edge *(the intermarginal jtrip)* and for about 2 mm beyond (to the *sulcus subtarsalis]* there is a transitional zone covered with stratified epithelium with the characteristics of both skin and conjunctiva. There are two layers of epithelium over the palpebral conjunctiva. The epithelium becomes gradually thicker from the fornices to the limbus, forming a s t r a t i fi ecTno'IT- kefalinized epithelium near the corneal margin. The rest of the palpebral conjunctiva lining the lids consists of thinner non-keratinized epithelium. Below the epithelium is an adenoid laver. consisting of loose connective tissue containing leucocytes, below which is a much denser fibrous layer, passing insensibly into the underlying tissues—lid or sclera. The palpebral conjunctiva is firmly adherent to the tarsus, while the bulbar portion is freely movable over the sclera except close to the cornea.

The blood supply of the conjunctiva is from the marginal arcade of the eyehd for the marginal conjunctiva, the peripheral arcade of the eyelid for the forniceal conjunctiva, the posterior conjunctival artery which is a branch of the peripheral arcade to within 4 mm of the limbus and the anterior conjunctival artery which is~a branch of the anterior ciliary for the limbus, and tne capillary arcades extending 1 mm into the cornea.

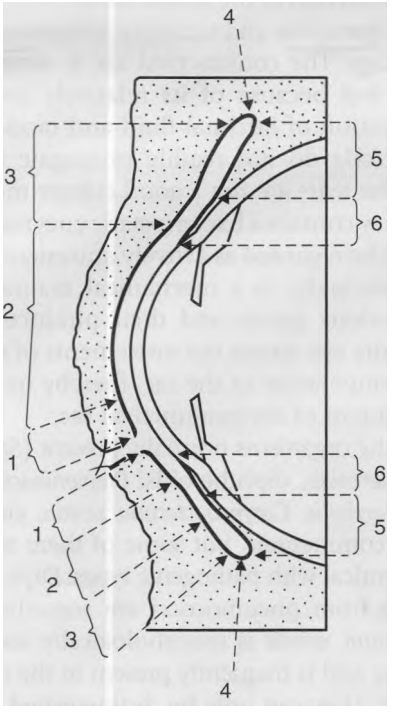
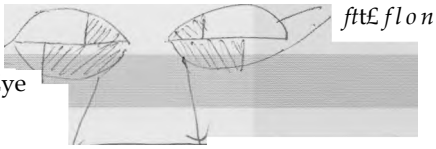


Fig. 14.1 The conjunctival areas: 1, marginal; 2, tarsal; 3, orbital; 4, fornix; 5, bulbar; 6, limbal.



The lymphatic drainage is to the^submandibular nodes) which drain the medial one-third of the superior conjunctiva and the medial two-thirds of the inferior conjunctiva; and the preauricular nodes which drain the lateral two-thirds of the superior conjunctiva and lateral one-third of the inferior conjunctiva.

The conjunctival nerve supply consists of branches of the ophthalmic division and branches of the maxillary division of the fifth cranial nerve.

The functions of the conjunctiva include tear production (mucin by the goblet cells and aqueous by the accessory lacrimal glands), supply of oxygen directly to the cornea when the eyes are open and protection of the eye by defence mechanisms which include non-specific measures such as presence of an intact epithelial barrier, lacrimation, provision of rich blood supply and mucin clumping; and specific immunologic mechanisms such as out pouring of mast cells, leucocytes, presence of an active mucosal-associated lymphoid tissue and antibodies in the form of secretory IgA.

The conjunctival surface is lubricated by the *tear film* which consists of a *mucinous layer* lining the conjunctival cells and corneal epithelium secreted by the goblet cells, an *aqueous layer* secreted by the lacrimal and accessory conjunctival glands, and a superficial *lipid layer* which is secreted by the meibomian glands and limits the evaporation of tears. This triple-layered sandwich maintains a smooth ocular surface and the oxygen dissolved in it from the atmosphere nourishes the corneal epithelium. The tears also help to wash off debris and play a role in immunological protection of the ocular surface with the help of the enzyme lysozyme and secretory immunoglobulin A.

Microbiology: The conjunctival sac is never free from organisms, but because of its relatively low temperature, evaporation of lacrimal fluid and moderate blood supply, bacteria do not readily propagate themselves. Moreover, the tears are not a good culture medium, and although they contain a bacteriostatic enzyme, lysozyme, they cannot be regarded as actively antimicrobial. Hence they act principally in a mechanical manner, washing away deleterious agents and their products. However, bandaging the eye arrests the movements of the lids and raises the temperature of the sac, thereby increasing the bacterial content of the conjunctival sac.

Most of the organisms normally present (*Staphylococcus albus* or *epidermidis,* diphtheroids, *Propionibacterium acnes, Neisseria catarrhalis, Corynebacterium xerosis,* etc.) are non-pathogenic commensals, but some of them are morphologically identical with pathogenic types. Diplococci indistinguishable from pneumococci are sometimes present. *Corynebactmum xerosis* is morphologically identical with *C. diphtheriae* and is frequently present in the normal conjunctival sac. They can only be distinguished by cultures. Staphylococci are often found and are relatively innocuous in the absence of other organisms but play an important part in mixed infections. Streptococci, *E. coli, B. proteus, N. gononhoeae, H. aegjptius, Moraxella,* etc. are pathogenic and rarely found in normal eyes. *Streptococcus pneumoniae, Neisseria gononhoeae* and *Pseudomonas pyocyanea* are among the most dangerous in ocular infections. Viruses as well as Chlamydia also play a large part in conjunctival disease. The common viruses are herpesvirus and the adenoviruses.

CLINICAL FEATURES OF CONJUNCTIVAL DISORDERS

Common symptoms of conjunctival disorders include redness, stickiness, foreign body sensation or grittiness, lacrimation and sometimes photophobia. Vision is generally normal but a slight blurring may occur if excess secretions form a film over the cornea. A substantial diminution of vision is indicative of associated involvement of the cornea or the presence of some other disorder, instead of or in addition to conjunctival involvement. Other possible symptoms include a burning sensation and dryness of the eyes. A growth on the conjunctiva sometimes invading the cornea may be another symptom in tumorous and timorous conditions.

Hyperaemia of the conjunctiva may be transitory, acute, recurrent or chronic. The first is caused by temporary irritation, as by a small foreign body in the conjunctival sac. Concretions in the palpebral conjunctiva, inspissated calcareous secretions in the meibomian glands or 'in-growing' lashes would cause acute and recurrent redness. Irritation limited to the lower fornix may be self-induced in malingerers and psychiatric patients. Chronic congestion may be caused by conditions such as dusty, ill-ventilated rooms or exposure to heat or diyness, but can also be due to causes unrelated to the conjunctiva itself, such as excessive ingestion of alcohol or allergic conditions such as hay fever. Hyperaemia, primarily or as a result of the underlying aetiology causes a sense of discomfort often described as tightness, grittiness, inability to keep the eyes open and tiredness, especially towards the evening or after near work. Bright light is resented, but true photophobia rarely occurs. If photophobia is present, associated corneal involvement or iritis must be looked for. The conjunctiva often looks normal until the lower fornix is examined, when the parts in contact are seen to be congested and sticky.

Conjunctival discharge refers to the production of excessive secretion in conjunctival disorders and is a prominent feature in conjunctivitis. This could be of various types depending on the nature of the disease, for example, watery or mucoid discharge occurs in viral and allergic types of conjunctivitis; and mucopurulent, or frankly purulenTdischarge is seen in bacterial conjunctivitis. The extent may vary from a mild'sUckmess^ffHFeyes, sticking together of eyelashes noticed on waking up in the morning, to severe copious discharge which needs to be cleaned

repeatedly. Pain with mild lid oedema and erythema may be present. Itching with a 'ropy! or 'stringy' mucoid discharge is characteristic of allergic conjunctivitis. In irritative conditions such as a conjunctival foreign body there is simply an increase in reflex secretion of tears referred to as excessive lacrimation, which presents as 'watering eyes' and should not be mistaken for epiphora or 'spill-over' of tears due to a blocked lacrimal drainage system.

F*oreivn body sensation* or grittiness may be a manifestation of dry eye, eye strain, trachoma, contact lens-induced papillary conjunctivitis, trichiasis, a foreign body, or could be due to involvement of the cornea.

Apart from assessing the obvious redness and nature of the discharge, the pattern of conjunctival inflammatory reaction and status of the tear film must be evaluated.

Conjunctival inflammatory reactions could be in the form of follicles, papillae or granulomas^Fo/fcfes Appear as yellowish-white, round elevations, 1-2 mm in diameter, and are due to localized aggregations of lymphocytes in the subepithelial adenoid layer (Fig. 14.2). Unless an acute inflammation is present, the conjunctiva over them remains normal.' *Papillae* are a hyperplasia of the normal vascular system with glomerulus-like bunches of capillaries growing into the epithelium in inflammatory conditions. Both follicles and papillae give rise to an irregular appearance of the conjunctiva and the slit-lamp may be necessary for their clinical differentiation. It is interesting that the conjunctiva of the XnewEom}is unable to produce follicles before 2 or 3 months of age, so that an infection very early mlife may appear initially as papillary conjunctivitis and develop into follicular conjunctivitis if it remains active for longer than 3 months.

The occurrence of follicles in the conjunctiva either as an acute, subacute or chronic manifestation of disease is relatively common; but does not occur in the normal conjunctiva. In all types of follicular conjunctivitis the histological nature of the follicles is identical. In trachoma, follicles are more numerous on the lippenpalpbral conjunctiva than the lower, which is unlike any other condition; also, degenerative changes and eventual scarring distinguish it from non-trachomatous types.

Subconjunctival haemorrhage, also called siihmninnctival ecchymosisjs due to the rupture of small vessels. The condition, though unsightly, is trivial. This can occur spontaneously in elderly people with fragile vessels or those with systolic hypertension or after local ocular trauma or eye surgery (Fig. 14.3). Very minute ecchymoses, or possibly thromboses, are seen in severe conjunctivitis; large extravasations accompany severe straining, especially in old people, as on lifting heavy weights or vomiting. They are not infrequently seen in children with whooping cough and may occur in scurvy, blood diseases such as purpura, or in malaria.

^Recurrent subconjunctival haemorrhagesfyvarrant investigations for a bleeding diatheses or leukaemia. The differential diagnosis includes Kaposi sarcoma. More serious are the large sub-conjunctival ecchymoses which seep forwards from the fomix following head injuries. They are due to an extravasation of blood^alonglhe'floor of the orbit, secondary to a fracture of the base of the skull. In fractures of the sphenoid the blood appears later on the temporal side than elsewhere. Haemorrhages also result from severe or prolonged pressure on the thorax and abdomen, as in persons squeezed in a crowd or by machinery.

The blood gradually changes colour and gets absorbed in from 1 to 3 weeks without treatment. The use of aspi-^ rin and non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided and if mild ocular irritation is present, artificial tears can be prescribed four to six times a day

Chemosis,/ otherwise known as oedema of the conjunctiva, is due to exudation from the abnormally permeable

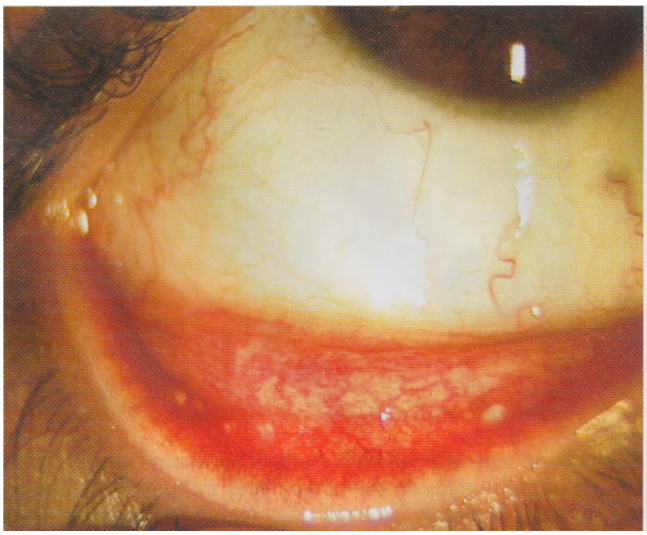


Fig. 14.2 Follicular conjunctivitis.

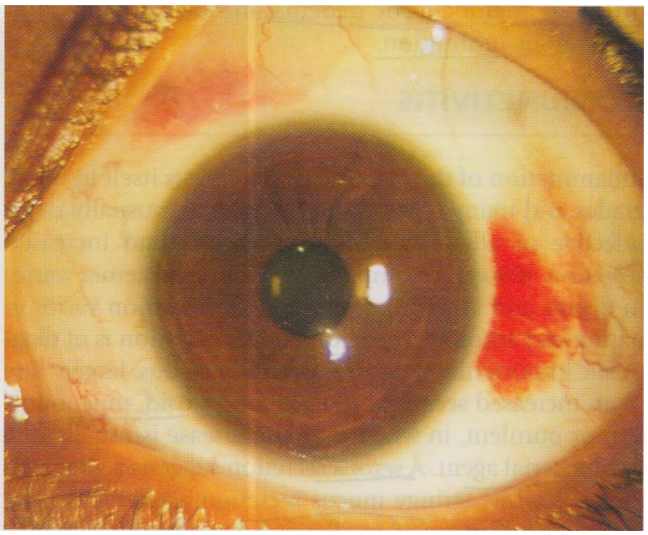


Fig. 14.3 Subconjunctival haemorrhage.



Fig. 14.4 Chemosis of the conjunctiva.

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capillaries. The exudate is retained within the mucous membrane which becomes swollen and gelatinous in' appearance, particularly in the loosely attached areas of the bulbar conjunctiva and fornices (Fig. 14.4). It may occur in: (i) acute inflammations; (ii) cases of obstruction to the circulation and (iii) abnormal blood conditions.

In the first group of cases the inflammation may be in the conjunctiva, as in gonorrhoeal conjunctivitis; or within the eyeball, as in panophthalmitis or hypopyon ulcer; it is also occasionally found in acute glaucoma. The inflammation may be in the accessory structures of the eye, as a.stye or an insect bite on the lid, dacrv-ocystitis, periostitis, orbital cellulitis or meningitis.

In the second group the pressure of an[ofb'ital tumour) may so interfere with the Jjmigh and, blood drainage as to produce chemosis; it is also found in pulsating exophthalmos or dvsthvroid eye disease.

The third group includes nephritis and the anaemia, urticaria, angioneurotic oedema, and occasionally lvm-~pEomatous infiltration.

CONJUNCTIVITIS

Inflammation of the conjunctiva manifests itself in many grades and many types (Table 14.1), but is usually of an infective or allergic origin. Hyperaemia and increased secretion always accompany it. The hyperaemia varies in degree and in distribution, and the secretion varies in nature and amount. The nature of the secretion is of diagnostic importance. It may be watery or serous, largely due to an increased secretion of tears; or mucoid, mucopurulent or purulent, in which case the disease is usually due to a bacterial agent. A serous secretion suggests a viral aetiology. A white stringy mucus secretion accompanied by itching is suggestive of an allergic aetiology. Occasionally, in acute allergic conditions such as a bee sting, chemosis occurs and the swollen membrane forms a wall around the cornea. The palpebral conjunctiva is little affected in insect bites because it is attached to the underlying tarsus and is less exposed, but the tissues of the lid are also often oedematous, so that the lids are swollen.

In the *diagnosis* of conjunctivitis, bacteriological investigation should always be supplemented by histological examination of the secretion and of *scrapings* of the palpebral conjunctival epithelium taken by a flame-sterilized platinum loop and stained with Gram, Giemsa and Papanicolaou stains for cytological examination when needed. Apart from the presence of bacteria or inclusion bodies in the cells, the cytological picture provides useful information in specific infections (Figs 14.5 and 14.6).

Conjunctivitis due to infections

Based on clinical presentation, the chief forms of infective conjunctivitis may be divided into two broad groups:

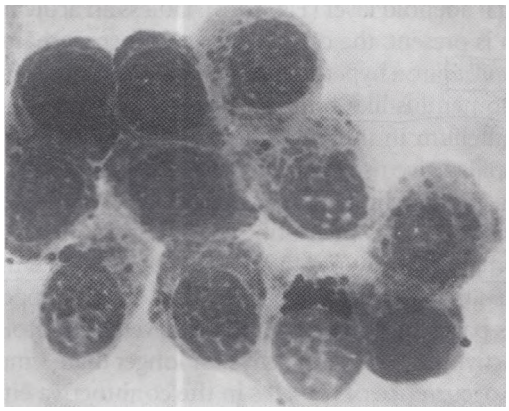


Fig. 14.5 Melanin granules in the cell form a 'cap' over the nucleus suggesting a chlamydial inclusion. (By courtesy of Yoneda)

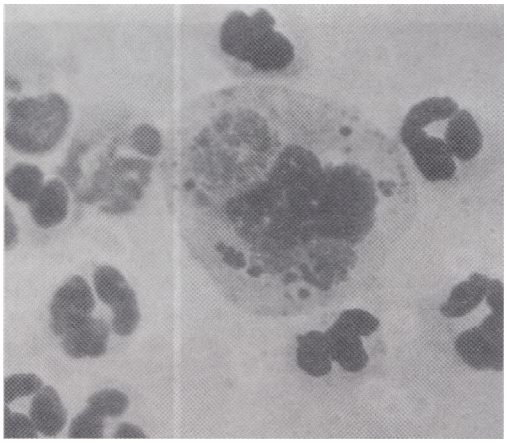


Fig. 14.6 An epithelial cell with multiple inclusions. Above and to the left of the nucleus an elementary body inclusion is deforming the nucleus. A dense, probably less mature, elementary body inclusion lies adjacent and to the right of the nucleus. (By courtesy of Yoneda)

(i)^cute^md (ii)(£ubaajte or chronigi *Acute conjunctivitis* (resolving in less than 4 weeks) may be further classified based on type of discharge, conjunctival reaction or aetiology. *Neonatal conjunctivitis* includes a limited spectrum of acute conjunctivitis and is dealt with separately. *Subacute* or *chronic conjunctivitis* (of more than 4 weeks' duration) includes non-specific conjunctivitis, angular conjunctivitis, some types of follicular conjunctivitis including trachoma, and granulomatous conjunctivitis (Table 14.1).

Acute conjunctivitis

This is usually bacterial, viral or due to *Chlamydia trachomatis* serotypes D-K.

Bacterial conjunctivitis

Acute purulent and mucopurulent conjunctivitis

Aetiology: Mucopurulent and purulent conjunctivitis may be caused by a number of bacteria (Table 14.1) and is contagious, being transmitted directly by the discharge.

Mucopurulent conjunctivitis also accompanies some viral infections in exanthemata such as measles and scarlet fever. The clinical presentation depends on the virulence "and "pathogenicity of the organism and the host's immune response.

Among the most common aetiological organisms is *Staphylococcus aureus,* which may also be responsible for other associated conditions such as blepharitis and eczema or impetigo of the skin. Staphylococci are Gram-positive, toxin-producing organisms whose pathogenicity is proportionate to their coagulase activity. Many other organisms (Table 14.1) may be responsible for the disease but two deserve special mention—*-Haemophilus aegyptius* and *Neisseria gonorhoeae.*

(Haemophilus aegyptiusf o^Koch-Weeks bacillus, is a very slenderT"Cram-negative rod, varying in length and staining poorly with the ordinary basic dyes. Groups of bacilli found in degenerated 'skeletonized' pus cells are characteristic. The organism may give rise to widespread repidemics^particularly in^sandyjsemi-tropical collntries)

Table 14.1 Classification of conjunctivitis

I Based on onset
- Acute
- Subacute
- Chronic

II Based on type of exudate
- Serous* (viral, allergic, toxic)
- Catarrhal* (allergic)
- Purulent (bacterial)
- Mucopurulent (bacterial, chlamydial)
- Membranous (bacterial)
- Pseudomembranous (bacterial)

III Based on conjunctival response
- Follicular (viral, chlamydial)
- Papillary (allergic)
- granulomatous (fungal, Parinaud oculoglandular syndrome, tuberculosis, syphilis, sarcoidosis, tularaemia, actinomycosis, sporotrichosis, parasitic, mviasis. foreign body)

IV Based on aetiology
- *Infectious*
  - Bacterial (*Staphylococcus aureus* and *albus, Haemophilus aegyptius, H. influenzae, N. gonorrhoeae, N. meningitides, Streptococcus pyogenes, Streptococcus pneumoniae, Moraxella lacunata, Proteus, Klebsiella, Escherichia coli,* diphtheroids, etc.)
  - Viral (herpes simplex, adenoviruses, picornaviruses [coxsackie virus, enterovirus 70], myxovirus [measles], paramyxoviruses [mumps, Newcastle conjunctivitis], molluscum contagiosum, etc.)
  - Chlamydial (adult or acute inclusion conjunctivitis [D–K], trachoma [A, B, C], lymphogranuloma venereum [L1, L2, L3])
  - Fungal *(Aspergillus, Candida, Nocardia, Leptothrix, Sporothrix, Actinomyces, Rhinosporidium seeberi)*
  - Parasitic
- *Non-infectious*
  - Allergic
  - Irritants (physical, foreign bodies, contact lens use, radiation)
  - Endogenous or autoimmune
  - Dry eye
  - Toxic (chemical or drug-induced)
  - Factitious or self-inflicted, artefacta
  - Idiopathic

*Serous: clear fluid resembling serum.

+Catarrhal: thick or viscid secretion resembling mucus.

often associated with severe corneal involvement, but in temperate countries the cases are usually mild and sporadic, although contact transmission is common. An attack confers immunity for some time.

Clinical features: In its milder forms an infection of the conjunctiva assumes the characteristics of a typical catarrhal inflammation of a mucous membrane. The picture of hyperaemia is associated with a mucus discharge, which gums the lids together, particularly in the mornings because of the accumulation during the night.

In the more severe cases, the whole conjunctiva is a fiery red Tpink eveT All the conjunctival vessels are congested, j phenomenon less marked in the circum-corneal ./one. Flakes of mucopus and eventually pus are seen in the fornices and often on the margins of the lids, .matting the lashes together with dirtv vellow crusts. Flakes of mucus passing across the cornea may give rise to coloured halos, owing to their prismatic action. These 'halos' must be carefully distinguished from those seen in glaucoma.

The presence of purulent or mucopurulent discharge is suggestive of bacterial infection and it is usually not possible to make a diagnosis of the organism clinically. However, certain clinical features do indicate an increased likelihood of certain specific infections; for example, there is usually more oedema (chemosis), small ecchymoses and a membranous film or 'pseudomembrane' in pneumococcal conjunctivitis. Iritis is a rare sequel of conjunctivitis, except in pneumococcal conjunctivitis and, if the cornea is involved, a hypopyon ulcer may develop.

A particularly severe form of acute purulent conjunctivitis is that due to *Neisseria gononhoeae.* It is associated with moderate to severe pain and lid swelling with copious purulent discharge and tender, sometimes suppurative, preauricular lymphadenopathy. In typical cases, the discharge re-accumulates within seconds of cleaningTThis form of conjunctivitis is also *termedfriypei'acute' conjunctivitis* or *acute*) *I hlennonhoea* by some. Gonococcal conjunctivitis occurs in two forms, as ophthalmia neonatorum in newborn babies and as severe purulent conjunctivitis in adults. Apart from *Neisseria gononhoeae,* infection with *Neisseria meningitides, Staphylococcus aureus, Streptococcus* species, especially beta-haemolytic streptococci, *Haemophilus aegyptius* and enteric Gram-negative bacilli can also present in this manner.

Complications: The disease reaches its height in 3 or 4 days. If mild and untreated or partially treated, it is liable to pass into a less intense, chronic condition. Complications are rare, but abrasions of the cornea are liable to become infected and to give rise to ulcers. Occasionally, marginal ulcers form or a superficial keratitis may develop.

Treatment: The treatment of mucopurulent conjunctivitis consists in the control of the infection by appropriate drugs. The eyes should not bejbandaged, as this prevents drainage of the secretion, but if there is any discomfort in bright light a sun-shade or dark goggles should be worn. Since the disease is contagious care must be taken to prevent its spread. The patient must keep his hands clean and no one else should be allowed to use his towel, handkerchief, pillow or other fomites.

Control of infection is most effectively achieved by the use of antibiotic drops. Ideally the appropriate drug should be chosen after tests of bacterial sensitivity have been made. Clinically, one or other of the 'broad-spec^. trum' antibiotics such as chloramphenicol, lomefloxacin, ofloxacin and ciprofloxacin in a frequency of four tn six times a day are prescribed empirically. An antibiotic ointment is applied by expressing a~small quantity directly into the lower fornix and is smeared along the lids at bedtime or, in the case of children, as often as they are put to sleep. It prevents the lids from sticking together—a two-fold benefit—of preventing discharge from being retained and obviating pain on opening them.

With control of the infection by antibiotics the pain, redness, discharge and other signs of inflammation start resolving. Topical steroid medication to hasten resolution should not be used in infectious conjunctivitis. After an attack of mucopurulent conjunctivitis the conjunctiva generally returns to normal. If the case has been neglected and chronic inflammatory signs persist, treatment should be the same as for chronic conjunctivitis/

Gonorrhoeal conjunctivitis

In developed countries gonorrhoeal conjunctivitis is now comparatively rare but is still seen in individuals and communities with poor personal hygiene.

Neisseria gononhoeae is a bun-shajgedGram-negative diplococcus, found within both leucocytes and epithelial cells. *N. catanhalis* and *N. meningitidis,* both gram-negative, are sometimes found in the conjunctival sac. They may be differentiated from the gonococcus by agglutination tests. *N. catanhalis* is rarely found in acute conjunctivitis, but may be seen in chronic forms.

Clinical features: The disease is acute, occurring usually in adult .males, often developing first in the right eve and is due to direct infection from the genitals. Apart from severe purulent conjunctivitis there is a marked tendency to involvement of the cornea. Constitutional disturbances, including a rise of temperature and mental depression, may also occur.

The incubation period is a!few hours to 3 davs. jrhereafter, the upper lid becomes swollen and tense, overhanging the lower lid and edged with pus., Eversion, which is difficult, shows that the palpebral conjunctiva is deep red and velvety; rarely there is a
There is" intense pain and the preauricular lymph node is enlarged and tender and may suppurate. After 2 or 3 weeks the purulent discharge diminishes, but subacute

conjunctivitis with papillary thickening of the conjunctiva persists for^^vefaTweeks longerTThe gonococcus is still present, a point of great importance, both in terms of contagion and treatment. No immunity is conferred by the attack.

The most important point in diagnosis is the coincidence of urethritis. The most important point in prognosis is the involvement of the cornea.

The gonococcus is capable of invading the normal cornea through an intact epithelium. Corneal complications are the rule, and constitute the cause of blindness. There may be diffuse haziness of the whole cornea, with grey or yellow spots near the centre. Ulcers may occur at any part, and are due to necrosis of the epithelium through direct invasion by the organisms. Marginal ulceration, which may extend completely round the cornea, may be due to retention of pus in the angle formed by the chemotic conjunctiva. When ulceration has commenced, it progresses rapidly and deeply and perforation is common with all its attendant dangers. The greatest care should therefore be taken to prevent injury to the cornea during diagnosis and treatment. Abrasions which may ulcerate are easily produced due to accidental trauma by the finger nails and even by cotton-wool swabs.

Iritis and iridocyclitis, with attendant complications, may arise independently of perforation of the cornea, and lead to serious diminution of vision. Gonorrhoeal arthritis is not uncommon, and endocarditis and septicaemia may arise as complications.

Treatment: Specific antigonococcal therapy is initiated based on the findings of intracellular Gram-negative diplococci on conjunctival scraping and smear examination or on clinical suspicion. The primary objective is to prevent or limit corneal involvement, protect the other eye and eliminate any systemic reservoir of infection.

If the disease is established and there is purulent discharge, the eye must be irrigated with warm saline and a 2-hourly intensive therapy given with antibiotic eyedrops (e.g. ofloxacin, ciprofloxacin, gentamicin or tobramycin), qr bacitracin ointment 6 hourly..... .....

Systemic treatment with a single dose ofjlg ceftriaxone as an intramuscular injection is usually adequate. Consultation for skin and venereal disease must be sought and the patient's sexual partner should be treated. If corneal involvement is present the patient should be hospitalized and treated with an injection of 1 g ceftriaxone given intravenouslv every 12 to 24 hours. G/doplepjrs^hould be used in all cases involving the cornea since this is always accompanied by some iritis; corneal complications require very active treatment topically and systemically. Treatment for any coexistent chlamydial infection is also recommended.

Patients who are allergic to penicillin or cephalosporins should be treated with tetracycline, particularly if there is coexistent infection with *Chlamvdia trachomatis*.

Membranous and pseudomembranous conjunctivitis

Aetiology: As in inflammation of the throat, a fibrinous membrane may cover the conjunctival surface in certain infections. *Corynebacterium diphtheriae,* beta-haemolytic streptococci, *Streptococcus pneumoniae, HaemopMus aegyptius, Neisseiia gononhoeae, Staphylococcus aureus,* and *Escheiichia coli* may all present in this manner. Diphtheritic infection occurs chiefly in children who have not been immunized and shows all degrees of severity. Streptococcal conjunctivitis, a very virulent form of conjunctivitis, occurs chiefly in children, in association with measles, scarlet fever, whooping cough and influenza. Streptococcal conjunctivitis may also be associated with erysipelas, which affects the skin of elderly patients and usually involves the face and sometimes the skin of the eyelids. Other non-bacterial causes include some viral infections, thermal and chemical bums.

In mild cases, there is some swelling of the lids and a mucopurulent or sanguinous discharge. On everting the lids the palpebral conjunctiva is seen to be covered with a white membrane which peels off easily without much bleeding; this form is often referred to as *pseudomembranous.*

In severe cases, the lids are more brawny; the conjunctiva is permeated with semisolid exudates, which impair mobility, compress the vessels, prevent the formation of a free discharge and tend to necrotize both the conjunctiva and cornea. In these cases the membrane separates less readily, with bleeding from the underlying surface, which is often described as *membranous* and is more common with diphtheritic infection. However, it has been placed beyond dispute that mild cases may be diphtheritic and severe non-diphtheritic. Also, membranous and pseudomembranous types cannot be distinguished clinically with certainty, hence it is best to make a diagnosis simply of membranous conjunctivitis until a bacteriological examination has been done.

The membrane may be patchy or cover the whole palpebral conjunctiva, often beginning at the edge of the lid, but is seldom found on the bulbar conjunctiva. The preauricular lymph node may be enlarged and may suppurate.

For 6-10 days there is great peril to the cornea from ulceration, usually due to secondary infection. About the same time, the slough also begins to separate and the discharge becomesjnor^profiise. In a few days the conjunctiva assumes a red and succulent appearance and there is danger of adhesions forming between the palpebral and bulbar parts ofthp conjunctiva (symblepharonl.

Cases of less severe but more chronic pseudomembranous conjunctivitis are occasionally seen. In *ligneous conjunctivitis* the membrane is cast off, but recurs; the pathology of these cases is not understood. Membrane fornSTonmay also occur as a complication of erythema multiforme.

Treatment: In children who have not been immunized, every case is treated as diphtherial unless films and cultures afford good negative evidence. This consists of

intensive topical (10 000 units/ml drops freshly made from injectable preparations) and systemic administration of penicillin together with the prompt injection of ant^giphtheritic serum (40uu-iu~D00 units repeated 12 hourly). Antitoxin given early and in adequate amounts both locally and systemically is curative, but has to be combined with the antibiotic.

Diphtheritic conjunctivitis is no longer that common and, after sending samples for cultures, membranous or pseudomembranous conjunctivitis is treated as described in purulent bacterial conjunctivitis. Removal of the membranes is not required and, if done, may precipitate a symblepharonT

In *streptococcal membranous conjunctivitis* the danger of necrosis of the cornea is considerable. Therefore, immediate local and systemic treatment is necessary, and careful observation as to clinical response to treatment is required.

Angular conjunctivitis (diplohacillarv conjunctivitis)

Aetiology: Such a condition may be caused by staphylococci but is typically due to *Moraxella lacunata,* a diplobacillus consisting of pairs of large, thick rods, placed end to end which stain well with basic stains, are Gram negativejmd easily recognized in films. They produce a proteolytic ferment, which acts by macerating the epithelium. The incubation period is 4 davs. The diplobacilli are strongly resistant to drying. They have been found in the nasal tract of healthy persons, and are often present in the nasal discharge in cases of angular conjunctivitis.

In this condition, reddening of the conjunctiva is limited almost exclusively to the intermarginal strip, especially at the i;tner and outer canthi, and to the neighbouring bulbar conjunctiva. There is also excoriation of the skin at the inner and outer palpebral angles, which may be a mere scruffiness, but is nearly always present. There is discomfort, with slight mucopurulent discharge and frequent blinking. If untreated, the condition becomes chronic and may give rise to blepharitis. Clear, shallow, corneal ulcers may occur, but are rare; they are usually marginal, but may be central and associated with hypopyon (*see* p. 194). A single attack does not confer immunity, and relapses are not uncommon.

Treatment: Diplobacillary conjunctivitis responds to tetracycline ointment. Eye drops containing/zinc inhibit the proteolytic ferment and are of great value although less rapidly effective, and may be used in addition.

Viral conjunctivitis

Viral infections usually cause a serous) or Jclear watir*yj* discharge and are further characterized byThe type of conjunctival inflammatory reaction they produce. In addition, many systemic viral illnesses such as influenza, mumps, measles and chickenpox can be accompanied by a non-specific conjunctivitis. The underlying systemic viral disease is treated as usual, supplemented with artificial tears four to eight times a day for the eyes.

Follicular conjunctivitis

This conjunctival reaction is most commonly caused by viruses, partirnlarlythnsp ntfhprpps and thpjpr|enovinises.} Isolated follicles, however, may occur particularly in the lower conjunctiva in any conjunctivitis of long standing and with the prolonged topical use of some medications.

Follicular conjunctivitis can be (i) acute, or (ii) subacute and chronic. *A^ite follicular conjunctivitis* is due to different causes, namely, chlamydial inclusion conjunctivitis, epidemic keratoconjunctivitis, pharvngoconjunctival fever, Newcastle conjunctivitis, haemorrhagic conjunctivitis, primary herpetic conjunctivitis and recurrent hejpes simplex conjunctivitis. *Subacute or chronic follicular conjunctivitis* is generally drug-induced (as in pilocarpine users), secondary to local lid lesions such as molluscum contagiosum a n d j)edkulosis.o r c^ejo_trachoma. *TPrl*

Epidemic Keratoconjunctivitis: This disease is usually caiisecrbyadenovi rus of serotypes 8 and 19, but also 3 and 7 and is characterized by a rapidly developing follicular conjunctivitis with markpd inflammatory symptoms and scanty exudate, associated with a preauricular adenopathy. Occasionally it takes on a membranouslorm. ^eypUoTeir dayslSterthe infection, £orjiealj: o implications appear— initially punctate. epithelial infiltrates followed by the development of discrete subepithelial opacities associated with photophobia (Fig. 14.7). The conjunctival manifestations gradually diminish and finally disappear but the comeal opacities may persist for many months or even years. The condition is markedly contagious and occurs in widespread epidemics, unfortunately often disseminated in clinics by contaminated solutions, fingers or tonometers. A n I i m m un o fl u ore scent test^detects the presence of the adenoviral group antigen m conjunctival secretions. Diagnosis is based on the demonstration of rising immunoglobulin titres in the blood. Treatment is non-specific with mild decongestive and lubricant drops to relieve discomfort and antibiotic drops to prevent secondary bacterial infection. Specific antiviral therapy is not necessary Acyclovir is not effective_against adenovj.rus infection.

Qmr^moconjunctival^Kr is caused by adenovirus serotypes 3;_4,and^7 and is characterized by an acute follicnlar conjunctivitis in association with pharyngitis, fever and occasionally preauricular adenopathy, seen chiefly in children in the epidemic form. Corneal involvement as a superficial, fine, punctate keratitis manifesting as epitheliopathy can occur but is rare. The disease is acute and transient and antibiotics have little effect. It is caused by one or other of the group of adenoviruses.

Newcastle conjunctivitis is clinically indistinguishable from the conjunctivitis of pharyngoconjunctival fever; the Newcastle virus is derived from contact with diseased jfowDD

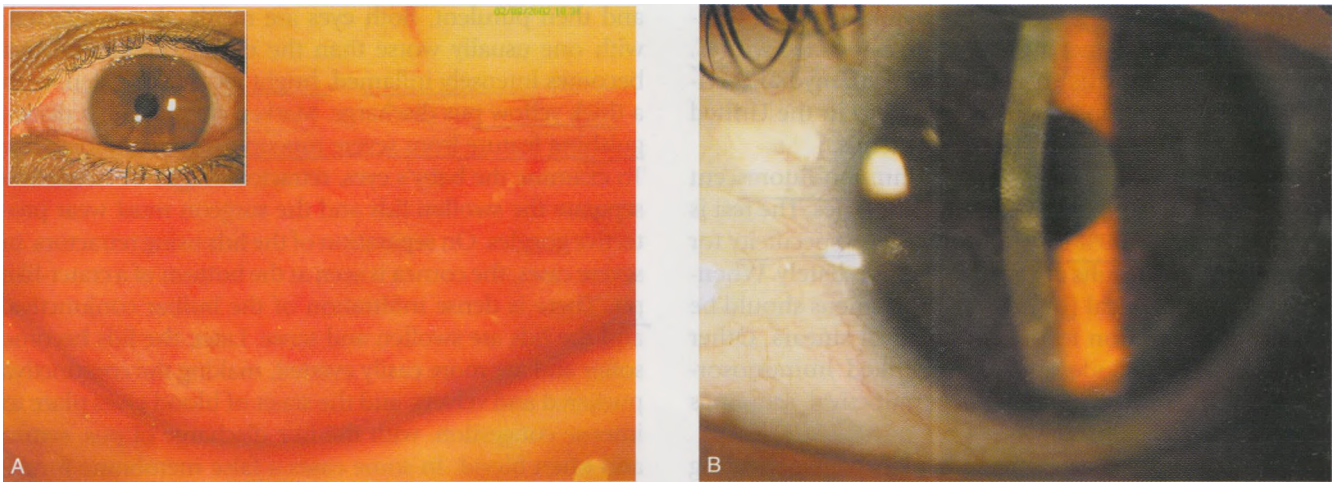


Fig. 14.7 Viral conjunctivitis. (A) Acute follicular reaction. The inset shows diffuse conjunctival congestion. (B) Subepithelial corneal opacities following adenoviral conjunctivitis.

P|POLLO /rn Eno fit tff) £ ;<r

Haemorrhagic conjunctivitis is due to picornavi ruses, namely, coxsackie virus and emerovirus *JQ*. It is also known asApcfflgronjunctivitis and occurs in a pandemic form producing a violent inflammatory conjunctivitis with lacrimation and photophobia. Subconjunctival haemorrhages and enlarged preauricular lymph nodes are common. The| cornea is usually unaffected

CAcutejnervetic coniunctivitis occurs as a primary manifestation of herpes; it is thus usually seen in young children who are, as a rule, infected by contagion from carriers of the virus. It is comparable with the more common acute stomatitis, which results from an initial herpetic infection and may be associated with vesicular lesions on the face. A preauricular adenopathy is present and the comeal vesicles may frequently merge to formIHendritic figures., The condition is acute, the follicles areTisually"large and corneal sensation is reduced.

Herpes simplex conjunctivitis may commonly occur in an atypical form in adults as acute follicular conjunctivitis without lesions of the face, eyelid or cornea and the condition then resembles epidemic keratoconjunctivitis. Mucosal involvement may be limited to tiny ulcers on the intermarginal portion of the evelid and can be demonstrated with fluorescein. Minute migwdendrites may be mistaken for the lesions of a coarse, punctate, epithelial keratitis but {educed comeal sensation is strongly suggestive of herpetic infection.

Where the"clinical evidence cannot differentiate herpes simplex conjunctivitis from epidemic keratoconjunctivitis, the viral antigen in epithelial cells may be detected by the fluorescent antibody technique, demonstrating a rising serum antibody titre during the first 1 or 2 weeks of illness or by isolating the virus. Treatment consists of the use of topical lubricating drops such as artificial tears 4-6 times a day with an initial follow-up every 2-5 days and then weekly till complete resolution, to detect corneal involvement at an early stage. It usually resolves in 1-2 weeks. If there is involvement of the cornea or of the skin of the eyelids, acyclovir 3% or vidarabine 3% eye ointment or trifluorothymidine 1% 1 drops five times a day are necessary.

Chlamydial conjunctivitis

Acute inclusion conjunctivitis Q - fc

The disease is caused by chlamydial infection (serotypes D-K) and produces inclusion bodies (Fig. 14.6) morphologicallv identical with those occurring in trachoma.

*QChlamydia inclusion conjunctivitis^* is generally spread by sexual transmission from a genital reservoir of infection. The primary source of infection is a benign subclinical venereal disease producing a mild urethritis in the male and cervicitis in the female. In adults the organism may be transferred from the genitals by the fingers, but a common mode of infection is through the water in swimming pools; thus the disease may occur in local epidemics *(sivimmim-tiool conjunctivitis.)*. It is also commonly transmitted from the mother to the newborn when follicle formation is less evident.

Inclusion conjunctivitis is characterized by a relatively acute onset, the incubation period varying fromjj ...to 10 days. The follicular hypertrophy is always more promment in thejower lid than the upper, although in acute cases the follicles may be partially obscured by papillary hypertrophy. The exudate, composed principally of neutrophils, may be moderately abundant, and the cornea is involved in a superficial punctate keratitis occasionally with some pannus-like peripheral vascnlarization.

CChlamydia trachomatis)is common in the developing and developed world, causing various genital and oculogenital infections. Associations have been reported with non-gonococcal and post-gonococcal urethritis, cervicitis, salpingitis, epididymitis, tsartftolmitis and Reiter disease. About half the cases of reactive inflammatory

arthritis occurring as a sequel to sexually acquired non-gonococcal genital tract infections are associated with C. *trachomatis.* Chlamydial urethritis and chlamydial cervicitis are the commonest venereal diseases in the United Kingdom and the United States of America.

The diagnosis is made by a direct immuno-fluorescent stain of smears using monoclonal anti-bodies, t he test is reported to have 100% sensitivity and 94% specificity for Chlamydia. The results are available immediately. Whenever possible, cervical (or urethral) specimens should be obtained in addition to the conjunctival smears. Other available tests include an enzyme-linked immunosorbent assay, Giemsa staining of conjunctival scrapings and McCov cell cultures.

The disease runs a relatively benign course, healing spontaneously if untreated in 3-12 months; the organism, however, is very responsive to treatment with broad-spectrum antibiotics or systemic treatment by tetracycline. 250 mg at 6-hourly intervals for 14 days or 100 mg doxycycline 12 hourly for 14 days or erythromycin 250 mg 12 hourly for 14 days. (Oral tetracycline and doxycycllhe are not recommended for young chiUren and lactating mothers.) New drugs include^azithromycin administered as a .single oral dose of lg and ofloxacin 300 mg orally twice daily for 7 days.

Ophthalmia neonatorum

Neonatal conjunctivitis is defined as a mucoid, mucopurulent, or purulent discharge from one or both eyes in the first month of life. It is a preventable disease occurring in a newborn child due to maternal infection acquired at the time of birth, and used to be responsible for 50% of blindness among children. The recent decline in the incidence of gonorrhoea as well as effective methods of prophylaxis and treatment have almost eliminated its occurrence and the seriousness of its sequelae. However, the disease is still prevalent and is a public health problem in communities with poor hygiene and limited access to proper health care. It may be due to *Chlamydia oculogenitalis, Streptococcus pneumoniae* or other organisms. Any discharge, even a watery secretion, from a baby's eyes during the first week should be viewed with suspicion, since tears are not secreted so early in life. The differential diagnosis oFa child with discharge from the eyes within the first month of life includes a congenitally blocked nasolacrimal duct, acute dacryocystitis, and congenital glaucoma.

In general, the aetiological differential diagnosis includes *Neisseria gononhoeae,* other bacteria such as staphylococci, streptococci, Cram negative coliforms, *Chlamydia trachomatis,* herpes simplex virus and chemical causes. A bacteriological examination should be made in every case.

Neisseria gononhoeae manifests earliest, typically within the first 48 hours of birth. In cases ofvirulent gonococcal infection, the discharge rapidly becomes mucopurulent and then purulent. Both eyes are nearly always affected, with one usually worse than the other. The conjunctiva becomes intensely inflamed, bright red and swollen, with a thick yellow pus discharge. Marked chemosis is a distinguishing feature from severe mucopurulent conjunctivitis. To examine the baby's eyes, retractors might be needed to separate the swollen lids and the surgeon must wear protective goggles. On separation of the lids using retractors, in severe cases, the cornea is seen at the bottom of a crater-like pit. There is dense infiltration of the bulbar conjunctiva, and the lids are swollen and tense. Later, the lids become softer and are more easily everted, making the conjunctiva puckered and velvety, and the stasis of blood gives place to intense congestion, with the free discharge of pus, serum and often blood. In some cases a false membrane forms, so that the case resembles a membranous conjunctivitis.

As the.^gonococcus has the power of invadmgjntactepithelium, there is anskoTameaftriceration in untreated gonococcal ophthalmia neonatorum. The slightest haziness of the cornea should be viewed with apprehension. Sometimes the child under observation has an already ulcerated cornea which may be perforated. Ulceration usually occurs over an oval area just below the centre of the cornea, corresponding to the position ot the lid margins when the eyes are closed and consequently rotated somewhat upwards. Rarely, oval marginal ulcers are formed as in the gonorrhoeal conjunctivitis of adults. The ulcers tend to extend rapidly, both superficially and in depth, resulting in perforation, usually manifesting clinically as a black spot or area in the ulcer caused by a prolapse of the iris. Sometimes perforation is sudden, a large~part ofthe iris prolapses and the lens iiiay-beextruded, while in the worst case there is a black hole in the cornea filled with clear vitteous.

Inadequate treatment may result in serious sequelae. If the corneal ulceration heals without perforation there is always much scarring of this tissue, but the nebula clears more in babies than in older people. Perforation may be followed by anterior synechiae, adherent leucoma, partial or total anterior staphyloma, anterior capsular cataract or panophthalmitis. When vision is not completely destroyed burseriously impaired by the corneal opacities, the development of centraj^m^ hich takes place during the first 3 weeks of life is impaired, resulting in the dpyplopmpnt of nystagmus which pprsists throughout fife.

Chlamydia trachomatis inclusion conjunctivitis manifests relatively late, usually over 1 week after birth. This is a relatively common cause of ophthalmia neonatorum. Bacterial examination is negative or inconsequential, but the characteristic intracellular inclusion bodies formed by *Chlamydia oculogenitalis* are found (Fig. 14.6). It is a venereal infection derived from the cervix or urethra of the mother.

The inflammation is less severe than in the gonococcal type but the conjunctivamay be considerably swollen and oedematous while the discharge may be purulent. In the absence of a [subconjunctival adenoid layer irTcKildren^

there are no follicles that appear, in contrast to infection in the adult, but if the disease is allowed to smoulder to the chronic stage these may develop after 3 months. A complicating superficial keratitis occurs as a rule and occasionally, in prolonged cases, the corneal periphery may be invaded hv a pannus. If left untreated, associated systemic disease such as chlamydial otitis and pneumonia may present or develop later.

Other bacteria manifest 48-72 hours after birth and herpes simplex virus infection presents 5-7 days after birth.

Chemical toxicity used to be seen within a few hours of prophylactic topical treatment withfsilver nitratej solution in some cases, and disappeared spontaneously in 24-36 hours. In the past, if maternal infection was suspected a drop of silver nitrate solution 1% was instilled into each eye (Crede's method). It is rarely seen nowadays as .erythromycin and tetracycline eye ointment have replaced silver nitrate for prophylactic use.

Where diagnostic tests are not available, the gram-stained smear is a useful and sensitive test with a high positive predictive value for identifying the aetiological agent of ophthalmia neonatorum. Conjunctival smears should be stained with gram and Giemsa stains and conjunctival scrapings obtained for the chlamydial immunofluorescent antibody test and specimens sent for viral, chlamydial and bacterial culture and sensitivity. Clinical judgement in terms of clinical features and time of onset should be used to judiciously advise relevant investigations for a particular case (Table 14.2). Gram-negative intracellular diplococci with polymor-phonuclear leucocyteslndlcate *NTgcmonhoeae*is the infecting organism. Gram-stained smears showing polymorphonuclear leucocytes and lymphocytes with-out bacteria or just the occasional bacteria *suggesCCKtamydia trachomatis* as the infecting organism. Gram-stained cDiijtmaival Smears with many bacteria and polymorphonuclear leucocytes are indicative of a bacterial infection such as *Staphylococcus aureus, Streptococcus pneumoniae* or *Haemophilus* spp.

Treatment: As the disease is preventable, *prophylactic* treatment is of prime importance. Any suspicious vaginal discharge during the antenatal period should be treated, and meticulous obstetric asepsis maintained at birth. The newborn baby's closed 1 ids should be thoroughly cleansed with sterile cotton-wool soaked in sterile normal saline and dried. If the mother is suspected to be infected with gonococci or *Chlamydia* then 1% tetracycline or erythromycin eye ointment should be applied. The eyes must be carefully watched during the first week. Considerable controversy still exists over the method of prophylaxis. Many authorities advocate the use of penicillin or other antibiotic drugs but all the organisms which could be present may not be susceptible to the administered drug.

If ophthalmia neonatorum is confirmed, the initial treatment is based on the immediate results of the Gram and Giemsa stains. The treatment should be on the lines already indicated forgonorrhoeal conjunctivitis and therapy can be modified according to the clinical response and culture results; fortunately most of the infections in ophthalmia neonatorum, including chlamydial infection, are amenable to penicillin and tetracycline topically and erythromycin given orally. The eyes are washed or irrigated with saline and if gonococcal infection is confirmed on smear examination or suspected clinically, or if the cornea is involved, the baby should be hospitalized, and gentamicin drops, bacitracin ointment and atropine added to the antibioticTFierapeutic regime.

The choice of antibiotic and mode of therapy for different organisms commonly causing ophthalmia neonatorum are summarized in Table 14.2. Penicillinase-producing *N. gononhoeae* is treated with a single intramuscular injection of either ceftriaxone 125 mg, or cefotaxime 50mg/kg i.v. or i.m. Jn three divided doses, or kanamvcin 25 mg/kg body weight. Local treatment consists of instilling gentamicin 0.3% drops in both eyes, repeated in 15 minutes and then after every feed for 3 days along with bacitracin eye ointment2-4 hourly

Table 14.2 Ophthalmia neonatorum: mode of presentation, differential diagnosis and treatment v

Time of onset after birth	Differential diagnosis	Treatment
Within the first 48 hours	*Neisseria gonorrhoeae „ O*	Ceftriaxone injection i.m., gentamicin drops, bacitracin eye ointment
	Chemical *To*i a TV*	Wash eyes, erythromycin ointment, observe, usually improves in 24 hours
48–72 hours	Other bacteria	Neomycin–bacitracin eye ointment, gentamicin or tobramycin drops
5–7 days	*Herpes simplex* virus (HSV II)	Acyclovir 3% eye ointment, systemic acyclovir for systemic involvement in consultation with a paediatrician
>1 week	*Chlamydia trachomatis* (D–K)	Erythromycin or chlortetracycline eye ointment, oral erythromycin for systemic infection

Chlamydial ophthalmia is treated with a suspension of ervthromvrin ethylsuccinate 50 mg/kg daily in four divided doses before feeds for 2-3 weeks,.or azithromycin 10 mg/kg for 3 days. Local treatment is with chlortetracycline 1% or erythromycin eye ointment after feeds. In all cases both parents must receive appropriate treatment for genital infection.

Bacterial ophthalmia other than gonococcal or chlamydial is treated locally with neomycin-bacitracin eye ointment after feeds, to both eyes. Once the sensitivity test is available, the antibiotic may be changed if required. The duration of treatment depends upon the response. However, conjunctivitis due tc^*Chlamydia trachomatis* persists as it is not affected by neomycin. If herpes simplex viral infection is present vidarabine 3% or acyclovir 3% eye ointment is used five times a dayfora week and then three times a day till resolution. Systemic acyclovir is recommended for systemic involvement after paediatric consultation. If chemical toxicity is suspected no treatment is needed as it is self-resolving. All affected babies must be re-evaluated daily for the first 48-72 hours and repeat cultures taken if required.

Chronic conjunctivitis

Conjunctivitis of more than 4 weeks' duration is termed chronic. Some types of acute conjunctivitis tend to become chronic if not treated in time or associated with other problems such as an underlying disorder of the ocular surface or dry eyes.

Trachoma

Once known as Egyptian ophthalmia and endemic in the Middle East since prehistoric times, it was spread far and wide in Europe by the French armies during the Napoleonic wars. It is now endemic in many parts of the world, particularly parts of the Eastern Mediterranean region, the Middle East, South West (Iraq and Iran) and Central Asia, drier regions of the Indian sub-continent (India, Pakistan, Bangladesh), Eastern Asia (China and Japan), Indonesia, the Pacific Islands, North and Central Africa, Central and large areas of South America. No race is exempt. It has been estimated that about one-fifth of the inhabitants of the world are affected. Trachoma, together with the complicating infections with which it is associated, is a major cause of blindness.

The disease flourishes among people living in unhygienic and crowded surroundings. In endemic areas, children are often infected in the first few years of life. It is contagious in its acute stages, and is spread by the transfer of conjunctival secretions through fingers or towels and, above all, by flies, which are attracted by the presence of profuse ocular discharge. On the other hand, scrupulous cleanliness prevents extension of the disease to healthy subjects.

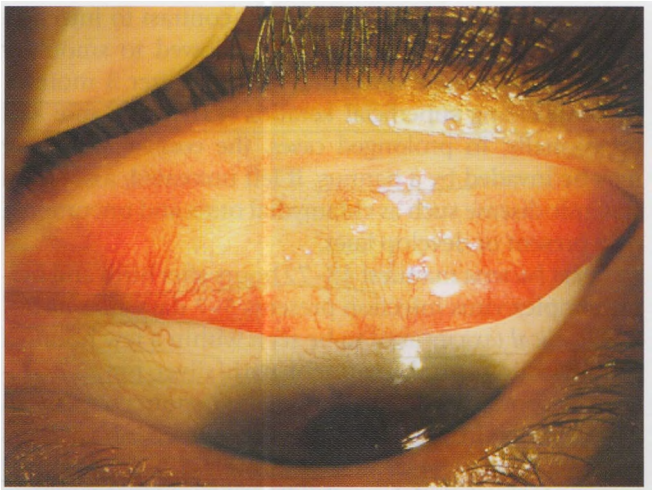


Fig. 14.8 Follicles in the upper palpebral conjunctiva.

The primary infection is epithelial and involves both the conjunctiva and the cornea. The typical *conjunctival signs* are the appearance of a diffuse inflammation characterized by congestion, papillary enlargement and the development of follicles. The conjunctiva covering the upper tarsus is usually most affected and appears red and velvety, a condition which may pass into a uniform jelly-like thickening. The essential lesion is the trachomatous follicle (Fig. 14.8). When small, these cannot be distinguished from those of follicular conjunctivitis but they can assume a width of up to 5 mm in diameter, an appearance never seen in non-trachomatous conditions. Their distribution is characteristic. They may commence in the lower fornix but in most cases they quickly appear in the upper fornix as well, where they are usually most accentuated, often forming a row along the upper margin of the tarsus. They are not, however, limited to these regions but may appear on the caruncle and the plica as well as generally over the palpebral conjunctiva. They are rare on the bulbar conjunctiva. Invasion of the lacrimal passages is not uncommon. Trachomatous infiltration may spread deep into the subepithelial tissues of the palpebral conjunctiva and even invade the tarsal plate. An important diagnostic feature is the appearance, at a relatively early stage, of signs of cicatrization of the follicles, often appearing as minute stellate scars visible with the slit-lamp.

Trachomatous *implication of the cornea* manifests itself initially as a superficial keratitis, usually so slight as to be evident only by slit-lamp examination after staining with fluorescein. It occurs typically in the upper part of the cornea where there are numerous epithelial erosions which later become associated with infiltrated areas in the substantia propria (corneal stroma).

At a later stage, *trachomatous pannus* develops as a lymphoid infiltration with vascularization of the margin of the cornea, usually limited to the upper half (Fig. 14.9) but tending to spread towards the centre and to involve the

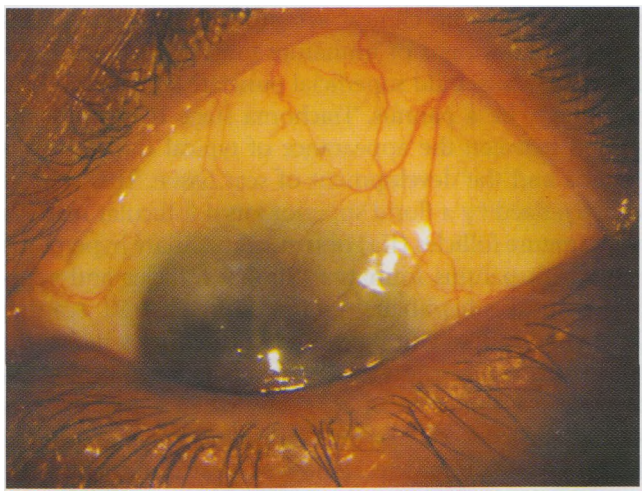


Fig. 14.9 Trachomatous pannus.

whole cornea. The upper part of the margin of the cornea becomes cloudy, and minute superficial vessels, springing from the corneal loops, grow inwards towards the centre. The haziness and vascularization increase until the upper half of the cornea is affected. At the same time, follicle-like infiltrations may appear near the limbus (Herbert pits). The vessels are all superficial and microscopic examination has shown that they lie at first between the Bowman's membrane and the epithelium, carrying in with them a small amount of granulation tissue. In the later stages, the Bowman's membrane disappears and the superficial layers of the substantia propria become involved. In more severe cases the vascularization is not limited to the upper part, but superficial vessels grow in from all sides and the whole cornea becomes vascularized and opaque.

In *progressive pannus,* the vessels are mostly parallel to each other and directed vertically downwards, anastomosing little. They extend to a level which forms a horizontal line, beyond which there is a narrow strip of infiltration and haze. In *regressive pannus* the infiltration shows evidence of receding so that the vessels extend a short distance beyond the area which is infiltrated and hazy. This difference is useful in estimating the results of treatment. *Corneal ulcers,* which may be chronic, may occur anywhere but are commonest at the advancing edge of the pannus. They are shallow, a little infiltrated and cause much lacrimation and photophobia.

The pannus may resolve completely, leaving the cornea quite clear apart from the obliterated vessels, if treated early, when the pannus has not destroyed the Bowman's membrane. In other cases a permanent opacity results.

Pathology: Trachoma is caused by *Chlamydia trachomatis* serotypes A, B, C, so called because it seemed to have a cloak (*chylamydos*) to the original observers, Halberstaedter and Prowazek. The organism is classified as a special type of bacterium which is a prokaryotic, obligatory intracellular parasite, and the two species of the genus are C. *trachomatis* and C. *psittaci.*

Chlamydia trachomatis is seen typically in conjunctival scrapings in the form of colonies in the epithelial cells as Halberstaedter-Prowazek inclusion bodies (Fig. 14.6). The inclusion is first composed of numerous initial bodies which divide until the cell eventually becomes filled with innumerable elementary bodies embedded in a carbohydrate matrix to form the inclusion body. The nucleus of the cell is displaced to one side and degenerates until eventually the cell bursts and the elementary bodies released attack fresh cells and increase in size to form initial bodies in the cytoplasm of these cells. Morphologically, identical inclusions are found in inclusion conjunctivitis, so although they are not histologically pathognomonic of trachoma, the finding of such bodies in scrapings from.the conjunctival epithelium is of considerable diagnostic importance. An infection confers little immunity since re-infection is relatively common; its occurrence has been proved experimentally and subsequent re-infections are progressively more acute.

Histologically there is lymphocytic infiltration involving the whole adenoid layer of the part of the conjunctiva affected. Special aggregations of lymphocytes, without a definite capsule, form follicles which are generally indistinguishable from those of follicular conjunctivitis except that they tend to show necrosis and contain large multinucleated cells (*Leber cells).* In the late stages, hyaline and other types of degeneration occur; and in all long-standing cases fibrous tissue forms around the follicles, later giving rise to cicatricial bands which are characteristic and never formed in other forms of follicular conjunctivitis. A characteristic white conjunctival scar (Arif *line)* is usually formed at the junction between the lower third and upper two-third of the superior tarsus. The grosser forms of cicatrization, however, are found only in cases that have been complicated by a superimposed infection.

The *onset* of the disease is usually subacute, but on massive infection—experimental, accidental or clinical—an acute onset may be observed. Its course is determined largely by the presence or absence of a complicating infection and repeated re-infection from flies and infected relatives. In the absence of such complications, a 'pure' trachoma may be a relatively mild, symptomless disease, so as to excite little or no attention until perhaps cicatrization manifests itself later in life. In such cases the discovery of follicles or other cicatricial remnants on the upper tarsal conjunctiva when the lid is everted may come as a surprise to the patient and his relatives. On the other hand, in many countries where the disease is endemic, secondary infections (as by *H. aegyptius,* the gonococcus or other organisms) result in an acute and incapacitating condition, liable to relapses as a result of re-infection, and leading to gross cicatricial sequelae which often lead to blindness.

Symptoms: As previously seen, the symptoms may be minimal in an uncomplicated trachomatous infection. When other infections confuse the picture the initial symptomatology depends on these. During the chronic stages there is usually considerable irritation, with photophobia and lacrimation when the cornea is involved; these symptoms are intensified in the presence of trichiasis. In such cases, the disability may be considerable and recurrent irritative phases may result in almost complete incapacity. In endemic areas where trachoma is rife, the economic loss thereby entailed may reach enormous dimensions.

Sequelae: Apart from the results of pannus and corneal ulceration, the most disabling effects of trachoma are caused by distortion of the lids. A peculiar drooping of the upper lids owing to dense infiltration is very characteristic, giving a sleepy appearance to the patient (*trachomatous ptosis).* There is always some scarring and, when extensive, alters the shape of the lids, especially the upper, a change aided by the infiltration of the tarsus, causing softening and later alteration of its fibrous tissue. By the later contraction of the newly formed scar tissue the lid margins may be turned inwards (*entropion*), causing the lashes to rub against the cornea often with disastrous effects (*trichiasis).* In late stages the tarsal plate may also become thickened *(tylosis).* These gross changes, however, rarely occur unless complicating infections have played a major part in the illness.

Diagnosis: Culture of C. *trachomatis* in irradiated McCoy cells is an expensive test. A simplified micro-immunofluorescence (micro-IF) test using pooled antigens rather than individual trachoma inclusion conjunctivitis (TRIC) serotypes has been developed, which is recommended for routine diagnostic use. McCoy cell cultures, monoclonal antibody direct tests and the IgA-IPA light microscopy tests form the best combination of diagnostic tools for chlamydial ocular disease. From the clinical point of view, the diagnostic features of trachoma depend on the following characteristics: (i) the presence of follicles more in the upper than lower palpebral conjunctiva; (ii) epithelial keratitis in the early stages most marked in the upper part of the cornea; (iii) a pannus in the upper part of the cornea; (iv) limbal follicles or their sequelae as Herbert pits and (v) in the later stages, typical stellate trachomatous scarring in the conjunctiva with linear conjunctival scarring of the upper tarsus. Depending on the stage of the disease, at least two of these signs should be present to establish the diagnosis. It is confirmed by the histological demonstration of inclusion bodies. Inclusion conjunctivitis can be excluded by culture of the organism.

As initially suggested by MacCallan, an English ophthalmologist who studied trachoma extensively in Egypt, the disease is frequently designated as occurring in four stages. Trachoma stage I designates the earliest stages of the disease before clinical symptoms are obvious. This stage includes signs of immature follicles present on the superior tarsus, mild superficial punctate keratopathy and there may be a pannus. Trachoma stage II includes the period between the appearance of typical trachomatous lesions and the development of scar tissue. This stage is characterized by a florid superior tarsal follicular reaction with mature follicles (Ila) or marked papillary hyperplasia (lib) with pannus formation, limbal follicles and superior corneal subepithelial infiltrates. In stage III, scarring is obvious along with the presence of follicles indicating persisting, active infection. In trachoma stage IV there is marked scarring of the upper tarsus, when a 'cure' appears to have been effected or the disease has become quiet so that there are no follicles. However, cicatrization gives rise to symptoms. Late complications include severe dry eye, trichiasis, entropion, keratitis, comeal scarring, superior fibrovascular pannus, Herbert pits (scarred limbal follicles), corneal bacterial superinfection and ulceration. The World Health Organization has suggested an alternative classification which is summarized in Table 14.3.

Treatment: The ideal antimicrobial treatment has yet to be developed. Tetracycline, erythromycin, rifampicin and the sulphonamides are effective when administered orally, but unfortunately, all of these have some side-effects. Sulphonamides have a high risk of allergic reactions such as erythema multiforme and the Stevens—Johnson syndrome. Oral tetracycline cannot be given to children less than 8 years of age, pregnant women or nursing mothers. Topical treatment with erythromycin or tetracycline eye ointment is far more ef fective than that with sulphonamides. Such treatment must be repeated in trachoma control programmes and given for five consecutive days a month for 12 months. Oral tetracycline or erythromycin 250-500mg four times a day or doxycycline 100 mg twice a day or clarithromycin 250-500mg twice a day for 3-6 weeks are also used to achieve a complete cure from active infection. A single-dose treatment with azithromycin (1 g) is also effective. Much of the dramatic effect which results is due to the elimination of secondary infection, which almost invariably flourishes in trachomatous eyes, but there is no doubt that the organism disappears and histological examination of scrapings from the conjunctiva demonstrates the disintegration of the inclusion bodies after the use of these drugs. It is to be remembered that well-formed follicles take a considerable time to resolve and dense infiltrative tissue does not disappear, so that the full effect of a course of such treatment cannot be assessed for some months. However, some cases appear to be resistant to this treatment and it may be that various strains of the organism have different sensitivities to antibiotic drugs, a variation which occurs in many organismal infections. It is desirable that antibiotic drugs be instilled several times a day until such time as the disease appears to be inactive.

Table 14.3 The World Health Organization (WHO) classification of trachoma (*FISTO)*

Trachomatous	Follicles	Implies active disease which needs treatment	Trachomatous inflammation, follicular: five or more follicles of at least 0.5 mm diameter on the upper tarsal plate should be present. Some papillae may be present in addition but the palpebral conjunctival blood vessels are visible. This stage implies that the patient, if properly treated, should recover with no scarring or minimal scarring
Trachoma	Intense	Severe disease which needs urgent treatment	Trachomatous inflammation, intense: the follicles and papillae are so numerous and inflamed that more than 50% of the palpebral conjunctival blood vessels cannot be seen clearly. This stage indicates a severe infection with high risk of serious complications
Trachomatous	Scarring	Old, now inactive infection	Trachomatous scarring: tarsal conjunctival cicatrization with white fibrous bands
Trachomatous	Trichiasis	Needs corrective surgery	Presence of at least one trichiatic eyelash
Trachomatous	Opacities	Corneal opacities from previous trachoma cause visual loss	Presence of a corneal opacity covering part of the pupillary region

Pannus requires no special treatment, for it quietens with the recession of conjunctival activity. Corneal ulcers must be treated on general principles *(see* p. 197). Trichiatic eyelashes are epilated or permanently removed by electrolysis; entropion should be surgically corrected *(see* Chapter 28).

Granulomatous conjunctivitis

Any unilateral conjunctivitis with a localized conjunctival inflammatory granuloma is termed granulomatous. If associated with regional lymphadenopathy it forms part of a spectrum of diseases known as Parinaud oculoglandular syndrome. The basic aetiopathogenesis of this form of conjunctivitis is usually the chance occurrence of some microorganism, which usually causes systemic disease, gaining entry into the body via the conjunctival route. It is rare but the causes are worth mentioning briefly because it is important to recognize this rare manifestation of some common diseases.

Parinaud oculoglandular syndrome

This term was used to describe conjunctivitis, usually of the follicular type, associated with ipsilateral preauricular (or sub-mandibular) lymphadenopathy.

It is due to infections caused by a number of different organisms including *Rochalimaea henselae* (cat-scratch disease), tularemia, tuberculosis, other mycobacteria, mumps, infectious mononucleosis, fungal infections, lymphogranuloma venereum and syphilis. Non-infectious causes include sarcoidosis, lymphoma and leukaemia.

Symptoms: It include redness, foreign body sensation and mucopurulent discharge. On examination, apart from follicular conjunctivitis and lymphadenopathy, there may be slight general malaise and fever with a skin rash.

Investigations: It include collection of conjunctival scrapings for Gram, Giemsa and acid-fast staining, cultures on blood agar, Sabouraud agar and Lowenstein-Jensen medium, complete blood count, FTA-ABS, chest X-ray, Mantoux test and serological tests for tularemia and cat-scratch disease.

Treatment: It includes warm compresses locally to the region of the tender lymph nodes, analgesics and antipyretics as required, and specific therapy for the underlying infection. Patients should be followed weekly till resolution. Conjunctival granulomas and enlarged lymph nodes may take 4-6 weeks to resolve.

Cat-scratch disease

This is caused by *Rochalimaea henselae.* There is usually a history of being licked or scratched by a cat 2 weeks or less before the onset of symptoms. The diagnosis is made by serological tests and the Hanger-Rose cat-scratch skin test. Treatment is supportive as the disease spontaneously resolves in 4-6 weeks. The organism is susceptible to tetracycline, trimethoprim/sulphamethoxazole and ciprofloxacin, which can be prescribed orally in the usual dosages for 4 weeks along with topical gentamicin drops four times a day and badtracin-polymyxin-B eye ointment four times a day for 4 weeks. There is no need to isolate the cat.

Lymphogranuloma venereum

This is a contagious venereal disease caused by *C. trachomatis* serovarieties LI, L2, L3. It manifests by an initial vesicle which bursts, leaving a greyish ulcer followed by frequently suppurative regional lymphadenitis.

The eyelids may be infected venereally or through accidental contamination in laboratory workers. Treatment is with any systemic anti-microbial drug effective

against *Chlamydia,* i.e. azithromycin 1 g as a single dose, doxycycline, tetracycline, erythromycin or ofloxacin.

Tuberculosis of the conjunctiva

This is rarely seen today but is described to occur typically in young people who are often free of clinical signs of tuberculosis elsewhere in the body, in which case it is a primary infection of exogenous origin. The disease is a rare manifestation of tuberculosis and nearly always produces ulceration. *Mycobacterium tuberculosis* is a non-motile, encapsulated, rod-like organism which stains with difficulty, but resists decolourization with strong mineral acids and is therefore referred to as acid-fast. Human and bovine varieties produce lesions in man.

Clinical manifestations: It may be multiple; small miliary palpebral conjunctival ulcers, follicular conjunctivitis, gelatinous excrescences in the fornix resembling a cock's comb, a pedunculated polyp-like growth or a tuberculoma-like nodule at the limbus. Conjunctival ulceration should always suggest either the presence of an embedded foreign body or a tuberculous or syphilitic lesion.

Pathology: Conjunctival scrapings may show acid-fast tubercle bacilli and histopathological sections of a biopsy of the lesion shows typical Langerhans giant-cell systems, while inoculation experiments may be carried out by the intraperitoneal inoculation of guinea-pigs.

The initial or primary lesion is an acute process, healing in a short time, and producing an inconspicuous parenchymal lesion with caseation of the draining lymph node. The post-primary lesion (re-infection) occurs in an individual who has developed a hyper-sensitivity to the organism, and is associated with severe parenchymal involvement with a minor effect on the regional lymph nodes.

The disease is chronic and the ulcers are indolent, but ^ there is little pain or irritation unless the ulceration is extensive.

Treatment: If the disease is a primary focus, it should preferably be eradicated by excision of the affected conjunctiva; if this is not feasible it should be thoroughly scraped and cauterized by diathermy. In all cases systemic antitubercular treatment is administered in conjunction with the physician.

Syphilis

Rarely, this manifests itself in the conjunctiva in the form of a *primary chancre,* which is less indurated than the ordinary genital chancre, and is usually acquired by contact with an infected oral lesion. A chronic ulcer or gummatous ulceration of the palpebral, or more commonly of the bulbar conjunctiva, is suggestive of the condition, particularly when the regional lymph nodes are enlarged. Scrapings should be taken and examined for spirochaetes. *Treponema* may be demonstrated by dark-ground microscopic examination. A primary chancre of the palpebral conjunctiva may be wrongly diagnosed and treated as a chalazion. *Treatment* is with topical tetracycline and systemic penicillin, the dose of which is determined by the stage of syphilis.

Tularemia

Tularemia has a widespread distribution in America, Europe and Asia and is caused by an organism (*Francisella tularensis)* derived from animals such as deer, cattle, sheep, beavers, muskrats, squirrels and rabbits. Infection is acquired by direct skin contact with any of these species or via an insect vector (such as ticks and deer flies). The most common portal of entry in human infection is the skin or mucous membranes through an abrasion or tick bite. In the oculoglandular form ulcers and nodules appear on the tarsal conjunctiva associated with swelling of the preauricular lymph node and accompanied by constitutional symptoms of fever, severe headache and general debility.

The diagnosis is made by an agglutination test and treatment is with streptomycin (1 g 12 hourly for 7 days) and topical gentamicin drops (2 hourly for 1 week, then 4-6 times a day) till the condition resolves. A physician must be consulted for control of the systemic infection.

Ophthalmia nodosa

This is a nodular conjunctivitis which may be mistaken for tuberculosis, and is due to the irritation caused by the hairs of certain caterpillars. Small semitranslucent, reddish or yellowish-grey nodules are formed in the conjunctiva, cornea and sometimes in the iris. On microscopic examination hairs surrounded by giant cells and lymphocytes are found. The nodules in the conjunctiva should be excised; otherwise the condition is treated on general principles.

Leprosy

Conjunctival involvement in leprosy is not uncommon. There may be lepromatous nodules on the eyelids, and lesions at the limbus or on the cornea. Non-specific conjunctivitis may develop independently or in conjunction with facial nerve paralysis and lagophthalmos with exposure keratopathy.

Fungal conjunctivitis

Fungal infections due to *Aspergillus, Candida albicans, Nocardia, Leptothrix* and *Sporothrix* can infrequently present as chronic conjunctivitis. Follicular conjunctivitis with lymphadenopathy is one mode of presentation. Ulcerative or pseudomembranous lesions may develop. Actinomycosis, sporotrichosis and rhinosporidiosis can present as granulomatous conjunctivitis.

Treatment is with topical miconazole or clotrimazole 1%. Rhinosporidiosis is a specific type of mycotic conjunctivitis caused by *Rhinosporidium seeberi,* described from certain

geographic regions such as Sri Lanka, Southern India, Central and South America, and Africa. Sessile or pedunculated fleshy exophytic granulomatous growths, whose surface is irregular and covered with minute white dots, are characteristic. The lesions are treated by complete surgical excision.

Non-specific chronic conjunctivitis

A non-specific chronic conjunctivitis may sometimes occur as a continuation of simple acute conjunctivitis in spite of conventional treatment. It is frequent when the eye is exposed to chronic irritation, i.e. smoke, dust, heat, bad air, late hours, alcohol abuse, etc. or when it is caused by hypersensitivity to an allergen which has not been eliminated. Permanent irritation from concretions (*see* p. 181) in the palpebral conjunctiva, misplaced lashes, dacryocystitis and chronic rhinitis are other possible causes. Unilateral chronic conjunctivitis should suggest the presence of a foreign body retained in the fornix, or inflammation of the lacrimal sac. It is often necessary to make a thorough and systematic investigation of the local and general condition before the cause can be found. It is not infrequently associated with chronic rhinitis or sinusitis, blepharitis and seborrhoea, particularly of the scalp, i.e. dandruff is a common accompaniment. The disease, though frequently regarded as trivial, may be a source of great discomfort.

The essential symptoms are burning and grittiness, especially in the evening when the eyes often become red while the edges of the lids feel hot and dry. Difficulty in keeping the eyes open is a common symptom. The lids may or may not be stuck together on waking as the discharge is slight, but there is frequently an abnormal amount of secretion from the meibomian glands.

Superficially the eyes may look normal but when the lower lid is pulled down the posterior conjunctival vessels are seen to be congested, and the surface of the mucous membrane is sticky. The upper and lower palpebral conjunctiva may be congested, with a velvety papilliform roughness; this is due to a hypertrophy of the normal vascularized papillae in the submucosa. Occasionally it is succulent and fleshy.

Treatment: This consists of eliminating the cause and restoring the conjunctiva to its normal condition. Chronic nasal catarrh is perhaps most likely to be overlooked. When heat is a prominent aetiological factor (as in cooks or in industrial workers) protective glasses may be ordered. A swab should be taken to eliminate the presence of infective organisms and, at the same time, the bacteriological flora of the nose and upper respiratory passages should be determined; any conjunctival or nasal infection should receive the proper treatment.

Local treatment consists of first eliminating any infection by a short course of a suitable antibiotic and then in diminishing congestion and restoring the normal suppleness and secretory activity of the conjunctiva. When there is an abnormal amount of secretion from the tarsal glands (*conjunctivitis meibomiana),* this should be squeezed out of the glands by warm compresses followed by repeated massage of the lid.

Non-infectious conjunctivitis

Allergic conjunctivitis

The allergic reactions of the conjunctiva may assume five forms: (i) seasonal allergic or 'Hay Fever' conjunctivitis, (ii) perennial allergic conjunctivitis, (iii) vernal conjunctivitis or keratoconjunctivitis, (iv) atopic keratoconjunctivitis and (v) giant papillary conjunctivitis.

Acute or subacute allergic conjunctivitis

This type of reaction shows few distinguishing characteristics from the corresponding types of inflammation due to organismal infection, except that itching is also a prominent symptom, hyperaemia is usually less marked, the watery secretion is not purulent and often contains eosinophil cells, and the condition shows a tendency to recurrences on renewed contact with the allergen.

It is a type I hypersensitivity reaction to pollen and other atmospheric exogenous allergens mediated by IgE as indicated by the accompanying eosinophilia. Some patients are symptomatic periodically (*seasonal allergic* or *hay fever conjunctivitis)* and others throughout the year (perennial allergic conjunctivitis).

Sometimes the allergen is a bacterial protein of endogenous nature, the most common being a staphylococcal infection in the nasal cavity or upper respiratory tract. A more characteristic picture is due to exogenous proteins, in which the conjunctivitis may form part of a typical hay fever and elevated IgE levels are demonstrable in the plasma and tears. Contact with animals (horses, cats), pollens or certain flowers (primula, etc.) are a frequent cause.

Some chemicals, cosmetics and eyelash dyes cause severe conjunctivitis and dermatitis. Drugs applied locally to the conjunctiva in susceptible persons may cause a typical allergic reaction of this type; it may sometimes be violent, almost erysipelatous, spreading widely over the lids and face. The most typical picture of such an acute reaction is that of atropine or brimonidine allergy, while other drugs tend to produce a more chronic response characterized by follicle formation (*see* p. 163).

Logically, *treatment* is removal of the allergen from the environment; if this cannot be done, desensitization may be attempted by a long course of injections. Temporary relief may be obtained by decongestant eye drops (naphazoline), antihistamine drugs (antazoline azelastine, chlorpheniramine) or mast cell stabilizers (sodium cromoglycate, olopatadine, ketotifen, etc). A short course

of corticosteroid drops frequently brings relief in severe cases, which do not respond to the topical use of 2% sodium cromoglycate drops.

In atropine irritation the drug should be avoided, and a suitable substitute used *(see* p. 153); but susceptible persons frequently develop an allergy to these drugs as well.

Vernal conjunctivitis (spring catarrh)

Also known as *vernal keratoconjunctivitis*, this is a recurrent bilateral conjunctivitis occurring with the onset of hot weather, and therefore rather a summer than a spring complaint, found in young children and adolescents, usually boys.

Burning, itching, some photophobia and lacrimation are the chief symptoms accompanied by a characteristic white, ropy secretion. In the cooler months the condition subsides and is symptomless although the lesions persist, but the symptoms recur with the return of heat. The disease is seen among all classes, is sporadic, and non-contagious. The long-term prognosis is variable. Children usually have a self-limited disease and eventually 'grow out' of the disease over a period of 5-10 years. Some young adults develop more severe manifestations of the disease, sometimes with indefinite recurrences.

Two typical forms are seen: (i) the palpebral form and (ii) the limbal or bulbar form and both may occur together.

The *palpebral form* is easily recognized. On everting the upper lid the palpebral conjunctiva is seen to be hypertrophied and mapped out into polygonal raised areas, not unlike cobblestones (Fig. 14.10A). The colour is bluish white, like milk, and this appearance may also be seen over the lower palpebral conjunctiva. The flat-topped nodules are hard, and consist chiefly of dense fibrous tissue, but the epithelium over them is thickened, giving rise to the milky hue. Histologically they are hypertrophied papillae, not follicles. Eosinophilic leucocytes are present in them in great numbers and found in the secretion. In addition, infiltration with lymphocytes, plasma cells, macrophages, basophils and eosinophils may also be seen. The palpebral form cannot be mistaken if typical, but may resemble trachoma. The type of patient, the milky hue, freedom of the fornix from implication and the characteristic recurrence in hot weather will usually prevent misdiagnosis.

The *limbal or bulbar form* is recognized by an opacification of the limbus (Fig. 14.10B) with nodules or a wall of gelatinous thickening at the limbus. White dots consisting of eosinophils and epithelial debris, known as Horner-Trantas dots, if seen at the limbus are a very characteristic feature.

Both types are complicated by a fine diffuse superficial punctate keratitis. The ultimate prognosis is generally good with the disease being usually self-limited over a period of a few years. However, in some individuals the disease is more severe with recurrences for several years with the development of severe dry eyes and corneal ulcers (shield ulcer), with scarring. Occasionally, some thickening and discoloration of the conjunctiva may remain.

Treatment: This is purely symptomatic. The irritation is best relieved by cold compresses, antihista mine eye drops and the topical instillation of steroid drops 4-6 hourly. After a few days, the acute irritation usually subsides and, thereafter, a maintenance dose three or four times a day along with topical mast cell stabilizing agents during the seasonal period of activity generally keeps the symptoms in check. Disodium cromoglycate 2% as drops 8 hourly or 4% drops 12 hourly are also useful. Olopatadine is a new mast cell stabilizer that is prescribed twice daily. Subtarsal injection of triamcinolone in severe cases may be helpful. As the symptoms and signs subside, topical steroids can be tapered off and discontinued, and mast cell stabilizers continued.

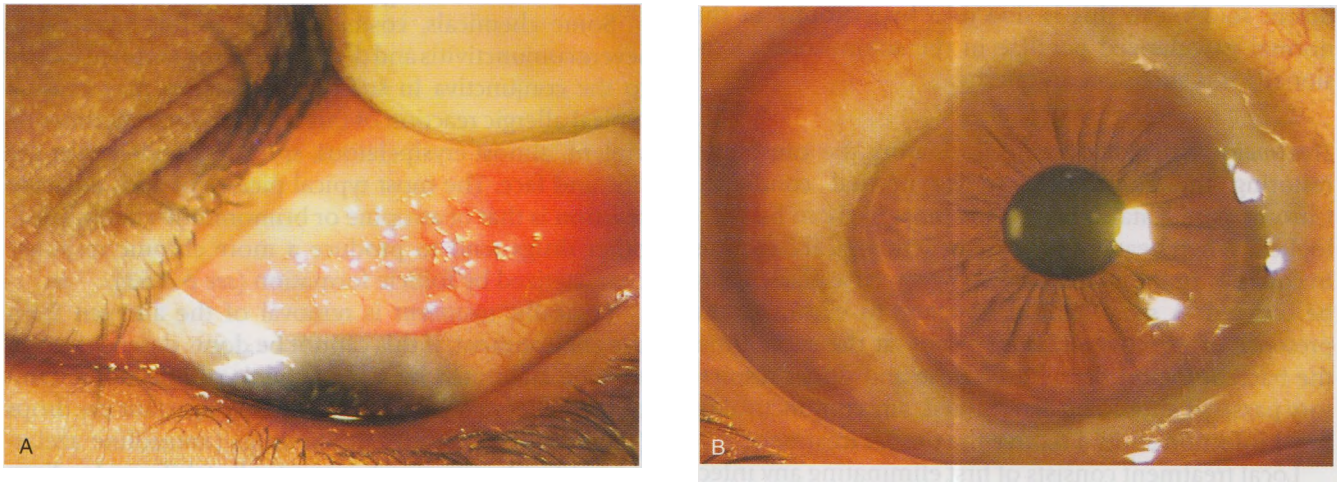


Fig. 14.10 (A) Vernal keratoconjunctivitis: palpebral form; (B) vernal keratoconjunctivitis: bulbar form.

Chronic steroid usage puts the patient at serious risk of silently developing steroid-induced glaucoma, or bacterial or fungal corneal superinfections which are all potentially blinding conditions. Hence steroids should be used only for short periods under the careful supervision of an ophthalmologist and indiscriminate use of steroids, particularly self-medication by patients or the parents in the case of children, is to be actively discouraged. Antibiotics are likely to set up an allergic reaction. The production of sticky mucus is characteristic. Acetyl cysteine used as 10 or 20% drops is useful in controlling excess mucus. Cold compresses and tinted glasses are often helpful and provide considerable comfort. The patient should be dissuaded from rubbing the eyes as this further induces mast cell degranulation with the release of histamines, setting up a vicious cycle. Cryotherapy of the nodules is sometimes useful.

Atopic keratoconjunctivitis

It is generally seen in young adults and often associated with a history of other atopic diseases such as asthma, allergic rhinitis, or atopic eczematoid dermatitis in the patient or his/her family. It is responsible for an extremely severe and chronic form of ocular surface disorder, though the disease spectrum varies in range of severity from mild to chronic persistent inflammation. It is similar in nature to vernal keratoconjunctivitis except that it tends to be more severe, chronic and extends into adulthood.

Giant papillary conjunctivitis

This is a specific type of allergic inflammation affecting the superior tarsal conjunctiva and is usually due to soft hydrophilic contact lens use, protruding suture ends or ocular prostheses. It can also occur rarely after many years of igid contact lens use. The underlying mechanism is a hypersensitivity reaction (types I and IV). The usual symptoms are itching, watering, foreign body sensation and, occasionally, blurring of vision. Signs include conjunctival congestion which is predominantly in the upper palpebral region with large polygonal papillae on the superior tarsal conjunctiva. Macropapillae are 0.3-1.0mm in size and giant papillae are l-2mm in size.

Treatment consists of discontinuing the use of soft contact lenses, removal of offending sutures, cleaning and polishing of any ocular prosthesis and replacing this with one coated with biocompatible material such as biocoat. Useful ancillary therapy includes mast cell stabilizers (lodoxamide 6 hourly, cromolyn sodium 6 hourly or olopatadine 12 hourly), along with artificial tears, antihistaminic drops and decongestants. Topical steroids can be administered for a short while and a subtarsal injection of long-acting steroid may be needed in severe cases, provided that the patient is not a steroid responder.

Endogenous or immune system-mediated conjunctivitis

Conjunctivitis occurring primarily because of an activation of the immune system and immunologically mediated inflammation includes various types of allergic conjunctivitis, drug reactions and autoimmune diseases known to affect the mucous membranes. Specific types are briefly described below.

Phlyctenular conjunctivitis

In phlyctenular conjunctivitis one or more small, round, grey or yellow nodules, slightly raised above the surface, are seen on the bulbar conjunctiva, generally at or near the limbus; they rarely occur on the palpebral conjunctiva, and the congestion of the vessels is limited to the area around the phlyctens. The disease may be complicated by mucopurulent conjunctivitis, in which the whole conjunctiva is intensely reddened.

There is considerable evidence that phlyctenular conjunctivitis is an allergic condition caused by endogenous bacterial proteins which in most cases are tuberculous, but in other cases may be derived from mild, long-standing infections such as those of the tonsils or adenoids. The condition used to be common but is rare today, a change that may in some degree be due to improved hygiene and the control of milk infected by bovine tuberculosis. However, it is still seen in populations where tuberculosis is still widely prevalent.

Phlyctens resemble blebs (Fig. 14.11) and show a true vesicular stage. They may be so small as to be seen only with difficulty, but usually measure about 1 mm in diameter. In the later stages the epithelium over the surface becomes necrotic and small ulcers are formed—on the conjunctiva this is of little consequence since healing takes place rapidly without the formation of a scar, but when it occurs on the cornea, as is very frequently the case, it is much more serious *(see* p. 204).

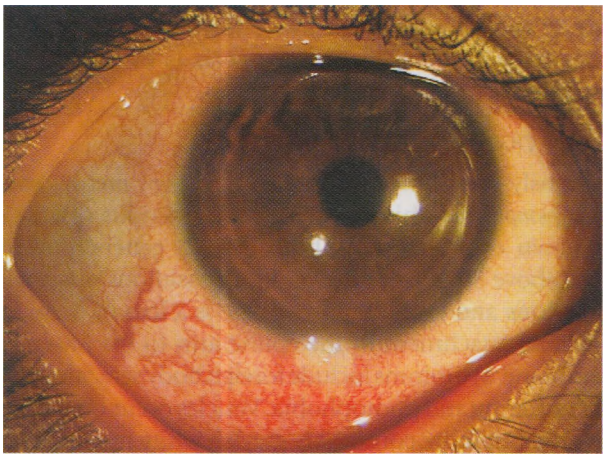


Fig. 14.11 Limbal phlyctenular conjunctivitis.

Simple phlyctenular conjunctivitis has few symptoms. There is some discomfort and irritation associated with reflex lacrimation. If there is no mucopurulent discharge and the cornea is not involved, there is little or no photophobia. If the condition persists, corneal spread is the rule and there is a marked intensification of the symptoms, particularly from phlyctens lying astride the limbus.

Treatment: Simple phlyctenular conjunctivitis is usually readily amenable to treatment, which must be both local and general. Steroids given as drops or ointment usually have a dramatic effect. If there is any corneal complication, or evidence of its imminence, antibiotics and a cycloplegic are added. Dark glasses or a shade may be used.

A number of syndromes related to *erythema multiforme* affect the conjunctiva in association with other mucous membranes such as those of the mouth, nose, urethra and vulva, as well as eruptions on the skin associated with general toxic symptoms, sometimes of considerable severity. The conjunctivitis may be mild but is sometimes severe when the condition is often known as the *Stevens—Johnson syndrome*; it may be pseudomembranous or vesicular and blindness may result from corneal complications. The disease is an immune vasculitis precipitated by the deposition of circulating antigen complexed with complement-fixing antibody.

In *Reiter disease* an acute conjunctivitis—catarrhal or purulent—is associated with urethritis and polyarthritis; keratitis and uveitis, sometimes with hypopyon, occasionally occur. The conjunctivitis associated with *Behcet disease* is usually mild. Treatment of all these conditions is unsatisfactory and corticosteroids and broad-spectrum antibiotics do not give consistent results. The formation of symblepharon is to be vigorously avoided and intensive lubricant therapy with artificial tears maintained lifelong.

Sarcoidosis

Patients affected with sarcoidosis not infrequently show lesions in the conjunctiva. These lesions are typically nodular, translucent and orange in appearance, usually located in the folds of the lower fornix. They are sometimes large and confluent. Diagnosis is by biopsy, and treatment is of the general condition.

Ocular cicatricial pemphigoid

Previously sometimes referred to as *benign mucous membrane pemphigoid,* this is a rare but very serious disease of unknown origin affecting both eyes. It generally affects those above 50 years of age and is of insidious onset with remissions and exacerbations. There is a loss of hemidesmosomal attachment of the epithelium to the basement membrane. Symptoms include foreign body sensation, redness, watering and photophobia. Vesicles occur on the conjunctiva, but more commonly greyish white membranous patches are seen. Progressive cicatrization follows, eventually leading to essential shrinkage of the conjunctiva, formation of inferior symblepharon, shallowing of the inferior fornix, severe dry eye, superficial punctate keratopathy, entropion, trichiasis, pannus, keratinization and consequent opacification of the cornea. Similar lesions maybe found in the nose, mouth, palate, pharynx, oesophagus, anus, vagina, urethra and, more rarely, on the skin. Somewhat similar lesions may complicate other aphthous affections of the mucous membranes such as *erythema nodosum, dermatitis herpetiformis, epidermolysis bullosa,* and *hydroa vacciniforme.* Stevens—Johnson syndrome, membranous conjunctivitis with scarring, severe bums, atopic vernal keratoconjunctivitis, radiation and squamous cell carcinoma can also produce a similar clinical picture. The diagnosis is made by conjunctival biopsy for immunofluorescent staining and dermatological, otorhinolaryngological and gastrointestinal specialist consultations. Depending on the severity of involvement, treatment is with artificial tears, protective moisture-retaining glasses, punctal occlusion, topical and systemic steroids, dapsone, immunosuppressive therapy, surgery by mucous membrane grafts and keratoprosthesis for end-stage corneal disease.

Local treatment, such as transplantation of the mucous membrane, is disappointing as is general treatment. Hydrophilic contact lenses together with artificial tears may be helpful.

Stevens-Johnson syndrome (Erythema multiforme major)

This is a type II hypersensitivity reaction usually due to an immunological reaction to drugs (sulphonamides, NSAIDs, antibiotics, antimalarials, antiepileptics (such as barbiturates and phenytoin) or systemic infections (caused by *Mycoplasma pneumoniae,* herpes simplex virus and some fungi). It is a serious disease, fatal in some patients, characterized by skin rash, erythematous lesions followed by bullae and epidermal necrosis, fever, malaise and ulcerative lesions of the mucous membranes, particularly the mouth and the eyes. Late ocular sequelae include severe dry eye, symblepharon, lid deformity (cicatricial enUopion), comeal vascularization and scarring. Ocular treatment in the acute stage includes supportive therapy with topical lubricants, antibiotics to prevent secondary bacterial infection, and lysis of adhesions forming between the bulbar and palpebral conjunctiva by passing a glass rod coated with antibiotic or plain paraffin ointment in the fornices. The late cicatricial stage can be treated medically to control the manifestations of a dry eye and lid deformities can be surgically corrected. Additional measures such as punctal occlusion, transplantation of conjunctival or buccal mucous membrane and transplantation of limbal stem cells with amniotic membrane to promote healing may be needed to restore the integrity of the damaged ocular surface.

Ocular rosacea

See Chapter 15.

Toxic and chemical conjunctivitis

Certain chemicals and toxins, including drugs such as neomycin, gentamicin, idoxuridine, trifluorothymidine drops, preservatives in drops such as benzalkonium chloride and thiomersal, and prolonged topical use of eserine, pilocarpine or phospholine iodide can produce follicular hypertrophy. The mechanism is believed to be a type IV delayed hypersensitivity reaction. Other drug reactions mimicking conjunctivitis include allergic blepharoconjunctivitis (brimonidine), reactive hyperaemia (latanoprost) and rebound hyperaemia (epinephrine, dipivefrine and apraclonidine). A form of toxic follicular conjunctivitis can also occur after exposure to other foreign substances such as cosmetics applied around the eyes, *Phthirus pubis* infestation along the lashes and pox virus (molluscum contagiosum) infection of the lid margins. Viral proteins and other related substances come in contact with the conjunctiva and lead to toxic reactions.

Traumatic conjunctivitis will be considered with ocular injuries when the action of chemicals and vesicant gases will be discussed *(see* Chapter 24). Malingerers sometimes induce conjunctivitis by inserting a multitude of irritants into the eyes. The irritation is most marked in the lower fornix, and usually the right eye is affected in right-handed people.

DEGENERATIVE CHANGES IN THE CONJUNCTIVA

Concretions ('lithiasis')

These occur as minute, hard, yellow spots in the palpebral conjunctiva, and are due to the accumulation of epithelial cells and inspissated mucus in depressions called Henle glands. They never become calcareous, so the term is a misnomer, but are so hard that when they project from the surface the cornea is scratched. This produces a sensation of a foreign body in the eye. They are common in elderly people who have suffered from trachoma and should be removed with a sharp needle.

Pinguecula

This is a triangular patch on the conjunctiva, usually found in elderly people, especially those exposed to strong sunlight, dust, wind, etc. It occurs near the limbus in the palpebral aperture, the apex of the triangle being away from the cornea and affects the nasal side first, then the temporal. It is yellow in colour and looks like fat, hence the name *(pinguis,* fat), but is due to hyaline infiltration and elastotic degeneration of the sub-mucous tissue. Since the pinguecula remains relatively free from congestion it is particularly conspicuous when the eye is inflamed; mistakes in diagnosis may then occur. It requires no treatment.

Pterygium

This is a degenerative condition of the subconjunctival tissues which proliferate as vascularized granulation tissue to invade the cornea, destroying the superficial layers of the stroma and Bowman's membrane, the whole being covered by conjunctival epithelium (Fig. 14.12). The lesion thus appears as a triangular encroachment of the conjunctiva upon the cornea with numerous small opacities lying deeply in the neighbouring part of the cornea in front of its blunt apex. The thick vascularized conjunctiva appears to be drawn onto the cornea from the canthus and is loosely adherent in its whole length to the sclera, the area of adherence being always smaller than its breadth so that there are folds at the upper and lower borders.

A pterygium frequently follows a pinguecula and, when single, is usually on the nasal side; when double

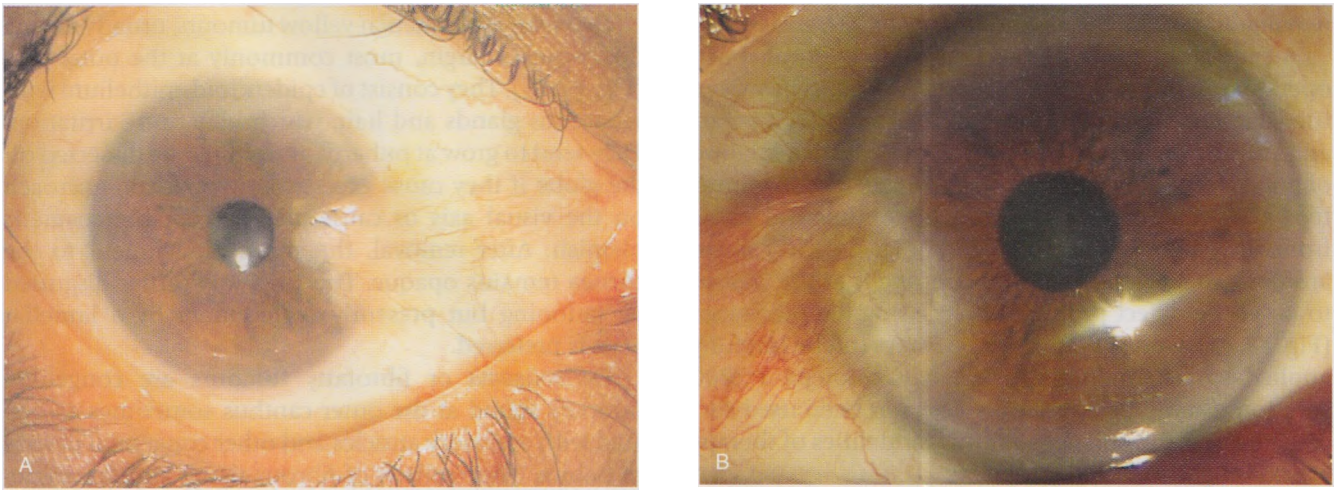


Fig. 14.12 (A) Pterygium presenting as a wing-shaped extension of the conjunctiva over the cornea. (B) Recurrence of pterygium after surgery with co-incidental arcus senilis.

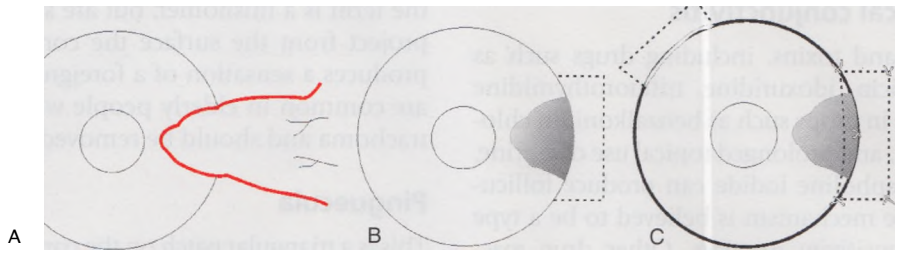


Fig. 14.13 Pterygium surgery. (A) Pterygium; (B) excised leaving an area of bare sclera; (C) autoconjunctival graft placed over the conjunctival defect.

the temporal lesion develops later. In the early stages it is thick and vascular, becomes thin and pale when it ceases to grow but never disappears. When it ceases to progress, consolidation occurs with the formation of dense fibrous tissue and the development of considerable corneal astigmatism. Ordinarily the condition is symptomless, but vision becomes impaired if it progresses into the pupillary area of the cornea.

The condition is common in dry sunny climates with sandy soils as in parts of Australia, South Africa, Texas, the Middle East and South and South-east Asia. Ultraviolet light is probably an aetiological factor.

Treatment: A pterygium is best left alone unless it is progressing towards the pupillary area, causes excessive astigmatism, a restriction of ocular motility or is disfiguring. It cannot be removed without leaving a scar unless a lamellar corneal graft replaces it.

Removal is effected by seizing the neck near the comeal margin with fixation forceps, raising it, and shaving or dissecting it from the cornea, starting from the apex. Care must be taken not to go too deep. The pterygium is freed from the sclera for about half the distance towards the canthus. Two parallel incisions are then made with scissors to excise as much of the pterygium as possible. The head of the pterygium is then excised and a bare area of sclera remains at the edge of the cornea (Fig. 14.13A and B).

A pterygium sometimes recurs after removal. Postoperative therapy with mitomycin C drops has been tried, but complications such as scleral necrosis, cataract and iritis have been reported. Another effective method of preventing recurrences is to perform an auto-conjunctival graft (taking a piece of limbal conjunctival tissue from the same or the other eye) (Fig. 14.13C) or an amniotic membrane graft and suturing it at the limbus to cover the defect produced by excising the pterygium (Fig. 14.13). Contact radiation by (3-rays can be carefully applied to the limbus. Alternatively, thiotepa 1:2000 solution given 6 hourly for 6 weeks has been used successfully in the past. The latter two modalities of therapy are no longer commonly used.

If the pterygium actually re-forms and extends towards the pupillary area, the apex should be freed, the lesion excised and a lamellar graft inserted over the affected area.

CYSTS AND TUMOURS

The only common cysts found in the conjunctiva are due to dilatation of lymph spaces. When small, these often form rows of little cysts on the bulbar conjunctiva *(lymphangiectasis).* Occasionally, single but multi-locular cysts occur (*lymphangiomata*). Larger *retention cysts* of Krause accessory lacrimal glands occur in the upper fornix. Subconjunctival *cysticercus* and *hydatid* cysts are rare. Non-parasitic cysts require simple removal of the anterior walls. *Epithelial implantation cysts* occur rarely after injuries or operations for strabismus.

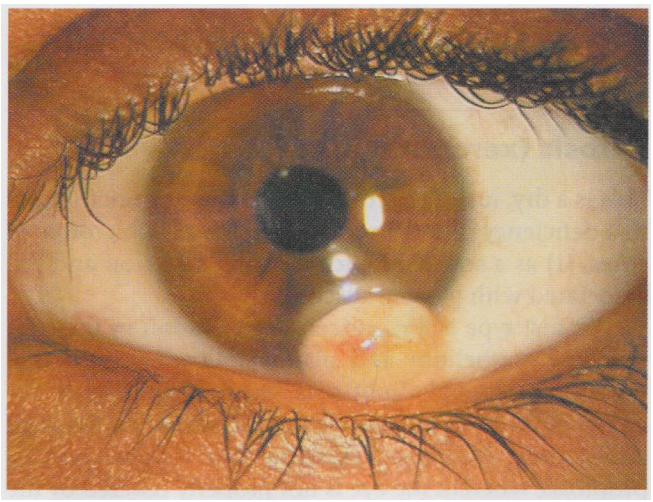
Tumorous conditions

In the conjunctiva these have a tendency to be polypoid owing to the perpetual movements of the globe and lids.

Congenital tumours: These include dermoids and dermolipomas. They are actually not true neoplasms but are in fact *choristomas* or a collection of heterotopic tissue (normal tissue in an abnormal location) which grow as tumours or tumour-like lesions.

Dermoids are lenticular yellow tumours, usually astride the corneal margin, most commonly at the outer side (Fig. 14.14). They consist of epidermoid epithelium with sebaceous glands and hair, which may cause irritation. They tend to grow at puberty, and should be dissected off the globe if they cause excessive astigmatism, encroach on the visual axis or cause an unacceptable cosmetic blemish. After removal, the site of attachment to the cornea remains opaque. This area was earlier disguised by tattooing but presently replacement by a lamellar graft is preferred.

Dermolipoma or fibrofatty tumours are congenital tumours found at the outer canthus sometimes associated with accessory auricles and other congenital defects in babies. They consist of fibrous tissue and fat, sometimes with dermoid tissue on the surface, and are not encapsulated. The main mass may be removed with care



Fig, 14.14 Limbal dermoid.

if cosmetically unacceptable, but it will be found that the fat is continuous with that of the orbit.

Both limbal dermoids and dermolipomas are more common in children with a congenital developmental anomaly known as Goldenhar syndrome (oculoauriculovertebral dysplasia). This syndrome affects structures derived from the first branchial arch leading to preauricular tags, deformities of the external ear and vertebral anomalies. Colobomas of the lids and iris and Duane retraction syndrome are other associated ocular abnormalities.

Papillomata: These occur at the inner canthus, in the fornices or at the limbus. They may become malignant and should be removed.

Simple granulomata: Simple granulomata consisting of exuberant granulation tissue, generally polypoid in form, often grow from tenotomy wounds or the sites of foreign bodies. They are common in empty sockets after excision, and at the site of chalazia which have been insufficiently scraped. They should be removed with a pair of scissors and sent for histopathological examination.

Pyogenic granuloma: Sometimes an infected polypoid or sessile granuloma develops after secondary bacterial infection following pterygium or squint surgery. The lesion is surgically excised and diagnosis confirmed by histopathological examination.

Squamous cell carcinoma (epithelioma): This occurs where one kind of epithelium passes into another; therefore, in the conjunctiva, it occurs chiefly at the limbus. Papillomata in old people often take on malignant proliferation. *Bowen intraepithelial epithelioma* or *carcinoma in situ* is also seen. Squamous cell carcinoma spreads over the surface and into the fornices, rarely penetrating the globe. They have the structural characteristics of such growths elsewhere. They must be removed as freely as possible, the base being cauterized by diathermy or treated with cryotherapy; and the diagnosis should be microscopically confirmed. On the slightest sign of recurrence with invasive squamous cell carcinoma, the eye must be excised and if recurrence takes place the orbit must be exenterated and radiation therapy given.

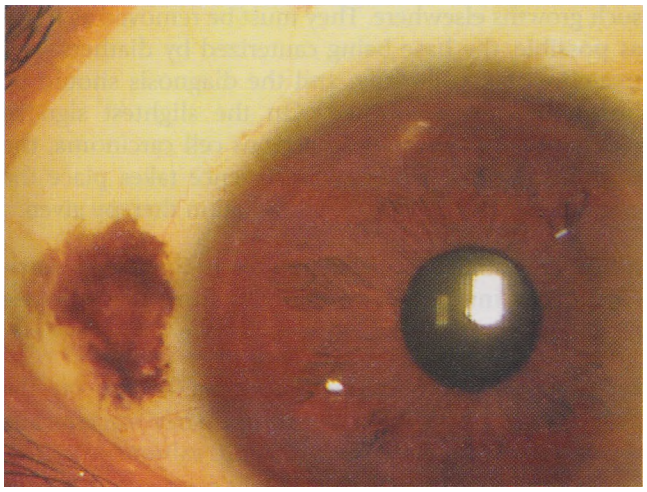
Basal cell carcinoma (rodent ulcer): Basal cell carcinoma may invade the conjunctiva from the lids (see Chapter 28).

Lymphomas: Conjunctival lymphoma occurs on the bulbar conjunctiva or in the fornix. They are typically described as painless, slow growing, salmon-coloured, i.e. light pinkish, mildly elevated, homogeneous lesions which can sometimes have small, round aggregations that look like fish eggs. An excision biopsy must be done to determine the diagnosis. Systemic lymphoma may be associated, hence a thorough systemic evaluation is mandatory. Radiotherapy is effective in treating localized conjunctival lymphomas.

Kaposi sarcoma: This specific type of tumour is seen in patients suffering from the acquired immune deficiency syndrome (AIDS) due to infection with the human immunodeficiency virus (HIV). It affects the skin or any organ and is common in southern Mediterranean regions, eastern Europe and Africa. If a conjunctival lesion is present there is a high association with AIDS and eye involvement can be the first manifestation. The lesion may also affect the skin of the eyelids and face. The tumour is highly vascular, with a bluish-red colour and presents as an elevated nodule somewhat resembling a subconjunctival haemorrhage. The lesion is malignant and its treatment is palliative with radiotherapy.

Pigmented tumours: These constitute an important type of neoplasia which introduces difficult clinical decisions: some are simple (naevus), some potentially precancerous (junctional naevus, precancerous melanosis, lentigo malignum) and some frankly malignant (malignant melanoma).

Naevi or *congenital moles* are not uncommon (Fig. 14.15). They are grey, gelatinous or pigmented nodules situated by preference at the limbus or near the plica semilunaris. They have the same structure as in the skin—groups, often alveolar, of 'naevus cells' in close connection with the epithelium. They are congenital and tend to grow at puberty, rarely becoming malignant. In view of this they should be excised completely before puberty, lest malignant changes follow the operative disturbance. It is to be noted that pigmentation at the limbus occurs normally in people with dark complexions, and dark patches are not uncommon in them.



Fig, 14.15 Naevus of the conjunctiva.

Precancerous melanosis is a diffusely spreading pigmentation of the conjunctiva, occurring rarely in elderly people, which may also involve the skin of the lids and cheek. It is liable to spread slowly and may eventually assume malignant characteristics, giving rise to metastases. The condition should, therefore, always be viewed as pre-cancerous and though radiosensitive at this stage; if allowed to progress to the malignant phase, some cases tend to become radioresistant in which case the only effective treatment is wide excision with exenteration of the orbit and extensive reconstitution by skin grafting. (3-irradiation, either primary or after tumour excision, is the treatment of choice for conjunctival melanomas.

Malignant melanoma is rare (Fig. 14.16A and B). It occurs typically at the limbus, is usually pigmented, and occurs mostly in the elderly. It spreads over the surface of the globe but rarely penetrates it; recurrences and metastases occur as elsewhere in the body. The neoplasm may be alveolar (derived from naevi) or round- or spindle-celled. The treatment is by excision of the globe or exenteration of the orbit.

DRY EYE SYNDROMES AND DISORDERS OF THE OCULAR SURFACE

Xerosis (xerophthalmia)

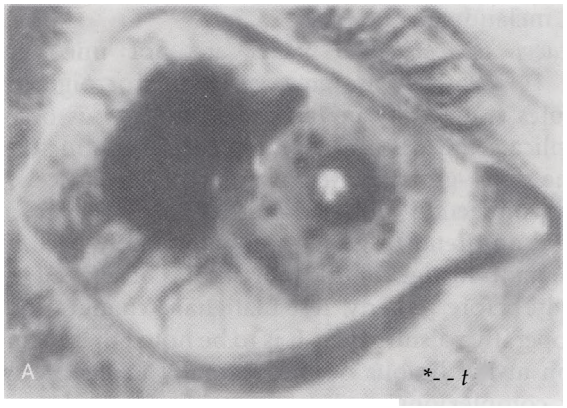
This is a dry, lustreless condition of the conjunctiva due to a deficiency of mucin, which occurs in two groups of cases: (i) as a sequel of a local ocular affection and (ii) associated with general disease.

The first type is a cicatricial degeneration of the conjunctival epithelium and glands following trachoma, burns, pemphigoid, diphtheria, etc. commencing in isolated spots, ultimately involving the whole conjunctiva and cornea. Prolonged exposure due to ectropion or proptosis, wherein the eye is not properly covered by the lids, also results in a 'dry' eye.

The chief changes are in the epithelium, which ceases to secrete mucus and becomes epidermoid like that of skin with granular and horny layers. A certain amount of vicarious activity is set up in the meibomian glands (*see* Chapter 28) which cover the dry surface with their fatty secretion so that the watery tears then fail to moisten the conjunctiva. C. *xerosis* grows profusely in these conditions, but this organism has no causal relationship and is of no importance.

It is to be noted that xerosis has nothing to do with any failure of function on the part of the lacrimal apparatus, as if the lacrimal gland is extirpated, xerosis does not follow. If, on the other hand, the secretory activity of the conjunctiva itself is impaired, xerosis may follow in spite of normal or increased lacrimal secretion.

In the second group of cases related to a systemic disorder, xerosis is usually mild and due to a deficiency of the fat-soluble vitamin A in the diet, found particularly in children and accompanied by night blindness *(see* p. 95). It is characterized by small, triangular, white patches on the outer and inner sides of the cornea, covered by a material resembling dried foam, which is not wet by the tears (*Bitot spots*, Fig. 14.17). These foamy spots are



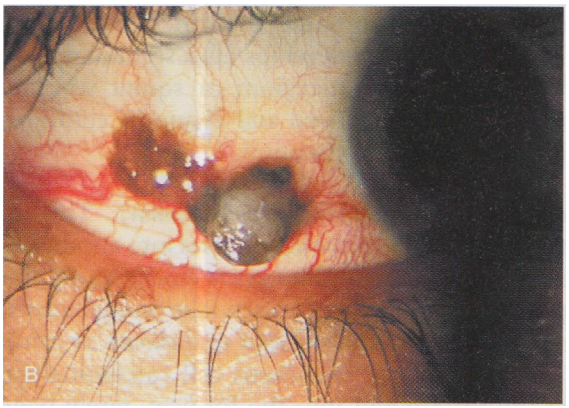


Fig. 14.16 (A) Malignant melanoma of the limbus; (B) malignant melanoma of the bulbar conjunctiva.

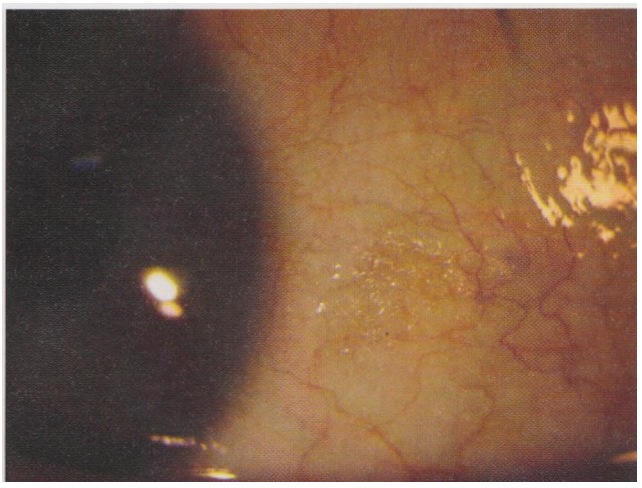


Fig. 14,17 Bitot spot.

due to gas production by *Corynebacterium xerosis* present in the horny epithelium. The cases usually occur during the summer months, and the children are often not conspicuously undernourished. A similar condition also associated with night blindness (nyctalopia), is found in marasmic children, associated with keratomalacia and necrosis of the cornea.

Treatment: Xerosis is a symptom and its treatment must therefore be purely symptomatic. Local treatment consists in relieving the dryness with artificial tears and mucomimetic agents *{see* p. 155). The frequency of medication varies from 1 hourly to 6 hourly, depending on the severity of symptoms. The dose is titrated by the subjective and objective clinical response to treatment. Dark glasses should be worn. In the vitamin A deficiency variety, nutrition should be restored by the administration of vitamin A.

Keratoconjunctivitis sicca (Sjogren syndrome)

Keratoconjunctivitis sicca is a condition caused by deficiency of the aqueous component of tears, i.e. the lacrimal secretion.

It is a general systemic and autoimmune disturbance usually occurring in women after the menopause and often associated with rheumatoid arthritis. It is characterized by deficiency of the lacrimal secretion leading to dryness of the eyes. This usually gives rise to chronic irritative symptoms and may be associated with epithelial erosions or filaments on the corneal surface. Damage to the epithelium of the cornea and conjunctiva may be demonstrated clinically by staining with Rose bengal. Pathologically, the lacrimal gland is found to be fibrotic and infiltrated with lymphocytes; similar changes in the salivary glands may lead to a dryness of the mouth, while desiccation may occur in other mucous membranes. A teanlysozyme ratio of 0.1 is typical of keratoconjunctivitis sicca.

Dry eye

A dry eye produces discomfort and reduced vision when the tear film becomes chronically unstable and repeatedly breaks up into dry spots between blinks, exposing the corneal and conjunctival epithelium to evaporation. Tear film instability may be the result of the following:

1. Deficiency of tears, as in Sjogren syndrome.
2. Deficiency of conjunctival mucus. Mucus from the goblet cells of the conjunctiva is necessary to keep the tear film stable. Lack of mucus causes pre-mature break-up of the tear film even in the presence of abundant tear fluid. Mucus deficiency occurs in Stevens-Johnson syndrome, ocular pemphigoid, avitaminosis, old trachoma or secondary to therapy with practolol.
3. Altered corneal surface changes and irregularities from past disease result in poor wetting with subsequent risk of further damage.
4. Insufficient wetting of the corneal surface by the lid as in decreased blink rate, lid paralysis or the formation of a dellen.

Symptoms arising from a dry eye may be mimicked by chronic blepharoconjunctivitis due to the staphylococcus, rosacea keratoconjunctivitis or allergic conjunctivitis. These diagnoses should first be eliminated. Features which help in the diagnosis of a moderately dry eye are the presence of particulate matter in the tear film due to mucus which is stainable with Alcian blue. Tear film break-up time should be less than 10 seconds, and dry, dead epithelium should be stained with 1% Rose bengal (Fig. 14.18) drops. Rose bengal also stains mucus. A teanlysozyme ratio between 0.9 and 0.6 or a Schirmer test producing wetting less than 6 mm support the diagnosis.

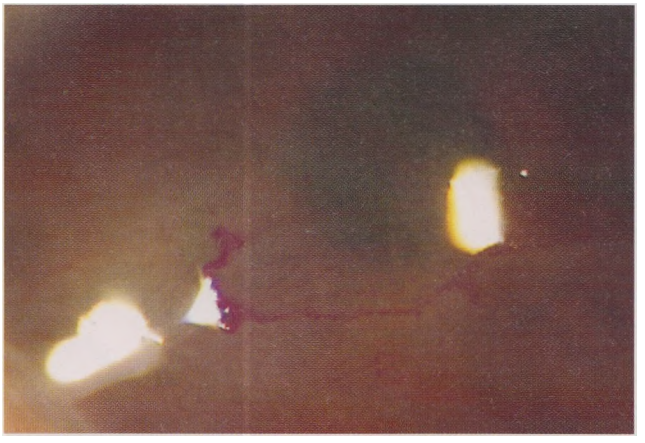


Fig. 14.18 Rose bengal 1% drops instilled in the conjunctival sac stain the devitalized epithelium in a patient with dry eye.

Several varieties of effective artificial tears are commercially available. The slow-release variety is a pellet of a cellulose compound without preservative that is inserted below the tarsus of the lower lid where it dissolves slowly providing a continuous source of tears. If obstruction of the canaliculi with gelatin plugs gives relief it is worth considering permanent obstruction of the lower puncta. Excess mucus may be treated by acetyl cysteine 5% drops buffered to pH 8.4 with sodium bicarbonate.

Squamous metaplasia of the ocular surface epithelium may play a part in the production of symptoms. This abnormality can be reversed by the application of topical transretinoic acid ointment with alleviation of discomfort.

Treatment to preserve the natural tears includes temporary occlusion of the puncta by inserting dissolvable collagen plugs, or permanent occlusion by inserting silicone plugs or by thermal cautery. Lateral tarsorrhaphy can also be performed to reduce the evaporation of tears.

Symblepharon

This is an adhesion between the bulbar and palpebral conjunctiva and occurs due to any condition which makes apposing surfaces raw and inflamed, allowing cicatrization and fibrosis. Chemical and thermal bums, cicatrizing conjunctival diseases such as Stevens-Iohnson syndrome and pemphigoid are common causes.

Treatment depends on the extent of symblepharon. Surgical release with mucous membrane or amniotic membrane grafting is needed in severe cases (Fig. 14.19).

Conjunctivochalasis

This is a condition seen in elderly people with laxity of the conjunctiva leading to folds usually visibly heaped on the lid margin (Fig. 14.20). It can be asymptomatic or produce ocular discomfort due to 'dry' eye and a foreign body sensation with tearing. Symptomatic relief can be provided by prescribing artificial tears 4 to 6 times a day, modifying the frequency as necessary. Sometimes surgical excision of redundant folds (conjunctivoplasty) is required.



Fig. 14.19 Symblepharon superiorly forming a pseudopterygium.



Fig. 14.20 Conjunctivochalasis.

Argyrosis

This is a deep brown staining of the conjunctiva from prolonged application of silver salts (silver nitrate, proteinate, etc.) for the treatment of chronic conjunctivitis and especially trachoma. Since these drugs are seldom used the condition is rarely seen nowadays. The staining, which is most marked in the lower fornix, is due to the impregnation of reduced metallic silver into the elastic fibres in the membrane and vessel walls.

SUMMARY

A healthy conjunctiva is important for the maintenance of a healthy intact ocular surface. Diseases of the conjunctiva manifest with symptoms of ocular irritation, lacrimation, mucoid or mucopurulent discharge, foreign body sensation, pain and redness. Signs of conjunctival congestion, papillae, follicles, pattern of involvement and type of discharge help in making a clinical diagnosis. It is important to examine the entire conjunctival surface carefully including lid eversion to look for foreign bodies and other signs. One should know how to differentiate conjunctival from circumcorneal congestion as this has important implications for correct diagnosis and treatment of different disorders. The diseases that affect the conjunctiva can be congenital, idiopathic, infectious, traumatic, iatrogenic and neoplastic.

SUGGESTED READING

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The special importance of diseases of the cornea lies in the fact that they often leave permanent opacities which substantially diminish visual acuity, while the associated complications which not infrequently follow them may even lead to complete loss of vision.

ANATOMY AND PHYSIOLOGY

The transparent cornea comprises one-sixth of th£ anterior eyeball. Its curvature is greater than the rest of the globe and the junction of the cornea with the sclera, anatomically called the *limbus,* is marked by a shallow sulcus also known as the *sulcus sclerae.* The cornea is convex forwards, but seen from the front its shape is somewhat elliptical with the horizontal diameter being slightly more than the vertical (Fig. 15.1 and Table 15.1). The corneal thickness is more in the periphery than in the centre and is affected by age, temperature, osmolality of tears, integrity of the epithelium and endothelium, intraocular pressure, disease and drugs.

The cornea consists of three layers (Fig. 15.1C): (i)the epithelium; (ii) the *substantia propria* or stroma and (iii) the endothelium. Between the epithelium and stroma lies the Bowman's layer or membrane and between the stroma and endothelium, the Descemet's membrane.

The normal healthy cornea is avascular and devoid of lymphatic channels. Corneal cells derive nourishment by diffusion from the aqueous, the capillaries at the limbus and oxygen dissolved in the tear film.

The metabolism of the cornea is preferentially aerobic and it can function only up to 6-7hours, anaerobically under normal conditions. The metabolically active cells are the endothelium, epithelium and stromal keratocytes. Oxygen is mostly derived from the tear film with a small contribution from the limbal capillaries and the oxygen gradient is from tears to the aqueous. Glucose supply for corneal metabolism is mainly (90%) derived from the aqueous and supplemented n6%rBvthe limbal capillaries.

Table 15.1 Anatomical dimensions of the normal cornea

	Corneal diameter (mm)		Radius of curvature (mm)
	Horizontal	Vertical	
Anterior surface	11.7	10.6	7.8
Posterior surface	11.7	11.7	6.5
Corneal thickness	Central	Peripheral	
	0.5–0.6	1.2	

The cornea is supplied by nerves which originate from the small ophthalmic division of the trigeminal nerve, mainly by the long ciliary nerves which run in the perichoroidal space and pierce the sclera a short distance posterior to the limbus. Here they form an annuhy^lexus from which branches travel radially to enter the corneal stroma. The nerve fibres lose their myelin sheaths and unite to form a subepithelial corneal plexus. Fine terminal branches then pierce Bowman's membrane and pass between the epithelial cells to form the intraepithelial plexus. There are no specialized nerve endings or sensory organelles. The axons do not have a Schwann rpll sheath. These naked axons are responsive to pain and temperature. Due to its dense nerve supply the cornea is an extremely sensitive structure.

The cornea is the most important refractive surface of the eye. Its refractive index is 1.38 (1.376) and the anterior surface is the main refractive surface. The tear film is important in maintaining a healthy normal environment for the corneal epithelial cells. The tear film consists of an inner mucin laver which lines the hydrophobic epithelium and makes it 'wettable', an aqueous layer and a superficial lipid laver which decreases evaporation.

The transparency of the cornea is due to its relatively dehydrated state, absence of blood vessels and pigment, uniform refractive index of all the layers and uniform spacing of the collagen fibrils in the stroma. The collagen fibrils are separated bv.a distance which is less than

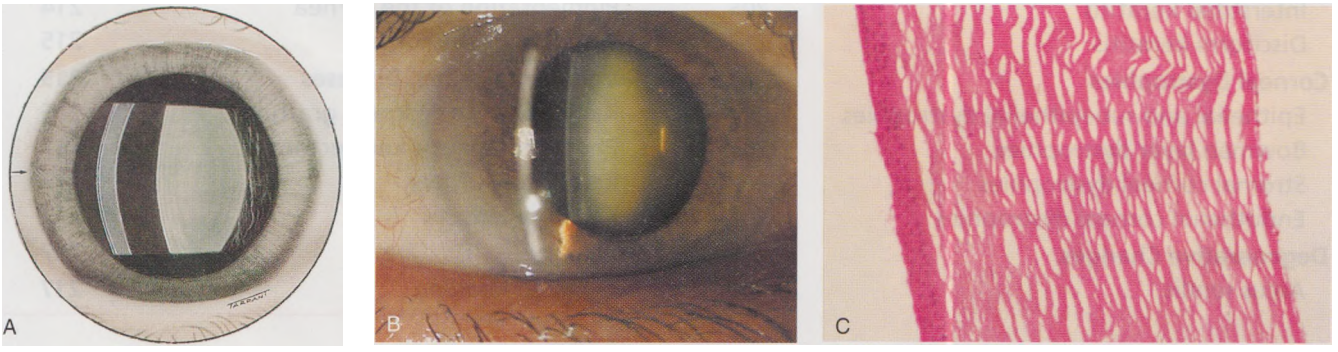


Fig. 15.1 (A and B) Diagrammatic representation of the normal eye, as seen with the slit-lamp. View of the front surface shows an elliptical shape. The light (arrowed) is coming from the left and in the beam of the slit-lamp the sections of the cornea and the lens are clearly evident. (C) Section of normal human cornea stained with haematoxylin and eosin. (By courtesy of S Kashyap)

the wavelength of light so that any irregularly refracted rays of light are eliminated by destructive interference. If there is an increase in separation of the stromal collagen or a disruption in their regular arrangement, for example, with an increase in tissue fluid, the cornea becomes opaque. This relative state of dehydration is maintained by the integrity of the hydrophobic epithelium and endothelium, the endothelial pump and the osmotic gradient, because the aqueous and tears are relatively hypertonic. The main role of the endothelial cells is to limit the fluid intake of the cornerfromTKTaqueous.

The functions oFTlTe cornea include: (i) allowing transmission of light by its transparency; (ii) helping the eye to focus light by refraction; (iii) maintaining the structural integrity of the globe; and (iv) protecting the eye from infective organisms, noxious substances and UV radiation *(see* Chapter 5).

With advancing age, the cornea becomes less transparent and develops dusFlike opacities due to condensations in the deeper parts of the stroma. There is also an increase in thickness oTTiow man's and Descemet's membranes.

In case the cornea sustains injury due to any cause such as trauma, infection or surgery, and if the injury is superficial involving only the epithelium, the stratified squamous epithelium covering the anterior surface of the cornea rapidly regenerates. This regeneration of corneal epithelial cells is mainly from stem cells, which are epithelial cells present as palisades of Vogt at the limbus. These mitotically activeTells with~anTncreased surface area of basal cells present in folds and palisades are ideally suited for this purpose. There is very little mitotic activity in the basal cells at the centre of the cornea. Bowman's laver, which is really a condensed part of the anteriormost layer of the stroma, serves as a barrier to the underlying stroma. When damaged,Jt jioes.-not-refienerate but is replaced by fibrous tissue, as is the stroma. On the other hand, Descemet's membrane, which is the basement membrane of the endothelial cell laver, can be regenerated by the endothelial cells to some extent when injured. Descemet's membrane is strong and generally resistant to trauma, but can develop tears or ruptures if the trauma is severe.^jt_is_elastic and if torn, the edges separate and are visible as parallel lines or if disinserted, curlsupin the anterior chamber. The endothelial cells are closely bound to each other and the entire endothelial layer can be stripped off as a sheet. The corneal endothelium does not regenerate but adjacent cells slide to fill in a damaged area. (V)(

The corneal epithelium and endothelium maintain a steady fluid content of the corneal stroma. They are lipid-rich and hydrophobic with good soliihilinTtTnTfiTHTand water but poor to ~salts.~The stroma is hydrophilic. The epithelial cells have junctional complexes which prevent the passage of tear fluidTnto the cornea and loss of tissue fluid from the cornea into the tear film. There are junctional complexes in the endothelium too, but the influx of aqueous humour into the cornea ^additionally limited by an active transport mechanism involving the *~Na⁺-^K^MTˢaM~pump* system. Trauma to either of these I aye rs pro <3uces~ o e de maoft h e stroma. The dense Bowman's layer, however, tends to limit the spread of fluid from the damaged epithelium into the deeper stroma.

Acute glaucoma, with a rise in intraocular pressure, can open ~up gaps between the endothelial cells pushing the aqueous into the corneal stroma and fluid may also accumulate beneath, between and within the epithelial cells.

The permeability of the cornea is related to the characteristics of the various components. Lipids in cell membranes have poor permeability to salts and are hydrophobic so as to help maintain the relative state of dehydration which is important for corneal transparency. The osmotic gradient maintained between the cornea and the hypertonic tears anteriorly and aqueous posteriorly limits movement of water into the cornea.
The hydrophilic stroma has better permeability to salts.

The cornea is normally avascular, but may be invaded by new blood vessels from the limbus in case of infection and inflammation. This brings the humoral and cellular defence mechanisms closer to the inflamed site for the purpose of immunological defence and repair. However, the transparency is compromised by this and a corneal opacity develops if the process continues. The new vessels can arise from the conjunctival superficial vascularjjkxus or the deep plexus from the anterior ciliary arteries. The capillaries~ansing from these plexuses normally end as loops at the limbus, but on stimulation new vessels can invade the cornea. When the stimulus is eliminated, these blood vessels can atrophy, regress and empty leaving behind ^ghost'vessels^

The cornea, being exposed to the external environment, is prone to atmospheric influences such as smoke, dust, heat, dry air and sand, which can all affect the ocular surface. Excessive exposure to ultraviolet radia-^,vjy tion can harm the cornea leading to solar keratopathy, < pterygium and climatic droplet keratopaffiyTVitamin A deficiency weakens the defences and healing potential and poor hygiene assists the spread of infection by eye-to-eye transmission. Hereditary disorders, dystrophies and other degenerations can affect the cornea.

PATHOLOGY

The major pathological changes that occur are broadly categorized as keratitis, and corneal 'ulceration', 'scarring' and 'opacification'.

Keratitis is the descriptive term used for any type of corneal inflammation. Inflammation anterior to Bowman's membrane (involving the epithelium and Bowman's

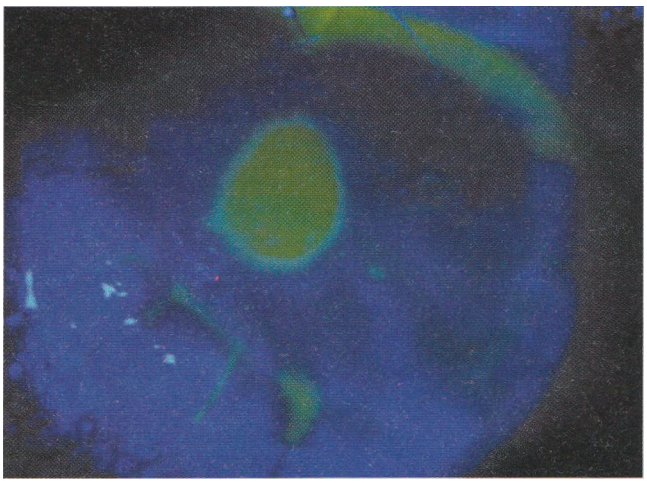


Fig. 15.2 Corneal epithelial defect stained with fluorescein.

membrane) is called *superficial keratitis.* If only occurring i njdiscrete_ jjatches, the latter is further categorized as *superficial punctate keratitis* (SPK). Inflammation in the stroma is called *deep keratitis.* Deep keratitis is further categorized as *stromal* or *interstitial keratitis* or *endo{hglitiE,* depending on tfie^cfi reel involvement of the endothelium in the inflammatory process.

A loss of epithelium is termed an *epithelial defect* and can be demonstrated clearly by staining with1% sodium fluorescein dye and viewed with cobalt blue filtered light (Fig. 15.2). If superficial without any inflammation, an epithelial defect is also called *an^raFrasion* or *erosion]*and usually heals withinJ^2-2£hours by regeneration of the epithelial cells from the periphery, which slide over to cover the defectjAloss of epithelium with inflamma tion in the surrounding cornea is called a *corneal ulcer* Inflammation in the cornea is visible as a greyish haze or loss of clarity. If accompanied by an outpouring of 'leucocytes the appearance is more off-white or yellowish and this hazy area is termed as an infiltration. Corneal ulcers can be infective or sterile.

A *corneal scar* is the final outcome of any inflammation. Unlike healthy transparent corneal tissue, scar tissue is white and opaque in varying degrees of severity. The nature, extent, pattern and density of scarring vary according to the nature of the original inflammatory disease. Non-inflam matory diseases can also lead to corneal opacification but the term 'scar' or 'scarring' is reserved for the opacity which follows inflammation.

Corneal opacity

If the corneal scar results in slight opacification allowing the details of the iris to be seen through the opacity it is called a *nebula* or a *nebular corneal opacity;* if rather more dense, through which the details of the iris cannot be seen

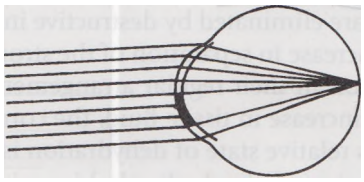


Fig. 15.3 The optical effect of a small central or paracentral complete leucoma. Light falling upon it is not irregularly refracted and does not distort the retinal image.

macula or a *macular corneal opacity;* if very dense and white and totally opaque obscuring the view of the iris and pupil, it is called a *leucoma* or a *leucomatous corneal opacity.* Old central leucomata sometimes show a horizontal pigmented line in the palpebral aperture, the nature of which is obscure but may be due to deposition of iron from the pre-corneal tear film. If the iris is adherent to the back of a leucoma following healing of a perforated corneal ulcer, it is called an *adherent leucoma.* Ifjjis tissue is incarcerated and incorporated within the scar tissue, as occurs in healing of a large sloughed corneal ulcer, it is called a *corneoiridic scar* or if ectatic. an *anterior staphyloma.*

A thin, diffuse nebula covering the pupillary area interferes more with vision than a strictly localized dense leucoma, so long as the latter does not block the whole pupillary area. This is because the leucoma stops all the light which falls upon it (Fig. 15.3), whereas the nebula refracts it irregularly, allowing many of the rays to fall upon the retina where they blur the image formed by the regularly refracted rays. An opacity does not necessarily prevent the light from being focussed upon the retina immediately behind it. Thus, a small central or paracentral opacity will not prevent the focussing of an object upon the macular region, for the rays passing through the clear peripheral parts of the cornea will be refracted towards the macula; only those rays which are incident on the opaque region of the corneal surface are cut off. There is thus a loss of brightness rather than of definition, although this is impaired by the superimposition of a diffuse entoptic image of the opacity upon the clear image of the external object.

Althoiiph so mp opacity always remains when Bowman's membraneiias-been-deatroyed, it usually clears considerably, a process more markedin younger patients. A clinical example of this is the healing process which takes place after excimer laser photo-refractive keratectomy (PRK).

Corneal oedema

Corneal oedema can affect the entire cornea but generally manifests itself first in the epithelium, which becomes steamy, an appearance due to the accumulation of fluid between the cells^ especially the basal cells. At the same time, the accumulation of fluid between the lamellae and

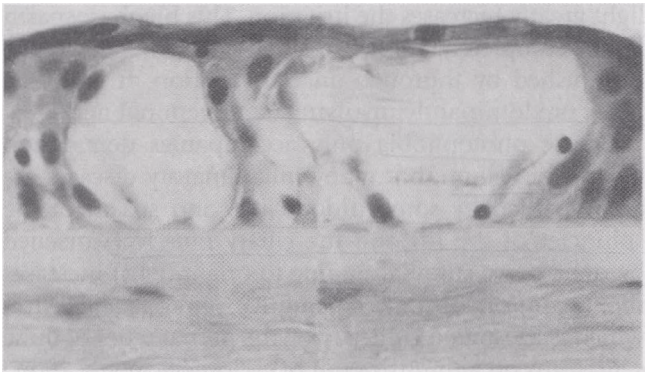


Fig. 15.4 Corneal oedema: vesicle formation.

around the nerve fibres of the stroma produces haziness throughout the entire cornea due to alterations in the refractive condition. If the oedema lasts for a Inna period the epithelinm tendsi.lu-he-jai.spjd-iBto-large-vesicles or bullae *(vesicular or bullous keratopathy)* (Fig. 15.4). This is a particularly intractable condition, which frequently gives rise to intense pain and symptoms of ocular irritation as the bullae periodically burst.

Such corneal oedema may occur in many inflammatory or degenerative conditions of long standing. It is common in glaucoma when the tension is high; it also tends to occur whenever the endothelium has suffered damage so that the aqueous can percolate through the stroma. After trauma or surgery such an oedema is characteristic of endothelial damage, particularly when strands of vitreous remamadherent to the posterior si irfacp of the cornea.

Striate keratopathy is a form of corneal oedema that is seen after operations upon the globe in which a peripheral corneal section has been made, as in cataract extraction. Here, delicate grey lines run from the wound and may pass completely across the cornea; they disappear spontaneously as the wound heals and are due to slight folding of the cornea where Descemet's membrane and the adjacent lamellae become^wrinkled. Radial striae are seen around wounds or ulcers, partly due to the cause and partly due to distension of the interlamellar spaces by oedema. The fine hatching which is seen around ulcers is similar.

Treatment is difficult unless the primary cause of the oedema can be eliminated. Some comfort may be obtained by the application of a bandage contact lens and the frequent instillation of a concentrated saline solution or an ointment containing 6% sodium chloride. An alternative which is frequently effective is to strip off the entire epithelium and to replace it by a thin flap of the conjunctiva. Visual improvement depends~nrr full-thickness keratoplasty.

Filamentary keratopathy

Filamentary keratopathy is the formation of epithelial threads (corneal filaments) which adhere to the cornea by one end while the other, which isoften club shaped, moves about freely(Fig. T37577 Such filaments produce symptoms of irritation and foreign body sensation and occur in degenerative conditions, inlong-standing corneal oedema, in cases of vTraTkeratitis particularly of the herpetic type, in the collagen vascular diseases and in (Try eyes due to any cause, i.e. keratitis sicca (*see* p. 185).

Keratic precipitates

Initially termed *keratitis punctata* or 'k.p.', these are depositions of leucocytes and other cells on the back of the cornea in cyclitis, iridocyclitis and occasionally in choroiditis. The greatest care must be taken not to overlook them, since they may be almost the only objective £ign offsenous disease) They may be~on the back of i clear cornea (*see* Fig. 11.12B) or the deeper layers may be infiltrated (Fig. 17.IB) as a result of the intraocular inflammation. Their appearance and nature will be described while discussing their cause (*see* p. 225).

Hypopyon

A hypopyon (*see* p. 195) consists of polymorphonuclear leucocytes which accumulate in the lowerangle of the anterior chamber and eventually become enmeshed in a network of fibrin. It is clinically seen in severe corneal ulcers as a collection of 'pus' in the anterior chamber. It may be so small that it is scarcely visible, being hidden behind the rim of sclera which overlaps the cornea. It may reach halfway up the iris, having a flat upper surface, determined by gravity, or it may fill the anterior chamber, wholly obscuring the iris. The hypopyon, if fluid, will be seen to shift, i.e. a change in fluid level with tilting or change in position of the head. Larger hypopyons and those due to fungal infections are usually less fluid owing



Fig. 15.5 Filamentary keratopathy.

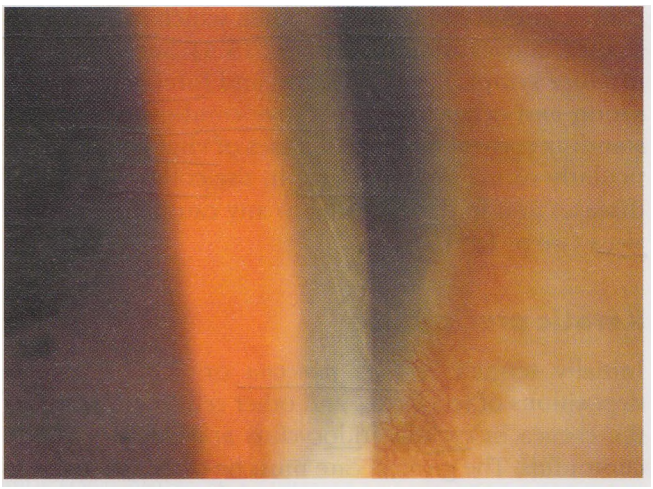


Fig. 15.6 Enlarged corneal nerves. <^U|\|C.A[L]

to the fibrinous network which imprisons the leucocytes in its meshes and direct invasion by fungal hyphae. These are immobile and are much less readily absorbed.

Prominent or enlarged corneal nerves

Prominent or enlarged corneal nerves may be asymptomatic and detected accidentally or may be associated with other local disease conditions such as keratoconus—Che corneal nerves are known to be en I arged~(Tlg!- l 5.6) in the multiple endocrine neoplasia (MEN) syndrome Type lib (combination of medullary carcinoma of the thyroid, phaeochromocytoma, mucosal neuromas and possibly marfanoid habitus). Other systemic diseases associated with prominent corneal nerves include neurofibromatosis and Refsum syndrome. Local ocular disorders with this clinical sign include keratoconus, keratitis (most characteristically seen in acanthamoebic keratitis), Fuchs endothelial dystrophy, trauma and congenital glaucoma.

CLINICAL FEATURES AND EXAMINATION

The cornea may be affected by infection, injury, inflammation, dystrophy, degeneration or cancerous conditions. The diseases manifest in different ways but certain common clinical features exist.

Common *symptoms* of corneal diseases are decreased vision, lacrimation, redness, photophobia, 'foreign body' sensation7~pain and a visible 'whiteness' of the cornea. They are present in varying degrees of severity and in different combinations.

Photophobia is the term applied to the discomfort experienced on exposure to bright light. In corneal disorders, this is accompanied by blepharospasm caused by corneal irritation due to stimulation of the terminal fibres of the corneal nerves. The slightest attempt to separate the lids, especially if the attempt is made in bright light greatly increases the irritation. This blepharospasm is not completely abolished in the dark, but is greatly diminished by thorough anaesthetization. It is thus a reflex predominantly involving-thp trippminal nerve.

Severe photophobia only accompanies denudation of the epithelium, but many inflammatory diseases are accompanied by some iridocyclitis, and spasm of the sphincter of the iris and the ciliary muscle (worsened bv optic nerve stimulation due to bright light) increases the discomfort. This has an additive 'photophobic' effect which is illustrated clinically by the partial relief of these symptoms on administration of cycloplegic medication.

Examination

External *examination* of the cornea can be performed with a torch, with a magnifying loupe and a slit-lamp *(see* p. 115). *Surface irregularities* can be detected by examining the *corneal reflex,* shape of the reflection of a window or byJZlacido^sj£CT^qscopic rings. Measurement of the *curvature* is donehv keratometry *(see* p. 67) and corneal topography *(see~pTTr^J7THF7:orneal thickness* can be measured manually by an optical pachymeter attached to a slit-lamp, with an ultrasonic pachymeter or a slit-scanning topography system. The *corneal endothelium* can be viewed with the slit-lamp in the *zone of specular reflection (see* Fig. 11.4) and cells counted using a specular microscope. All the layers of the cornea can be studied in detail and images stored for analysis using the confocal microscope (Fig. 15.7).

INFLAMMATION (KERATITIS)

Inflammation of the cornea may arise from three sources:

1. *Exogenous infections:* The cornea is primarily affected by exogenous organisms, including virulent organisms already present in the conjunctival sac, gaining access to the corneal tissues and causing keratitis.
2. *Endogenous infections or inflammation:* These are typically immunological in nature. The avascularity of the cornea allows immunological changes to persist for an unusually long time; examples are phlyctenular keratitis related top tuberculosis] and interstitial keratitis' related to j syphilis *]* and \ measles.) Sometimes the cornea is affected by a hypersensitivity or autoimmune reaction rather than related to a specific infection. These changes are common near the limbal blood vessels close to the corneal margin and are called *marginal keratitis* or *marginal corneal ulcers.*
3. *Contiguous spread from the ocular tissues:* Owing to direct anatomical continuity, diseases of

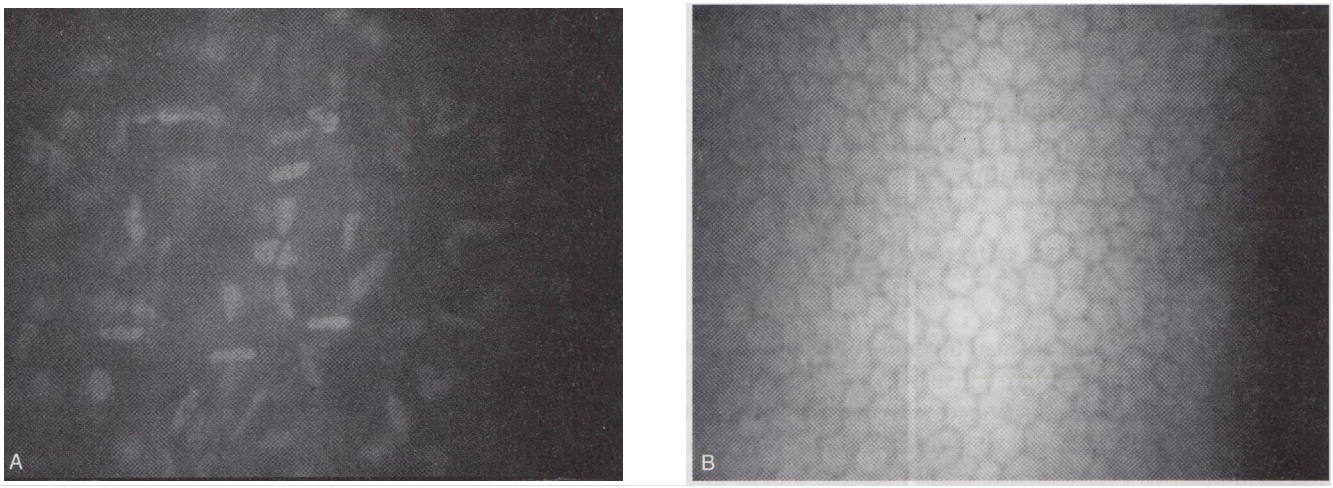


Fig. 15.7 Corneal keratocytes (A) and endothelial cells (B) recorded with the confocal microscope. (By courtesy of M. Vanathi)

the conjunctiva readily spread to the corneal epithelium (such as , trachoma and vernal keratoconjunctivitis); those of the sclera to the stroma (e.g. sclerosing keratitis); and of the uveal tract to the endothelium (e.g. herpetic nvpi.t.k-with endothelitis).

From the clinical point of view, corneal inflammations are best divided into categories: (i) based on location: superficial and deep and (ii) based on the nature of the aetiology: infectious, immune-mediated, degenerative, neoplastic and traumatic (including chemical and thermal injuries).

INFECTIONS AFFECTING THE CORNEA

Corneal infections can be *suppurative* (purulent) or *non-suppurative* (non-purulent) depending on whether 'pus' is formed; they can be *ulcerative* or *non-ulcerative* and the aetiological agents can be bacterial, fungal, viral and parasitic (protozoal or helminthic). Most corneal infections begin as superficial keratitis but can later become deep.

Superficial purulent keratitis includes corneal ulcers which are characterized by an epithelial defect with infiltration of the underlying and surrounding stroma. Superficial non-purulent keratitis includes a number of conditions of varied aetiology. Many of them are viral infections or parasitic (acanthamoebic, microsporidiosis, onchocerciasis) while others such as phlyctenular and rosacea keratitis are of constitutional origin. Superficial keratitis, if untreated or inappropriately treated, evolves into deep keratitis.

Certain conditions begin with deep stromal involvement in which case the term *deep stromal keratitis* is applied. The deep forms of keratitis comprise those due to infections where organisms enter the cornea from the body through the limbus, for example, syphilis, onchocerciasis, tuberculosis; or some forms of immunological inflammation in viral infections *tdisciform keratitis)* and lesions of indeterminate origin or due to the spread of scleral inflammations (sclerosing keratitis, *see* p. 221).

Infectious crystalline keratopathy (ICK) is a special variety of stromal keratitis distinguishable bv the appearance *of* crystalline arborifoem white opacities or deposits in the corneal stroma with minimal or no associated inflammatory reaction. It is typically seen in immunocompromised corneas such as following corneal grafts, long-term topical corticosteroid use or contact lens wear (Fig. 15.8). It is hypothesized that commensal organisms from periocular skin or the ocular surface gain access to the stroma via suture tracks or through compromised unhealthy corneal epithelium.

Microorganisms that can produce this type of infection include alpha haemolytic streptococcus, peptostreptococcus, pseudomonas and Candida and "prolonged treatmentwith topical vancomycin, moxifloxacin or gatifloxacin eye drops with discontinuation or minimization

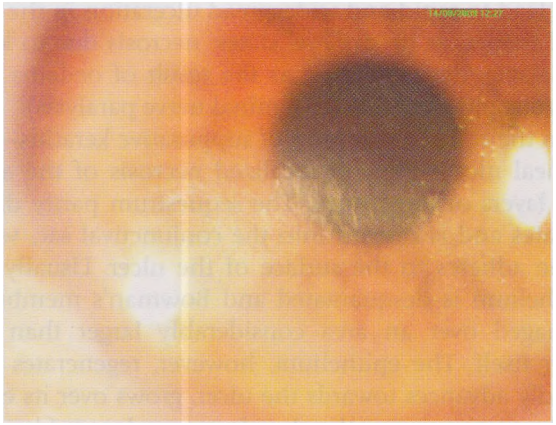


Fig. 15.8 Infectious crystalline keratopathy.

of topical steroid use is generally required. Recurrence of infection and stromal scarring are common which may then require keratoplasty. Differential diagnosis of crystalline deposits in the cornea includes Schnyder's crystalline corneal dystrophy, and hypergammaglobulinaemia, cystinosis and lipid keratopathy.

Bacterial ulcers and purulent keratitis

Aetiology

Suppurative keratitis or corneal ulcer is due to organisms that produce toxins which cause tissue death (necrosis) and pus formation in the corneal tissue. Purulent keratitis is nearly always exogenous, due to pyogenic bacteria such as *Pseudomonas, Staphylococcus aureus* and *albus, Pneumococcus, Neisseria gonorrhoeae, Escherichia coli,* etc.), which invade the cornea from without. It has been noted that the only organisms known to bp ahlp to invade normal corneal epithelium are/N. *gonorrhoeae) and(Coiynebactenum diphtheriaefrbut* most other bacteria (e.g. pneumococci) are capable of producing ulceration when the epithelium is damaged. Organisms such as staphylococci may lead to superficial erosions initially, which coalesce to form frank ulcers.

Pathology

Although minute abrasions of the cornea are probably of everyday occurrence, highly virulent, pathogenic organisms are not always present in the conjunctival sac and, if they are, the tear film and the resistance of the normal tissues suffice to deal with them. However, there are certain specific predisposing factors which increase the risk of developing corneal ulceration. These are: introduction of organisms during trauma, prolonged use of topical steroids, dry eyes, entropion with trichiasis, lagophthalmos due to neuroparalysis (facial nerve), wearing of contact lenses, bullous keratopathy and poor local hygiene. Apart from actual abrasions a diminished resistance of the epithelium will allow the entry of organisms and lead to rapid and widespread ulceration in the corneal tissues, as in 'dry eye' states, necrosis due to keratomalacia, desquamation as the result of oedema and neurotrophic keratitis (trigeminal nerve paralysis).

In the commonest form of suppurative keratitis—the corneal ulcer—there is localized necrosis of the anterior layers of the cornea. The sequestrum partly disintegrates and is cast off into the conjunctival sac, while some adheres to the surface of the ulcer. Usually the epithelium is desquamated and Bowman's membrane damaged over an area considerably larger than the ulcer itself. The epithelium, however, regenerates and rapidly advances towards the ulcer, grows over its edge, and sometimes over the slough or purulent infiltration which forms the floor.

The ulcer is usually saucer-shaped, and the walls project above the normal surface of the cornea owing to swelling caused by the fluid imbibed by the corneal lamellae. The surrounding area is packed with leucocytes and appears as a grey zone of infiltration. This is the *progressive stage.* A line of demarcation forms, as in necrosis elsewhere in the body. Here, a wall of polymorphonuclear leucocytes forms a second line of defence while leucocytes macerate and dissolve the necrotic tissues. When the necrotic material has been shed off the ulcer is somewhat larger, but as the surrounding infiltration and swelling disappear, the floor and edges become more smooth and transparent, and the *regressive stage* is reached.

Meanwhile, vascularization develops and minute superficial vessels grow in from the limbus near the ulcer to restore the loss of substance; they also supply antibodies and therefore play an important role in resolving bacterial infections. Sometimes their exuberance oversteps the limits of utility, as in a fascicular ulcer.

The healing of a corneal ulcer: When an ulcer has become vascularized, cicatrization occurs which is carried out by the regeneration of collagen and the formation of fibrous tissue. The newly formed fibres are not arranged regularly as in the normal corneal lamellae, hence they refract the light irregularly and the scar is, therefore, more or less opaque. If it is large and dense, some of the larger vessels persist while the smaller ones disappear. Bowman's membrane is never regenerated, and if it has been destroyed, as is the case in all but very superficial abrasions, some degree of permanent opacification remains. However, in some mild scars, restoration of transparency does occur over time. Here, vascularization plays a considerable part as is shown by the fact that the opacities clear first in the immediate vicinity of the vessels.

The scar tissue which replaces the destroyed portions of the cornea usually fills in the gap exactly, so that the surface is level. It is quite common, however, for some deficiency to remain so that although the resultant cicatrix may be almost transparent, the surface could become flattened or even faceted. Such *corneal facets* can be seen only by careful examination of the corneal reflex but they may cause considerable diminution of visual acuity.

Symptoms and signs

While these events occur in the cornea, irritative signs are always found within the eye. Some of the toxins produced by the bacteria diffuse through the cornea into the anterior chamber, just as topical medications do when instilled into the conjunctival sac. They exert an irritative effect upon the vessels of the iris and ciliary body, so that hyperaemia of the iris occurs with ciliary injection resulting in *keratouveitis.* If the irritation is

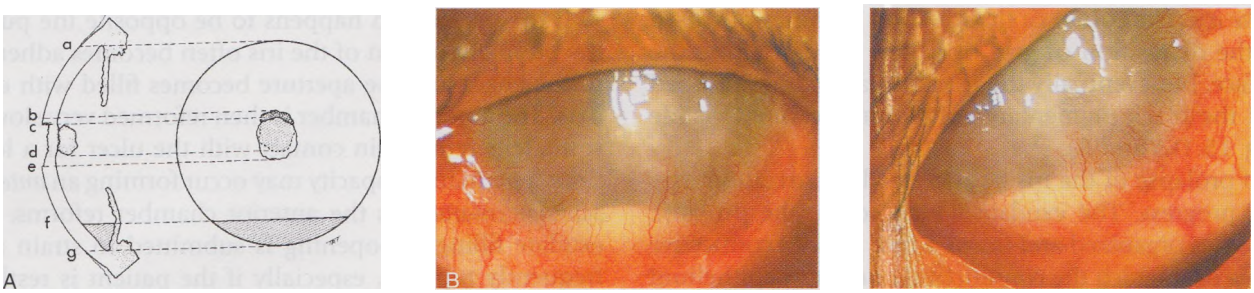


Fig. 15.9 (A) Hypopyon ulcer: c–e, the extent of the ulcer; b–c, actively infiltrated border; c–d, mass of leucocytes and fibrin adherent to the endothelial surface; f–g, hypopyon. (B) Hypopyon (left) with shifting fluid level on tilting the head (right) in a case of bacterial keratitis.

great, leucocytosis takes place, and polymorphonuclear cells poured out by the vessels pass into the aqueous and gravitate to the bottom of the anterior chamber where they form a *hypopyon* (Fig. 15.9A and B).

Symptoms of a corneal ulcer are marked. During the progressive stage there is lacrimation, photophobia, blepharospasm, pain and photophobia owing to the exposure of the terminal fibres of the ophthalmic division of the trigeminal nerve and varying degrees of diminution of vision.

The clinical assessment of a corneal ulcer requires careful examination with a slit-lamp. The ulcers can be graded according to size, area of infiltration and depth of involvement (superficial or deep) to indicate their severity (mild, moderate or severe), location and extent of possible threat to vision.

Complications

Superficial ulcerations commonly heal with varying degrees of scarring but if the ulcer is deep, the loss of tissue may lead to a marked thinning of the entire cornea at the site of the ulcer so that it bulges under the influence of the normal intraocular pressure. As the cicatrix becomes consolidated the bulging may disappear, or it may remain permanently as secondary keratectasia, an *ectatic cicatrix.*

Some ulcers, especially those due to pneumococci and septic organisms, extend rapidly in depth so that the whole thickness of the cornea, except Descemet's membrane and a few corneal lamellae, may be destroyed. Descemet's membrane, like other elastic membranes, offers great resistance to inflammatory processes. It is, however, unable to support the intraocular pressure by itself and, therefore, herniates through the ulcer as a transparent membrane called a *keratocele* or *descemetocele* (Fig. 15.10). This may persist, surrounded by a white cicatricial ring, or it may eventually rupture.

Perforation of an ulcer is usually caused by sudden exertion by the patient, such as coughing, sneezing, straining at stool or spasm of the orbicularis muscle. Any such activity causes a rise in the blood pressure, which at once manifests itself by a rise in the intraocular pressure and the weak floor of the ulcer, unable to support the sudden strain, gives way. When an ulcer perforates, the aqueous suddenly escapes and the intraocular pressure falls to the atmospheric level, the iris and lens being driven forwards into contact with the back of the cornea. The effect upon the nutrition of the cornea is good; owing to the diminution of intraocular pressure the diffusion of fluid through the cornea is facilitated, extension of the ulceration usually ceases, pain is alleviated, and cicatrization proceeds rapidly. The complications which follow a perforation are, however, of extreme danger to sight as well as preservation of the eye. These complications vary according to the position and size of the perforation.

Usually the perforation takes place opposite some part of the iris which is drawn into the aperture when the aqueous escapes. If the perforation is small the iris becomes gummed down to the opening, the adhesion organizes forming a layer of scar tissue over the adherent iris which is referred to as a 'pseudocornea' and an *anterior synechia* is formed. The blocking of the perforation with the iris allows the anterior chamber to be reformed as fresh aqueous is rapidly secreted. If the perforation is large, a portion of the iris is carried not only into the opening but through it causing a *prolapse*

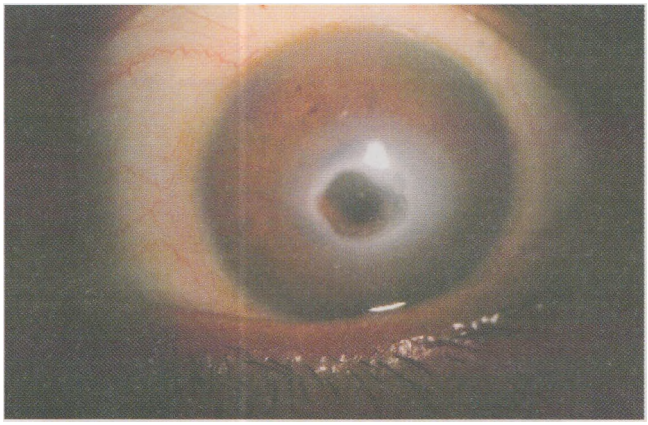


Fig. 15.10 Descemetocele.

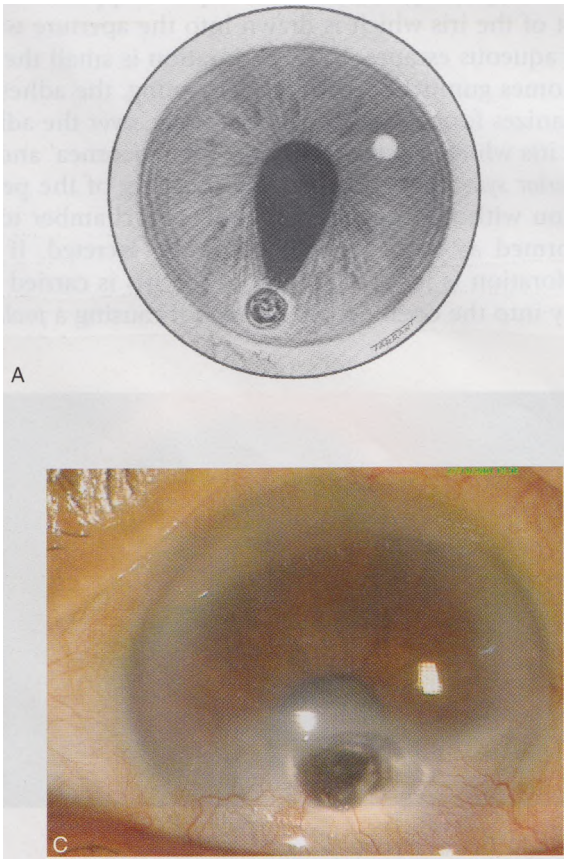
of the iris. The colour of the iris soon becomes obscured by the deposition of grey or yellow exudate upon the surface, but eventually the iris stroma becomes thinned and the black pigmentary epithelium becomes visible (Fig. 15.11A and B).

If prolapse of the iris has occurred, cicatrization may still progress. The exudate which covers the prolapse becomes organized and forms a thin layer of connective tissue over which the conjunctival or corneal epithelium rapidly grows. Contraction of the bands of fibrous tissue tends to flatten the protruding prolapse. It rarely, however, becomes absolutely flat; more commonly the iris and cicatricial tissue are too weak to support the restored intraocular pressure, which is often increased owing to the development of a *secondary glaucoma.* The cicatrix therefore tends to become ectatic. An ectatic cicatrix in which the iris is incarcerated is called an *anterior staphyloma* which, depending on its extent, may be either partial or total. The bands of scar tissue on the staphyloma vary in breadth and thickness, producing a lobulated surface often blackened with pigment; hence the name. Histopathologically, in case the iris tissue is completely enmeshed in corneal tissue one would expect to see the iris tissue within the remnants of corneal tissue rather than just being adherent to the posterior surface of the cornea. It is therefore sometimes labelled as a *corneoiridic scar* which may or may not be ectatic.

If the perforation happens to be opposite the pupil, the pupillary margin of the iris often becomes adherent to the edges and the aperture becomes filled with exudate. The anterior chamber is then reformed very slowly; if the lens remains in contact with the ulcer for a long time, a permanent opacity may occur forming an *anterior capsular cataract.* As the anterior chamber reforms, the exudate filling the opening is submitted to strain and frequently ruptures, especially if the patient is restless. This process may be repeated, so that the opening may become permanent forming a *corneal fistula.*

Sometimes the whole cornea sloughs with the exception of a narrow rim at the margin, and a *total prolapse of the iris* occurs. The pupil usually becomes blocked with exudate, and a false or *pseudocornea* is formed consisting of the iris covered by exudate. If, however, the perforation takes place suddenly the suspensory ligament of the lens is stretched or ruptured, causing subluxation of the lens, or even anterior dislocation and *spontaneous expulsion of the lens and vitreous* through the perforation.

The sudden reduction of intraocular pressure when perforation occurs dilates the intraocular blood vessels, which may rupture causing an *intraocular haemorrhage.* Rupture of the retinal vessels gives rise to a vitreous haemorrhage; choroidal, a subretinal or subchoroidal haemorrhage. It may indeed be so profuse that the contents



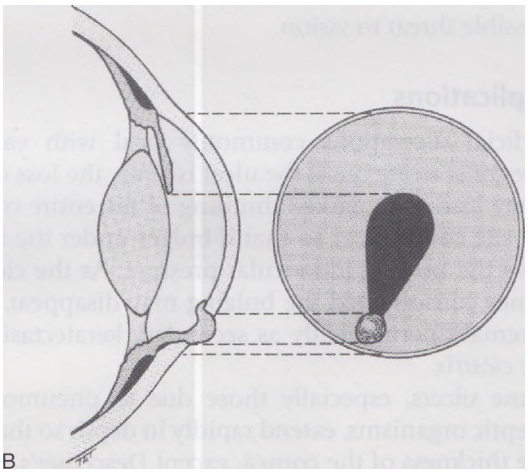


Fig. 15.11 (A) Perforated corneal ulcer with a prolapse of the iris. (B) A longitudinal section of the topography of the lesion. (C) Perforated corneal ulcer with iris prolapse and pseudocornea formation with evidence of vascularization and scarring as part of the healing response.

of the globe are extruded along with the out-flowing blood, i.e. *expulsive haemorrhage.*

Finally, the organisms which have caused the ulceration of the cornea may gain access to the interior of the eye as a result of perforation. *Purulent iridocyclitis, endophthalmitis* or even *panophthalmitis* may occur.

Treatment

Treatment of uncomplicated ulcers: Control of infection, symptomatic relief, cleanliness, heat, rest and protection are the fundamental principles of treatment for corneal ulcers. Control of infection is attained by the use of antimicrobial drugs; heat is employed to prevent stasis and encourage repair, while local rest is attained by the use of cycloplegics such as atropine.

Before starting treatment, preliminary microbiological investigations to identify the causative organism are mandatory. Corneal scrapings are obtained from the edges and base of the ulcer after instilling a local anaesthetic and using sterile disposable blades, disposable needles or a Kimura spatula. Multiple scrapings are obtained and smeared onto slides and plated on culture media for culture and sensitivity (blood agar, chocolate agar, thioglycollate broth for bacteria, non-nutrient agar with *Escherichia coli* overlay for *Acanthamoeba* and Sabouraud dextrose agar without chlorhexidine for fungi). Smears are stained with Gram and Giemsa stains to identify the causative agent and study the morphology of the inflammatory cells. Treatment can be started empirically by a general practitioner if an ophthalmologist is not available, but urgent referral to an ophthalmologist, preferably a corneal specialist, is a must after instituting first-line antibiotic therapy.

The antibiotics used in the treatment of a simple, uncomplicated bacterial corneal ulcer are outlined in Table 15.2. The infection is controlled by the intensive local use of fortified antibiotic drugs as already explained (*see* p. 147). Fortified drops are not commercially available and have to be prepared from available injectable preparations. Monotherapy with a single fluoroquinolone has also been recommended but is not a standard practice as resistance to fluoroquinolones is high in some countries. It has been observed that perforation is more likely in ulcers treated with ofloxacin.

Atropine, administered either as drops or ointment (1%), should be instilled in the affected eye two or three times a day as this drug prevents ciliary spasm and forestalls some of the dangerous results of iritis such

Table 15.2 Antibiotics for the treatment of bacterial corneal ulcers

Antibiotic	Concentration	Preparation	Frequency
Fortified cephazolin*	5% (50 mg/ml)	Add sterile water to 500 mg cephazolin dry powder to make 10 ml of solution Refrigerate and use within 7 days	Administer 1 hourly round-the-clock for the first 48 hours then decrease to 2 hourly during the day and 4 hourly at night. Once healing is ensured, further decrease to 4–6 hourly
Fortified tobramycin*	1.3% (13.6 mg/ml)	Inject 2 ml of tobramycin (40 mg/ml) injection in a 5 ml bottle of commercially available 0.3% tobramycin drops Refrigerate and use within 14 days	Administer 1 hourly round-the-clock for the first 48 hours then decrease to 2 hourly during the day and 4 hourly at night. Once healing is ensured, further decrease to 4–6 hourly
Alternative drugs			
Fortified vancomycin	0.30%	Add sterile water to 500 mg vancomycin dry powder to form 10 ml solution. Refrigerate and use within 4 days	Administer 1 hourly round- the-dock for the first 48 hours then decrease to 2 hourly during the day and 4 hourly at night. Once healing is ensured, further decrease to 4–6 hourly
Fluoroquinolones (ciprofloxacin, ofloxacin, moxifloxacin or gatifloxacin)		Commercially available drops	Administer 1 hourly round-the-clock for the first 48 hours then decrease to 2 hourly during the day and 4 hourly at night. Once healing is ensured, further decrease to 4–6 hourly

'Both are started empirically as first-line management and are instilled alternately every half hour. Therapy can be changed if needed after the culture and sens reports become available.

as prevention of posterior synechiae which always complicate corneal ulceration. Much comfort can also be obtained by local heat.

If the inflammation is severe and persists after the infective component is cured, steroids administered either as drops or an ointment may help to promote healing and prevent florid vascularization but should only be used when it is apparent that antibiotics are controlling the infection. Steroids are a double-edged sword and once the inflammation ceases, they should be discontinued since they may retard epithelialization and inhibit repair by fibrosis. Steroids should be used with extreme caution under the careful supervision of an ophthalmologist. In case of any doubt, steroids are best avoided.

If the ulcer progresses despite therapeutic measures, the removal of necrotic material may be hastened by repeated scraping of the floor with a spatula, the ulcer may be cauterized, or therapeutic keratoplasty undertaken.

Cauterization may be performed with pure carbolic acid (100%) or trichloracetic acid (10-20%). Carbolic acid has the advantage of penetrating a little deeper than it is actually applied, thus extending its antiseptic properties more widely; it acts both as a caustic and an antiseptic. Although the parts touched immediately turn white, the normal epithelium rapidly recovers. Cauterization is contraindicated in ulcers with excessive thinning or perforated ulcers. The acid must not, however, touch the conjunctiva lest adhesions form between the lids and globe. Povidone iodine 5% can be used as an alternative.

When cicatrization is complete and all irritative signs have passed, attempts to render the scar more transparent are usually disappointing. Cicatrices clear considerably in young patients and in many others a gratifying improvement may be noticed in the course of some months. The residual corneal scar may cause surface irregularity and irregular astigmatism; therefore, vision can sometimes be improved in cases of nebular corneal opacities with the use of a rigid gas-permeable contact lens. Dense corneal scars in eyes with visual potential are treated with *corneal grafts* (*see* p. 215). *Lamellar keratoplasty* may be advised for superficial scars (*see* p. 216) whereby the superficial defective lamellae are replaced by a correspondingly shaped corneal graft. When the scar traverses the greater part or the whole of the corneal thickness, *a full-thickness* (*penetrating*) *graft* is used.

In eyes with corneal scars with no visual potential a *cosmetic contact lens* to hide the blemish is the only option. *Tattooing* such scars in otherwise blind eyes with Indian ink or impregnation with gold (brown) or platinum (black) or drawing ink after stromal punctures are other methods which have been tried with varying success.

Treatment of a peiforated ulcer: If perforation has occurred, the treatment depends upon its size and situation. If it is small and in the pupillary area, prolapse of the iris is not to be feared. Rest, the continued use of antibiotics, atropine, and a firmly applied bandage or bandage contact lens suffice. All forced expiration—blowing the nose, coughing, etc.—must be avoided. The patient must be reassessed twice daily for response to treatment. If a small perforation is over the iris, adhesion to the cornea usually occurs to form an adherent leucoma. This may become detached when the anterior chamber reforms, or may remain as a fine adhesion, in which case no special treatment is required.

A further option is the use of a *tissue adhesive* such as N-butyl 2-ethyl cyanoacrylate monomer which is available in a 0.5 ml glass ampoule. It is applied to the area of perforation after careful debridement. The surface is dried with a sponge and a small drop of the tissue adhesive from the undersurface of a bent iris repositer or a hypodermic needle is placed immediately over the perforation. Drying of the adhesive may take 5-10 minutes, after which the anterior chamber may reform. Following this, a continuous-wear soft contact lens can be applied or a definite surgical procedure such as a *therapeutic penetrating keratoplasty* or *conjunctival flap* undertaken.

The commonest cause of failure in treatment is the development of secondary glaucoma, a complication which usually occurs in elderly people. If the intraocular pressure rises it adversely affects the corneal metabolism and thus its resistance. The rise of tension is an indication for oral or intravenous acetazolamide, intravenous mannitol and topical antiglaucoma therapy.

If there is an underlying source of infection such as a mucocele of the lacrimal sac it should be treated by dacryocystorhinostomy.

Special types of bacterial corneal ulcers

Hypopyon ulcer: Every corneal ulcer is associated with some iritis owing to the diffusion of toxins elaborated by bacteria into the eye. The resultant iridocyclitis may be so severe and the outpouring of leucocytes from the vessels so great that these cells gravitate to the bottom of the anterior chamber to form a *hypopyon.*

It is important to remember that a hypopyon is sterile, since the leucocytosis is due to toxins, not to actual invasion by bacteria which, indeed, are as incapable of passing through the intact Descemet's membrane as are leucocytes. This accounts for the ease and rapidity with which the hypopyon is often absorbed. It may develop in an hour or two, rapidly disappear, and as readily reappear. Such hypopyons are fluid, always moving to the lowest part of the anterior chamber depending on the position of the patient's head. The fact that the hypopyon is sterile has great practical importance—it is unnecessary to remove the pus, as is the rule in other



Fig. 15.12 (A–C) Bacterial corneal ulcer with hypopyon.

parts of the body; if the ulcerative process is controlled, the hypopyon will be absorbed.

The development of a hypopyon depends on two factors—the virulence of the infecting organism and resistance of the tissues. Many pyogenic organisms (staphylococci, streptococci, gonococci, *Moraxella)* may produce this result, but by far the most dangerous are *Pseudomonas pyocyanea* and pneumococci, which are not infrequently present in the normal conjunctival sac and are particularly likely to be present if there is any inflammation of the lacrimal sac (dacryocystitis). The presence of dacryocystitis is, therefore, a constant menace to the eye. On the other hand, the agent causing ocular trauma may carry the infection. The commonest causes are scratches with the finger nail and rubbing of the eyes with infected hands, following the presence of minute foreign bodies, especially in those working in stone or coal quarries or mines.

Unless the organism is very virulent, some lack of resistance on the part of the tissues must be present. Hence hypopyon ulcers are much more common in old, debilitated or alcoholic subjects. These ulcers also occur during or after acute infectious diseases such as measles or scarlet fever.

Hypopyon ulcers vary in type according to the infective agent and the age of the patient. In adults the ulcer caused by pneumococci is characteristic and called an *ulcus serpens* due to its tendency to creep over the cornea in a serpiginous fashion. The typical ulcus serpens is a greyish-white or yellowish disc-like lesion near the centre of the cornea. The opacity is greater at the edges than at the centre and is particularly well marked in one special direction. A cloudy grey area, made up of fine lines, surrounds the disc, but is also more marked in the same direction. The entire cornea may be lustreless. There is a violent iritis and the aqueous is cloudy or there may be a definite hypopyon varying in size from hour to hour.

An untreated or inadequately treated ulcer increases in size and depth. On the side of the densest infiltration, which often looks like a yellow crescent, the tissues break down and the ulcer spreads (Fig. 15.12); on the other side it may be undergoing simultaneous cicatrization and the edges may be covered by fresh epithelium. In this manner it travels forwards. Often there is infiltration just anterior to Descemet's membrane at a spot exactly opposite the floor of the ulcer, while the intervening lamellae are normal. This fact accounts to some extent for the tendency to perforate, since the inflammatory process is going on, as it were, from both surfaces of the cornea. As might be expected, the intraocular pressure is often raised.

If left to pursue its natural course the hypopyon increases, becomes fibrinous and the ulcer perforates, usually forming a large opening through which the iris prolapses. The whole cornea, except the narrow rim nourished by the limbal vascular loops, may necrose, and panophthalmitis destroy the eye.

Treatment: In all cases of hypopyon ulcer the treatment already indicated for corneal ulcers must be initiated at once and must be energetic. If all else fails a therapeutic penetrating keratoplasty becomes necessary to save the eye.

Fungal corneal ulcers

Mycotic or *fungal keratitis* is frequently seen in tropical countries, rural areas and in immunocompromised individuals. It is commonly due to *Aspergillus, Fusarium* or *Candida albicans.* Fungal ulcers are typically seen after injury with vegetable matter such as a thorn or wooden stick and are characterized by a relatively indolent course. Symptoms are much milder than the clinical signs would suggest. The slough in these ulcers is dry in appearance with feathery borders, surrounded by a yellow line of demarcation which gradually deepens into a gutter and there may also be a hypopyon (Fig. 15.13). An immune ring (*Wesseley*) may be visible due to deposition of immune complexes and inflammatory cells around the ulcer. Satellite lesions may also be seen. There is marked ciliary and conjunctival congestion, but symptoms of pain, watering and photophobia are disproportionately less as compared to those in cases of bacterial corneal ulcers. The hypopyon, if present, is thick and immobile, and is due to direct invasion into the anterior chamber of fungal hyphae enmeshed in thick exudates.

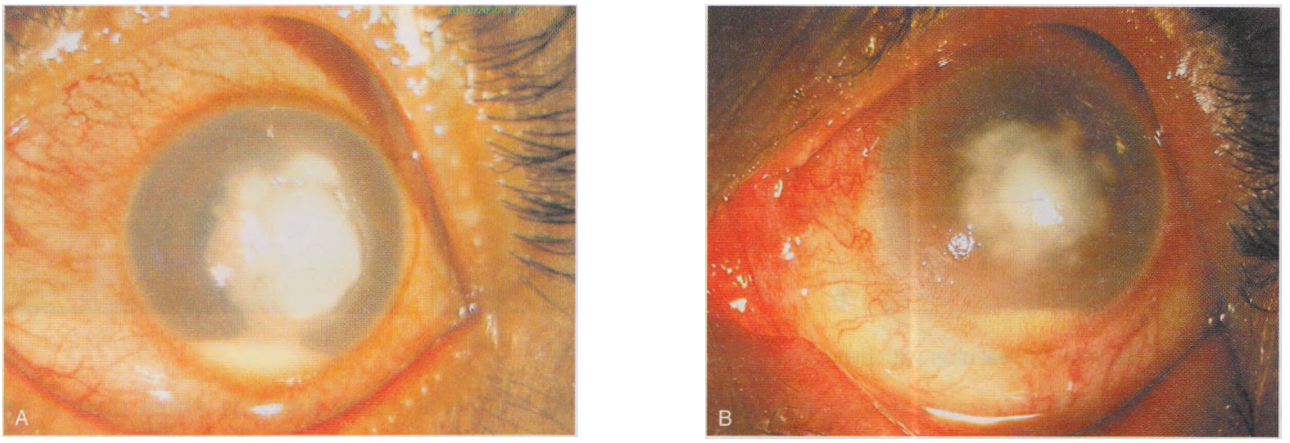


Fig. 15.13 (A) Fungal corneal ulcer showing a dry looking ulcer with feathery margins and thick hypopyon and (B) fungal corneal ulcer showing satellite lesion.

Treatment is by means of local natamycin and amphotericin B drops, and miconazole ointment; these are effective against *Aspergillus* and *Fusarium.* Nystatin is effective against *Candida.* Oral antifungal agents may be needed if the ulcers are severe and there is a suspicion of endophthalmitis. Ultrasonography is useful in looking for evidence of exudates in the vitreous suggestive of endophthalmitis in severe ulcers with opaque media. If endophthalmitis is confirmed ancillary measures such as a vitreous tap and intravitreal injection of antibiotics and antifungals (amphotericin B) are indicated. However, medical therapy is often ineffective and the infected cornea has to be replaced with a corneal graft or covered with a conjunctival flap.

Viral infections of the cornea

Superficial keratitis may result from a number of infections, most of which are viral. Of these, the most common are herpes zoster, the adenoviruses and *Chlamydia trachomatis* and inclusion conjunctivitis; the last two conditions have already been discussed. Rarely, the viruses associated with measles, vaccinia, infectious mononucleosis and mumps, as well as immunoinflammatory disorders such as Behcet syndrome and Reiter syndrome, may affect the cornea, while a secondary keratitis may follow a lid infection with the viruses of molluscum contagiosum and warts (verrucae). These viral infections give rise to different clinical pictures, but the same appearances may be associated with infection by several types of virus, while one virus may give rise to more than one type of lesion.

Punctate epithelial erosions (multiple superficial erosions) are the most common manifestation of viral infections. In this condition the cornea shows multiple minute defects in the epithelium, which stain with fluorescein. This is frequently acute in onset and associated with conjunctivitis. There is considerable pain, photophobia and lacrimation. As a rule, the infection is characterized by recurrences when fresh erosions appear in successive crops after the initial lesions have quietened or the original erosions have healed. If these recurrences persist for a considerable time, superficial vessels may invade the cornea. However, a completely non-specific lesion of this type may be caused by several other agents; for example, it may be caused by the toxin of staphylococci, the organism also giving rise to a blepharitis or conjunctivitis. Some chemical irritants produce the same picture. Associated with a general febrile disturbance, this is a well-established manifestation of an infection by one or other of the adenoviruses and also constitutes the characteristic picture of early trachomatous keratitis. Treatment is with lubricants and topical broad-spectrum non-epitheliotoxic antibiotic drops such as chloramphenicol to prevent secondary bacterial infection. Steroids should not be used.

Punctate epithelial keratitis (superficial punctate keratitis) is usually a viral infection of both eyes which runs a course of months or sometimes years. It attacks the deeper layers of the corneal epithelium and is sometimes associated with opacities extending into Bowman's membrane and superficial layers of the stroma *(punctate subepithelial keratitis).* The epithelial opacities appear as superficial, slightly raised grey dots scattered over the central area of the cornea which do not stain readily with fluorescein but turn a deep red with Rose bengal. A combination of epithelial and subepithelial punctate lesions is also a common occurrence in viral infections *[epidemic keratoconjunctivitis, pharyngoconjunctival fever, herpes, vaccinia* and others *(see* p. 168*)]*, but may occur without any known cause *(Thygeson superficial punctate keratitis).*

Treatments of most of these conditions is symptomatic with lubricant drops (artificial tears). Topical steroids have a marked suppressive effect but the lesions recur on withdrawal of the steroids which must, therefore, be used with caution and careful follow-up maintained as



Fig. 15.14 Herpes simplex of the skin.

numerous potential serious side effects such as steroid-induced glaucoma, fungal and bacterial superinfection may develop.

Herpes simplex

Ocular involvement with the herpes simplex virus has varied manifestations which include blepharitis, conjunctivitis, keratitis and iridocyclitis. The corneal involvement can be epithelial (dendritic or geographic keratitis), stromal (necrotizing and non-necrotizing stromal keratitis) and endothelial.

The herpesvirus has a widespread distribution. It can be grown in tissue culture and elementary bodies can be found by suitable staining methods in the vesicular fluid. There is some evidence that the virus has antigenic properties but, in practice, immunity does not develop after an attack and a person once infected frequently becomes a carrier. Periodic attacks tend to break out on the lips, nose and cornea with herpes simplex virus type I (HSV I) and on the genitals with herpes simplex virus type II (HSV II), the recurrences taking place particularly in association with intercurrent diseases such as a cold, pneumonia, a relapse of malaria or exposure to sunlight (Fig. 15.14).

In a primary lesion (usually in children), herpes may manifest itself as a severe follicular keratoconjunctivitis, but in the usual recurrent form the conjunctiva is spared apart from the occurrence of a nondescript conjunctivitis. The initial corneal lesion is a *superficial Punctate keratitis*—numerous minute whitish plaques on the cornea often arranged in rows or groups. They quickly desquamate, forming erosions which may heal rapidly leaving no opacity, but are accompanied by great irritation, lacrimation and blepharospasm. Usually, however, fresh crops appear and the condition may prove very obstinate. After the plaques have desquamated leaving minute shallow clear facets, the distinguishing features are the shape of the lesions, the total absence of vascularization, their grouping, the crenated edges where several have coalesced and the persisting filamentary shreds of diseased epithelium. In all cases the cornea is relatively insensitive.

In severe forms, *dendritic ulcers* develop. The infiltrates, spreading in all directions, coalesce and form a large shallow ulcer with crenated edges. More often grey striae extend in one or more directions, increase in length, and send out lateral branches which are generally knobbed at the ends so that a dendritic figure, not unlike a liverwort, is formed. This resembles no other condition and is pathognomonic (Fig. 15.15B and C). The surface over the infiltrates breaks down and an extremely irritating and chronic ulcer is produced, persisting with exacerbations for weeks or months, sending out fresh branches but never extending in depth. Generally only one or two of the infiltrates stain with fluorescein at any given time, but fresh spots are continually being formed and the disease frequendy recurs; alternatively, a large confluent ulcer may be formed (Fig. 15.15A). Meanwhile the stroma may be implicated and a *disciform keratitis* (Fig. 15.15D), sometimes of considerable extent, may develop. This is an immunological reaction resembling an Arthus reaction. An iritis is invariably associated with a severe herpetic keratitis, sometimes of considerable severity, and occasionally a hypopyon may occur. The herpesvirus has been isolated from the aqueous in a few such cases. Diagnostic tests are limited to immunofluorescence and mltnrp of epithelial scrapings or tissue biopsies.

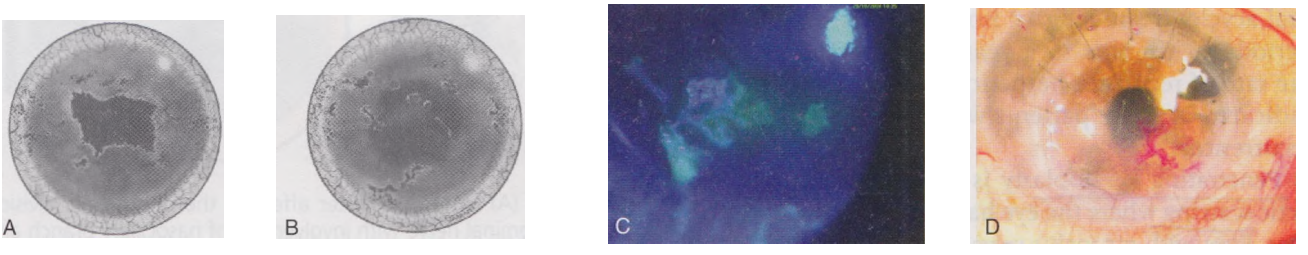


Fig. 15.15 Herpetic keratitis. (A) Large confluent ulcer with outlying areas of staining; (B) multiple dendritic ulcers (By courtesy of Barrie Jones); (C) dendritic ulcer stained with fluorescein and (D) dendritic corneal ulcer in a corneal graft stained with rose bengal dye.

Treatment: The treatment of herpes simplex eye disease depends on the nature of ocular involvement and requires the judicious use of topical and svstpmic antivirals, topical steroids and supportive therapy with lubricants (artificial tears) and cycloplegics.

Commercially available antiviral agents include 5% idoxuridine (5-iodo-2-deoxyuridine, IDU), 1% trifluridine (trifluorothymidine, F3T) eye drops, 3% acyclovir eye ointment, 3% vidarabine eye ointment and oral acyclovir (400 mg and 800mg tablets).

Epithelial keratitis responds well to topical antivirals which are prescribed along with topical antibiotics to prevent secondary bacterial infection, lubricants to relieve discomfort and cycloplegics if required. Debridement of the edges of the dendritic ulcer with a moistened, fine cotton-tipped applicator is also useful in reducing the load of active virus-infected cells. Eighty-five per cent of initial dendritic ulcers treated with IDU drops five times a day are cured within 2 weeks. Trifluridine 1% drops four times a day, or acyclovir 3% ointment five times a day, or 3% vidarabine ointment five times a day produce resolution of herpes simplex viral keratitis in approximately 95% of patients. It is uniformly accepted that topical steroids are contraindicated in the presence of active viral replication as occurs in. herpes simplex epithelial keratitis.

Stromal keratitis (including disciform keratitis), endotheliti s and iridocyclitis. These are treated with a combination of topical steroids, topical antiviral drugs and cycloplegics.

Certain aspects of treatment have become clearer after the results of the multicentre Herpetic Eye Disease Study (HEDS) were published. In the absence of accompanying herpes simplex virus epithelial keratitis, stromal keratitis improves more rapidly when corticosteroid eye drops are used along with a topical antiviral agent. Oral acyclovir (400 mg five times a day) does not seem to prevent the occurrence of iridocyclitis or stromal keratitis following epithelial keratitis treated with trifluridine, and appears to provide no extra benefit over topical steroids and trifluridine in the treatment of stromal keratitis. However, oral acyclovir may be added to a regimen of a topical antiviral agent and corticosteroids in treating patients with herpes simplex virus iridocyclitis. Also, low-dose oral acyclovir (400 mg 12 hourly) prescribed for long periods (6 months to a year or longer) does reduce the rate of recurrent herpetic eye disease and hence is indicated in those patients who are prone to frequent recurrences.

Penetrating keratoplasty is useful _in cases with herpetic scarringwhere the eye has been free of activity for a year. Eyes with extensive vascularization invite rejection of a graft, and recurrence of active herpetic infection in the transplant is often a problem.

Herpes zoster

Herpes zoster is caused by the same virus that causes chickenpox (varicella zoster virus). After an infection with chickenpox in childhood or youth, the virus lies dormant to appear later, particularly in elderly people with depressed cellular immunity, causing the clinical picture of zoster. In zoster ophthalmicus the chief focus of infection is the Gasserian ganglion from where the virus travels down one or more of the branches of the ophthalmic division of the tiigeminal nerve, so that its area of distribution is marked out by .rows of vesicles or the scars left by them (Fig. 15.16A), exactly asTn zoster in other parts of the body. The supraorbital, supra- and infratrochlear branches are nearly always involvecOfequently the nasal branch; and only rarely the infraorbital branch. It is nearly alwaysjonilateral ancTdoes'not crossTfref midline. It may be biMeral only in disseminated zoster seen in immunocompromised conditions.

There may be feverand malaise at the onset, and the eruption is preceded by severe neuralgic pain along the course of the nerves which are so Characteri sfic'oTzoster that they should arouse suspicion of the nature of the disease before the vesicles appear. The pain sometimes ceases after the outbreak of the eruption, but may continue for months or even years. The skin of the lids and other areas affected become red and oedematous, so that the disease may be mistaken for erysipelas, but the characteristic distribution and especially the strict limitation to one side of the midline of the head should obviate this error. The vesicles often suppurate, bleed and cause small, permanent, pitted scars. The active eruptive stage lasts for about 3 weeks and is followed by some degree of anaesthesia of the skin. Ocular complications arise as the eruption is subsiding, but may be overlooked during the acute stage owing to the difficulty in examining the eye; they are generally associated with involvement of the nasociliary branch of the trigeminal nerve (Fig. 15.16B).

With the slit-lamp, numerous rounded spots composed of minute white dots are seen in the epithelium

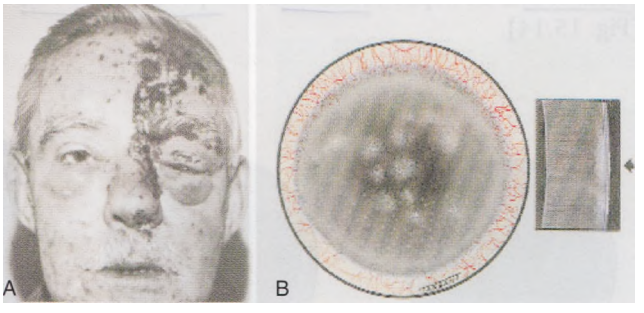


Fig. 15.16 (A) Left-sided zoster affecting the ophthalmic division of the trigeminal nerve with involvement of nasociliary branch and (B) herpes keratouveitis. The large coin-shaped subepithelial lesions are known as nummular keratitis; the small dots below are keratic precipitates.

which soon involve the stroma to form a coarse subepithelial punctate keratitis. Larger discoid lesions are also termed 'nummular' keratitis. Similar lesions are also seen in other forms of viral keratitis.

Sometimes the infiltration spreads deep and diffuses into the stroma to be associated with iridocyclitis. The cornea is usually insensitive. This is tested by touching it with a wisp of cotton-wool and comparing the reaction with that in the fellow eye; the slightest touch is followed by a reflex closure of the lids if the cornea is sensitive. Similar nodules leaving grev-scarred areas may appear on the sclera and patches of sectoral atrophy may develop on the iris. The intraocular pressure is sometimes diminished in the early stage, but subsequently a secondary glaucoma is not unusual. The ocular lesions and the corneal anaesthesia are very obdurate and often persist long after the disease has otherwise resolved. In some cases, there is associated paralysis of the motor cranial nerves, especially the oculomotor, abducens and facial, which usually passes off within 6 weeks. Facial palsy is dangerous as it causes exposure of the cornea. Acute retinal necrosis develops in some patients shortly after cutaneous varicella zoster infections. The time interval between the skin infection and the retinal necrosis may vary from 5 days to 3 months. Another late complication is ootic neuritis.

Treatment: A course of 800 mg acyclovir five dines daily for 10 days is recommended for herpes zoster to reduce the period of viral shedding, accelerate the time for healing by 50%, reduce the incidence of new lesions and the severity of acute pain. In addition, acyclovir in this dosage reduces the incidence of post-herpetic neuralgia. The drug should be administered as early as possible, preferably no later than 4 days after the onset of rash. Pain during the first 2 weeks of an attack of herpes zoster is usually severe and is treated with strong oral analgesics. If this proves ineffective then opioid analgesics may be tried.

Topical antiviral and antibiotic ointments are applied on the skin and lids. In the eye itself, topical antivirals are not indicated but an antibiotic ointment is useful in the acute stage of the disease to prevent secondary bacterial infection when lid vesicles are discharging and forming crusts.

When the herpetic infection gives rise to scleritis, sclerosing keratitis or iritis, dexamethasone 0.1% drops 4 hnnrlv are used along with an antiviral ointment five times a day and steroid ointment at night. This tends to reduce the ischaemia and fibrotic scarring which may develop. Systemic steroids are recommended in cases of progressive proptosis with total oculomotor nerve palsy and optic neuritis. These conditions are probably due to occlusive vasculitis. The initial dose is 60 mp per dav and is rapidly reduced to a maintenance dose. Systemic non-steroidal anti-inflammatory drugs (NSAIDS) such as oxyphenbutazone are sometimes useful in severe cases of scleritis which have not responded to steroids.

Artificial tears are required following an attack of herpes zoster if there is any dryness of the eyes or rapid formation of dry spots on the cornea.

Neurotrophic ulcers of herpes zoster are best treated bytarsorrhaphy of the lateral half of the lids. Neglected disciform keratitis and sclerokeratitis often give rise to dense scarring and lipoid deposits in the central cornea. Such patients may require penetrating corneal grafting if the cornea is not too vascularized.

Parasitic infestations

Protozoal infections

Acanthamoebic keratitis: Acanthamoebic keratitis can be a devastating infection if not recognized early. Its occurrence is frequently associated with the wearing of soft contact lenses. The usual source of infection is the saline solution used to clean or store the lenses. It has also been seen to occur in non-contact lens wearers and may be related to swimming or bathing in contaminated water. There may be no antecedent trauma and the infection is often unilateral with the formation of a ring infiltrate; the epithelium is intact initially but has a mottled, dendritiform appearance and later breaks down (Fig. 15.17). Ocular pain is severe, perhaps due to deep linear stromal infiltrates localized along the corneal nerves. However, the diagnosis is usually missed in the early stages as the clinical appearance mimics viral keratitis, a non-healing corneal abrasion and fungal keratitis.

When diagnosed, early keratitis may be treated successfully with topical propamidine isethionate 0.1% and polyhexamethyl biguanide (PHMB) 0.02%. The organism is also susceptible to treatment with topical chlorhexidine 0.02%, neomycin and miconazole.



Fig. 15.17 Acanthamoebic keratitis.

Helminthic infections

Onchocerciasis: Corneal involvement in patients suffering from onchocerciasis includes punctate or fluffy 'snowflake' corneal opacities due to the presence of living or even dead microfilariae, peripheral corneal scarring due to sclerosing keratitis, irregular pigmentation and even calcification. The scarring could be due to the death of the microfilariae or as the result of a reaction to the presence of living microfilariae. In the early stages of punctate keratitis, the corneal lesions are reversible but once more advanced scarring due to sclerosing keratitis develops, the visual loss is permanent.

IMMUNOLOGICALLY MEDIATED DISEASES

Phlyctenular keratitis

It has already been pointed out that phlyctens are commonly found at the limbus; they may also occur within the corneal margin. The fact must be emphasized that the disease is essentially conjunctival, and when the cornea is affected it is the conjunctival element of the cornea—the epithelium and the superficial layers underlying it—which suffers. As has already been noted, it is an allergic reaction to an endogenous allergen, commonly tuberculoprotein *(see* pp. 179-180).

The corneal phlycten is a grey nodule, slightly raised above the surface and if the epithelium breaks down, a yellowish ulcer is formed. Corneal phlyctens are localized infiltrations of exactly the same nature as conjunctival phlyctens but cause much pain and reflex blepharospasm (photophobia). They may become absorbed without destruction of the superficial layers of the stroma, in which case they cause no permanent opacity. The epithelium, however, is readily destroyed and the denuded surface easily becomes infected, usually by staphylococci, leading to the formation of a small superficial ulcer.

Treatment of phlyctenular keratitis is the same as that of phlyctenular conjunctivitis *(see* p. 179) until ulceration has occurred; thereafter atropine combined with corticosteroids and antibiotics should be administered as drops or ointment.

Acne rosacea

This is generally seen in elderly women, and is associated with ocular irritability and lacrimation. In addition to slight mucopurulent conjunctivitis, yellowish-white infiltrates and small ulcers appear in the cornea near the limbus, which always becomes heavily vascularized. The ulcers can be intractable and frequently recur. In severe cases iritis is also present (Fig. 15.18A and B).

Local treatment is disappointing but is similar to that for phlyctenular keratitis; the greatest relief usually follows the instillation of corticosteroids as drops or ointment. The essential treatment, however, is that of the skin condition. A course of systemic tetracycline is often helpful. Patients receive 250 mg tetracycline orally four times daily or 100 mg doxycycline twice daily for 3 weeks of each month. The dosage is then slowly reduced each month and the drug is stopped if improvement is maintained.

Marginal ulcer (catarrhal ulcer)

These ulcers occur near the limbus, especially in old people, as an immune reaction to toxins produced by staphylococcal organisms residing in the conjunctival sac or lids in patients with chronic meibomianitis or blepharitis; they also occur in association with a chronic conjunctivitis and may be caused by *Moraxella* or *Haemophilus* (Fig. 15.19). They are typically located at the points of contact of the eyelids with the cornea, i.e. at 4-, 7-, 10- and 2 o'clock positions. They are shallow, slightly infiltrated with a clear area between the lesion and the limbus, often multiple, and may be accompanied by neuralgic pain in the face and head. Sometimes they heal rapidly but recur just as rapidly, so that the process tends to

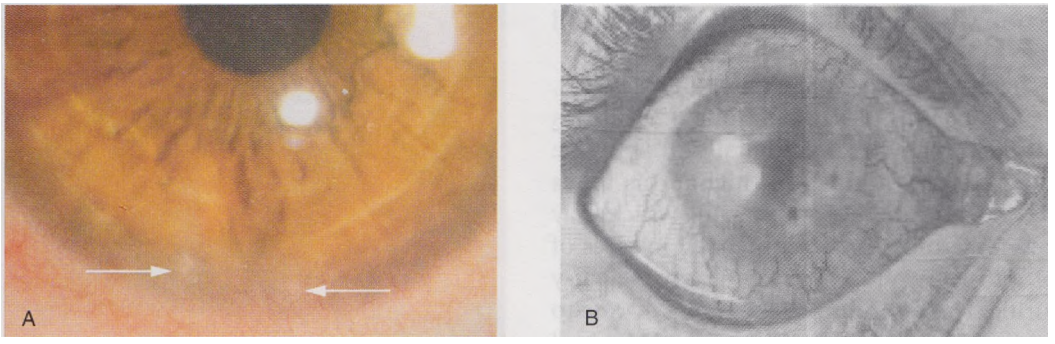
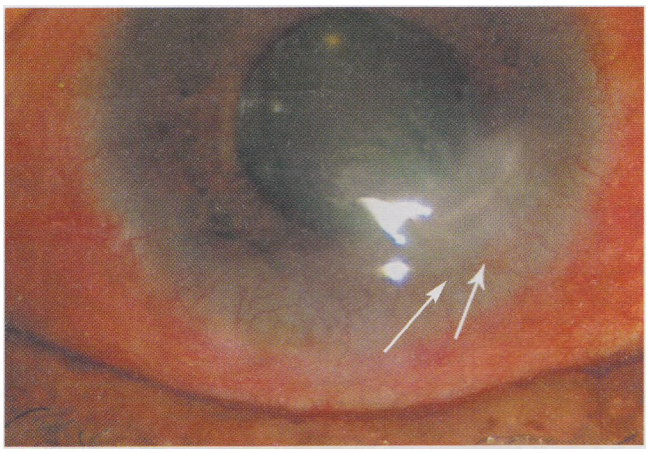


Fig. 15.18 (A) Mild marginal keratitis in a patient with acne rosacea keratitis. Infiltrates are visible at the inferior limbus. (B) Severe rosacea keratitis.



Fig, 15,19 Marginal corneal ulcer secondary to staphylococcal hypersensitivity.

drag on indefinitely. Frequently the ulcers become vascularized and the vessels persist. More serious rare forms of deep marginal ulceration also occur in patients with polyarteritis nodosa, systemic lupus erythematosus or Wegener granulomatosis caused by deposition or formation of antigen-antibody complexes at the limbus and constituting a ring ulcer, sometimes leading to necrosis of the whole cornea.

Treatment: The infection should be treated with an appropriate antibiotic. Steroid drops or ointment may be beneficial. In severe cases associated with systemic autoimmune disorders, systemic steroids and cytotoxic drugs may be indicated.

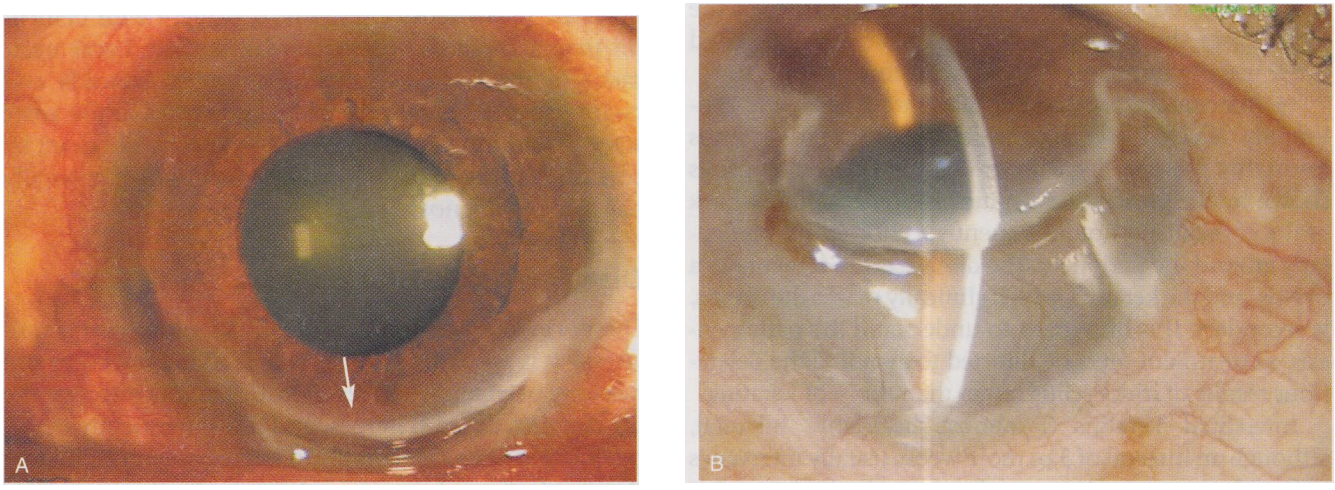
Chronic serpiginous ulcer (rodent ulcer, mooren ulcer)

This is a rare, degenerative, superficial ulcer, starting at the corneal margin and spreading circumferentially and axially over the whole of this tissue (Fig. 15.20). The exact underlying cause is unknown. Erosion is initiated by autoimmune lysis of the epithelium with consequent release of collagenolytic enzymes. It is accompanied by severe and persistent neuralgic pain and lacrimation. It commences as one or more grey infiltrates, which break down, forming small ulcers that spread and sooner or later coalesce. The ulcer undermines the epithelium and superficial stromal lamellae at the advancing border, forming a whitish overhanging edge which is characteristic, while the base quickly becomes vascularized. It rarely perforates, but progresses with intermissions for months until eventually a thin nebula is formed over the whole cornea and sight is greatly diminished. Bilateral involvement with severe pain and relentless progression ('malignant') is more common in young adults, while a milder, usually unilateral, less painful form is seen in elderly patients. Mooren ulcer is a diagnosis of exclusion after all other systemic disorders predisposing to marginal ulceration are ruled out.

Treatment: This is difficult as ischaemia is the underlying cause. Excision of a 4-7 mm strip of adjacent conjunctiva may prove successful by eliminating conjunctival sources of collagenase, proteoglycanase and other inflammatory mediators. Topical antibiotics and steroids are usually ineffective. If perforation occurs, ulcer debridement, cyanoacrylate adhesive and soft contact lenses may be tried. Lamellar keratoplasty with intravenous methotrexate therapy may halt the process.

Interstitial keratitis

This is an inflammation affecting chiefly the stroma of the cornea. It is of infective or more often allergic origin. Interstitial keratitis and deafness (Cogan syndrome) is a rare disease affecting young adults. The keratitis is associated with vertigo, tinnitus and deafness.



Fig, 15.20 Mooren ulcer showing a peripheral marginal ulcer with an overhanging edge. (A) Early stage and (B) late stage.

Interstitial keratitis due to inherited syphilis most commonly affects children between the ages of 5 and 15 years. Delayed interstitial keratitis occasionally occurs in patients above 30 years. After slight irritative symptoms with some ciliary congestion, one or more hazy patches appear in the deep layers of the cornea near the margin or towards the centre. If they start near the margin they migrate towards the centre; until finally the whole cornea looks lustreless and dull. In 2-4 weeks the whole cornea is hazy with a steamy surface, giving a general ground glass appearance in which denser spots can always be seen. As a rule, the iris is dimly visible, but in the severest of cases the whole cornea becomes opaque, so that this tissue is hidden (Fig. 15.21).

Meanwhile, deep vascularization occurs *(see* Fig. 11.7), consisting of radial bundles of brush-like vessels, and since they are covered by a layer of hazy cornea, their bright scarlet is toned down to a dull reddish pink ('salmon patches') wherein separate vessels can be seen only with difficulty. The opacity extends a little beyond the vessels, which seem to push the opacity in front of them and at the height of the condition the vessels run in radial bundles almost, but seldom quite, to the centre of the cornea. There is often a moderate degree of superficial vascularization, but it never extends far over the cornea, and at the limbus the conjunctiva may be heaped up.

After the disease has reached its height, the cornea clears slowly from the margin towards the centre, which may remain hazy for a long time, but finally improves except in the worst cases. As the cloudiness disappears the vessels become obliterated; although they cease to carry blood they remain permanently as fine opaque lines, the characteristic radial course of which indicates the previous occurrence of the disease.

Since the infiltration of the cornea is almost entirely limited to the deeper layers lying immediately anterior to Descemet's membrane, the corneal surface rarely becomes ulcerated. It is frequently stippled, steamy and slightly uneven, and this condition may persist. In the worst cases the cornea may be enormously thickened but it usually improves with some useful vision.

In interstitial keratitis, the uveal tract is always profoundly affected and a considerable degree of iritis is invariably present. Sometimes there is severe cyclitis, as shown by the presence of keratic precipitates on the back of the cornea, and not infrequently a choroiditis, particularly around the periphery. The disease is fundamentally a uveitis, and the keratitis, which clinically masks the uveitis, is secondary. It is important to understand the pathogenesis, as treatment must be directed to avoiding the deleterious results of iridocyclitis rather than those of keratitis.

Interstitial keratitis is almost invariably bilateral, although an interval of 3 or more weeks usually intervenes before the onset in the second eye; rarely the interval is several months. The acute stage lasts at least 6 weeks and may extend to several months. The cornea takes weeks or months to clear, but little improvement can be expected after 18 months.

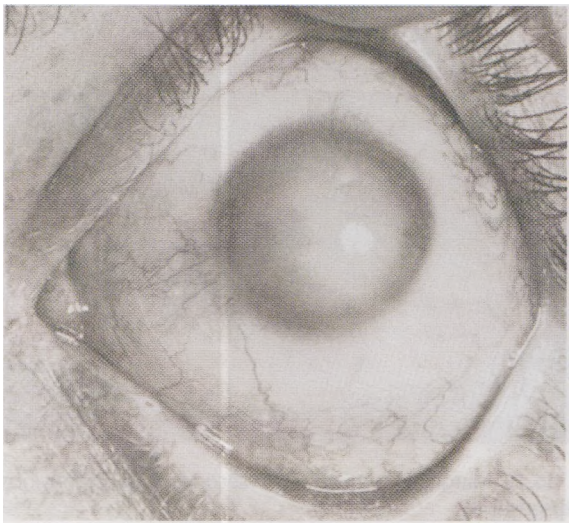


Fig. 15.21 Syphilitic interstitial keratitis.

Diagnosis: A diagnosis depends on other evidences of congenital syphilis and positive serological reactions to this disease. The characteristic signs of late congenital syphilis are prominence of the frontal eminences, flatness of the bridge of the nose, Hutchinson teeth (notching of the two upper central incisors in the permanent dentition), rhagades at the angles of the mouth, shotty cervical nodes and periosteal nodules, particularly on the tibiae.

Treatment: It is doubtful if antisyphilitic remedies have any influence over the course of the keratitis, partly because the cornea is non-vascular and partly because the reaction is probably largely allergic. It is possible, however, that intensive systemic treatment with penicillin may shorten the course of the disease. Local treatment in the form of lubricants, topical steroids and cycloplegics to control the uveitis is helpful in the acute stage. In the later stages the best results are obtained by corneal grafting of the penetrating type, which generally has a good prognosis.

Disciform keratitis

Disciform keratitis occurs generally in adults and is unilateral. It is probably associated with a viral infection and has long been known to result from vaccinia affecting the lid margins, or from herpes, and not infrequently develops from a SPK. The condition is probably not due to a direct infection of the corneal stroma by the virus from the epithelium but seems to be the expression of a tissue

response, sometimes involving necrosis, due to the reaction between antigens liberated by the virus in the epithelium and antibodies produced in the stroma or carried there by the blood stream. The pathology may thus be analogous to that of syphilitic interstitial keratitis.

The disease is characterized by the gradual appearance of a central grey disc lying in the middle layers of the stroma, usually with a denser central opacity. The slit-lamp shows thickening of the cornea and often folds of Descemet's membrane and an immune ring of the Wesseley type. It is accompanied by moderate irritation which persists for weeks or many months, leaving a permanent opacity. The cornea may become anaesthetic but ulceration does not occur. Owing to its central situation, vision is considerably impaired. It is associated with some degree of uveitis.

It is completely a difficult condition to treat, but generally the symptoms and the extent of the permanent opacity may be ameliorated by the local administration of corticosteroids along with topical or systemic antiviral agents such as acyclovir.

CORNEAL DYSTROPHIES

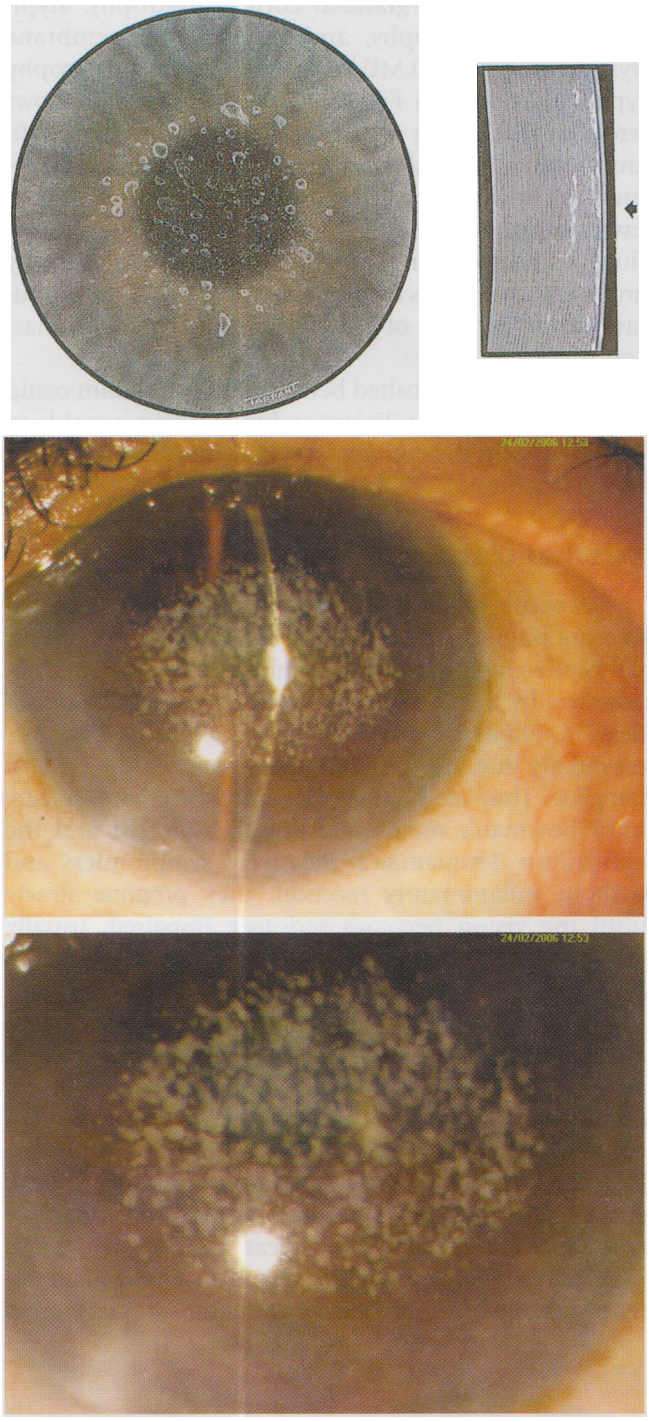
Corneal dystrophies are non-inflammatory, hereditary corneal disorders which are characterized by bilateral, non-vascularized corneal opacities. They mainly affect a particular layer of the cornea. A variety of classification systems have been used in the past. The International Committee for Classification of Corneal Dystrophies (1C3D) established in 2005 has devised a current and accurate nomenclature supplementing the anatomic classification with updated clinical, pathologic and genetic information.

Epithelial and subepithelial dystrophies

These involve the anteriormost layer of the cornea, generally present in adults, who may be asymptomatic or suffer from bouts of recurrent corneal erosions associated with pain, lacrimation and blurring of vision with varying extent of corneal haziness. Prominent examples in this group are epithelial basement membrane dystrophy (EBMD, map-dot-fingerprint dystrophy, Cogan microcystic epithelial dystrophy, anterior basement membrane dystrophy), Meesman corneal dystrophy (MECD, juvenile hereditary epithelial dystrophy) and gelatinous drop-like corneal dystrophy (GDLD, subepithelial amyloidosis, primary familiar amyloidosis [Grayson]).

Bowman layer dystrophies

These autosomal dominant dystrophies usually present in childhood with recurrent corneal erosions and gradual visual impairment due to corneal opacities which are typically reticular (honeycomb) in pattern



Fig, 15.22 Reis–Buckler corneal dystrophy.

in Thiel-Behnke corneal dystrophy (TBCD, corneal dystrophy of Bowman layer, type II [CDB2], honeycomb-shaped corneal dystrophy, anterior limiting membrane dystrophy, type II [ALMD2]) and irregular, coarse, geographic shaped opacities at the level of Bowman layer and superficial stroma in Reis-Biicklers corneal dystrophy (RBCD, corneal dystrophy of Bowman layer type I

[CDB1], superficial granular corneal dystrophy, atypical granular dystrophy, anterior limiting membrane dystrophy, type 1 [ALMD1], granular corneal dystrophy type 3) as seen in Fig 15.22. Histopathology shows irregular thickening of the epithelium with focal deficiencies in epithelial basement membrane and replacement of Bowman layer by a fibrocellular layer with a saw-toothed wavy pattern visible between the epithelium and stroma in Thiel-Behnke corneal dystrophy and a sheet of connective tissue with fibrillar or granular hyaline deposits of protein that stain red with Masson trichrome.

The material deposited beneath the epithelium could be removed by blunt dissection but is now amenable to treatment with the excimer laser by laser phototherapeutic keratectomy (PTK).

Stromal corneal dystrophies

These occur bilaterally around puberty. They are of obscure origin involving the central area of the cornea, rarely affecting the corneal margin. The lesions are characterized by the development of discrete areas of opacification, mainly in the superficial layers of the stroma, essentially due to hyaline deposits between the corneal lamellae. They tend to increase in number and density until Bowman's membrane becomes eroded and the epithelium desquamates. Relatively symptomless and without inflammatory reaction, they progress slowly until the vision becomes seriously impaired, usually above the age of 40 years. Once this occurs, treatment is best by keratoplasty.

A few main forms have been differentiated. In *granular corneal dystrophy (nodular or granular dystrophy of Groenouw)* (Fig. 15.23), in which the heredity is autosomal dominant, the opacities formed due to the abnormal accumulation of hyaline protein assume a discrete granular form and subsequently coalesce into various irregular shapes. The intervening cornea between the opacities and peripheral cornea remain clear.

A *lattice form* (Fig. 15.24), also with an autosomal dominant heredity, is characterized by bifurcating criss-cross

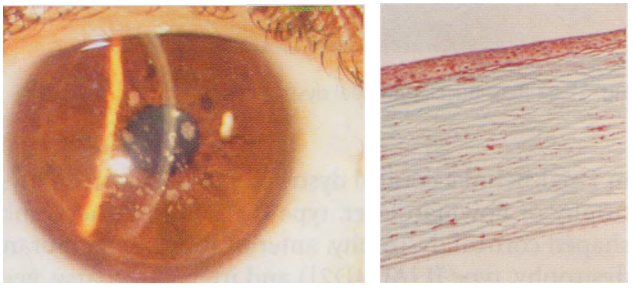


Fig. 15.23 Granularcorneal dystrophy. Histological section (By courtesy of S Kashyap) stained with Masson trichrome shows deposition of hyaline protein in the stroma.

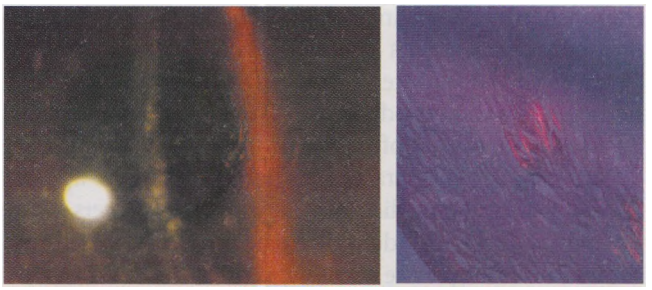


Fig. 15.24 Lattice corneal dystrophy. Histological section (By courtesy of S Kashyap) stained with Congo red shows amyloid deposition in the stroma.

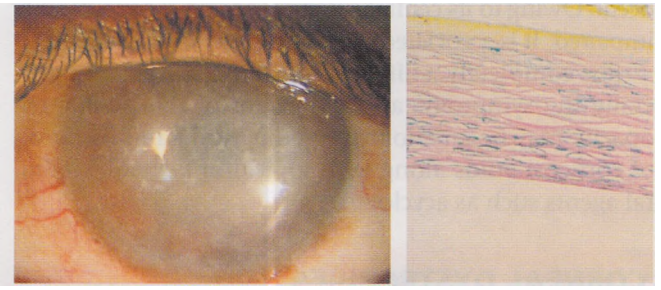


Fig. 15.25 Macular corneal dystrophy. Histological section (By courtesy of S Kashyap) stained with colloidal iron shows deposits of mucopolysaccharide glycosaminoglycans in the stroma.

lines associated with punctate opacities. It is a localized form of amyloidosis.

A *macular form* (Fig. 15.25) has a recessive heredity and in it the visual acuity tends to be affected at an early age. The opacities are present throughout the cornea with no clear spaces between. Histopathological examination of the cornea by special stains after keratoplasty demonstrates the nature of the material deposited. Intracellularly and extracellularly in the corneal stroma, endothelium and Descemet's membrane.

Endothelial corneal dystrophies

These occur rarely, the most common being the *endothelial dystrophy of Fuchs* (Fig. 15.26). It is seen in elderly people, particularly females, and is due to changes in the endothelium with the formation of hyaline excrescences on Descemet's membrane *(cornea guttata)* and the eventual atrophy of the endothelial cells. These deep changes are followed by a diffuse oedema of the stroma and epithelium clinically visible as the formation of microvesicles or even bullae in the epithelium, with an opacification in the stroma. Characteristically, patients complain of seeing halos in the morning, which disappear later in the day as the massaging effect of reflex blinking and evaporation leads to subsidence of corneal epithelial oedema. Periodic rupture of the epithelial bullae can be painful and the eye is prone to secondary infection. Ultimately the entire cornea turns opaque and insensitive. Treatment

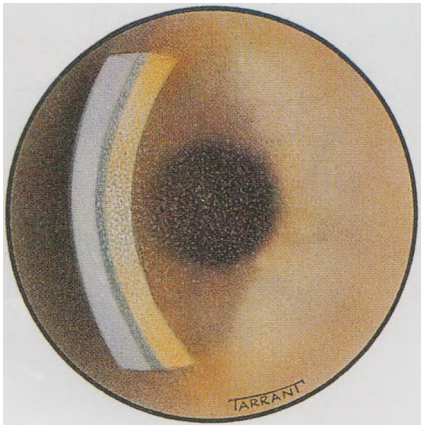


Fig. 15.26 Fuchs endothelial dystrophy.

is difficult; hypertonic solutions such as sodium chloride 5% eye drops 6 hourly or sodium chloride 6% eye ointment at night can help deturgesce the cornea if epithelial oedema is prominent. Finally, treatment by penetrating keratoplasty is required.

DEGENERATIVE CHANGES

A variety of degenerative conditions occur in the cornea, many of which are of clinical importance. They are distinguished from dystrophies as being non-hereditary and usually unilateral. These are conveniently divided into three categories: primary degenerations, secondary degenerations depending on long-standing changes in the eye itself, and infiltrations associated with metabolic disturbances.

Arcus senilis

This is a lipoid infiltration of the cornea seen in the elderly. It is almost universally present to some extent in people who are above 60 years of age. It commences as a crescentic grey line or whitish arc concentric with the upper and lower margins of the cornea, the extremities of which finally meet so that an opaque line, thicker above and below, is formed completely round the cornea. It is characterized by being separated from the margin by a narrow zone of comparatively clear cornea, being sharply defined on the peripheral side, fading off on the central. It is never more than about 1 mm broad, is of no importance either from the point of view of vision or of the vitality of the cornea (*see* Figs 15.27 and 14.2) and is unrelated to secondary forms of hypercholesterolaemia.

Arcus juvenilis

This is exactly like arcus senilis but is a rare condition. If it appears below the age of 40 years, a serum lipid profile is indicated to eliminate a hereditary anomaly with



Fig. 15.27 Arcus senilis.

a serious prognosis for life. The characteristic diagnostic feature is the presence of a line of clear cornea between the opacity and the limbus. This feature is occasionally also found in old sclerosing keratitis, but in this case the opacity is usually localized to one part of the cornea and extends further towards the centre.

Terrien marginal degeneration

Terrien marginal degeneration is usually bilateral, but may be unilateral. This condition is often asymptomatic initially and there is slow progressive thinning of the peripheral cornea, sparing the limbus, which manifests typically superiorly and is more frequently seen in men (Fig. 15.28). The eye is typically quiet with no redness or inflammation. A fine vascularized pannus is noticeable over the thinned involved area with a yellow deposit of lipid in the affected part. The lesion may slowly extend circumferentially and lead to either myopic or irregular astigmatism. The epithelium over the thinned cornea usually remains intact but perforation can occur with minor trauma.

Band-shaped keratopathy

This is a common condition in chronic uveitis, especially in blind shrunken eyes, and in children suffering from Still disease. It is also common in aphakic eyes which

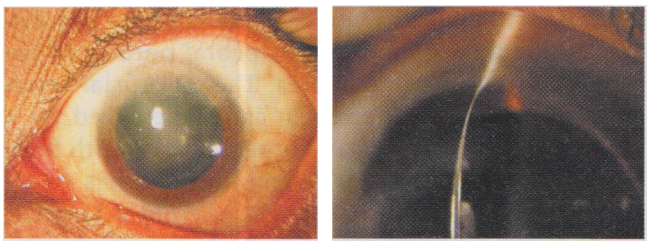


Fig. 15.28 Terrien marginal degeneration.

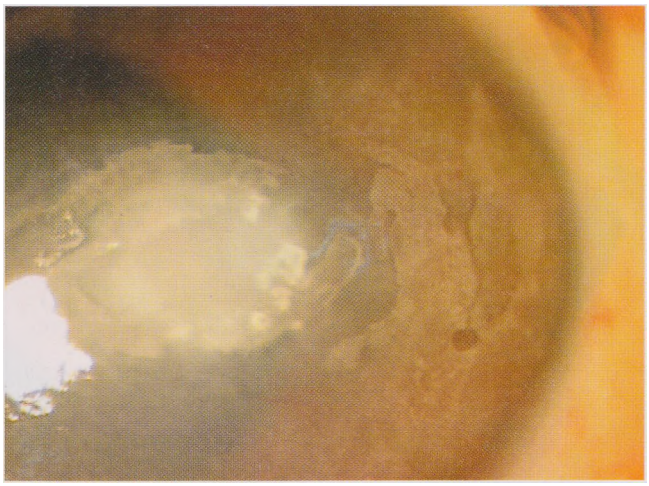


Fig. 15.29 Band-shaped keratopathy.

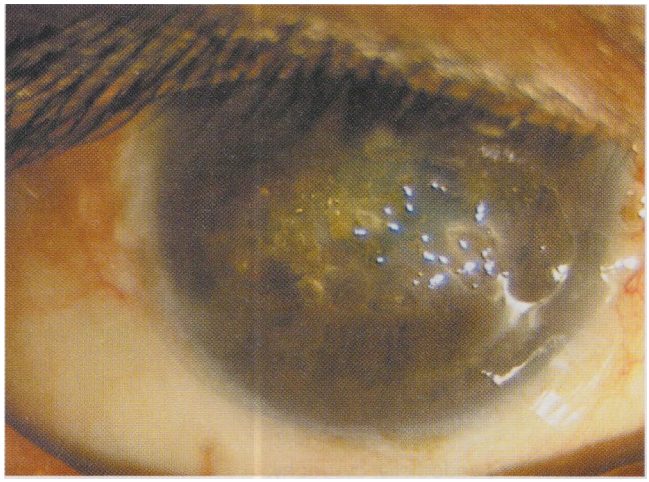


Fig. 15.30 Climatic droplet keratopathy.

have undergone vitrectomy with silicone oil if the oil is allowed to remain in the eye for long. Occasionally, it is associated with hyperparathyroidism, vitamin D poisoning or sarcoidosis. Rarely, it is found bilaterally, in otherwise healthy eyes, as a horizontally oval area in the palpebral fissure. A whitish band appears in the interpalpebral area, commencing at the inner and outer sides and progressing until it forms a continuous band across the cornea, interspersed with round 'holes' or cleaves in the band itself (Fig. 15.29). Close to the limbus, however, the cornea is generally relatively clear, as in so many degenerative conditions, probably owing to the better nutrition close to the blood vessels. The condition is due to hyaline infiltration of the superficial parts of the stroma, followed by the deposition of calcareous salts.

Treatment: Improvement of vision may be obtained by scraping off the opacity, which is usually calcareous and quite superficial, or dissolving it with the sodium salt of ethylenediamine tetra-acetic acid (sodium edetate). It can also be removed with the excimer laser (phototherapeutic keratectomy).

Climatic droplet keratopathy

Also called *oil droplet keratopathy* or actinic droplet keratopathy, this form of degeneration is common in those exposed to a hot, dry, dusty environment and outdoor activity in the sun, such as farmers. The disease affects the exposed interpalpebral portion of the cornea sparing the limbal area. The superficial layers are predominantly affected. It is characterized by a superficial non-vascularized corneal opacity with focal lesions in the epithelium resembling droplets of oil (Fig. 15.30). If vision is severely affected a lamellar keratoplasty or excimer laser phototherapeutic keratectomy can be done.

Salzmann nodular degeneration

This is a degenerative condition characterized by bluish-white, avascular nodules appearing in the superficial layers of the stroma and Bowman's membrane, occurring in persons who have suffered previous corneal disease (Fig. 15.31). The condition tends to be slowly progressive and may be treated by lamellar keratoplasty.

Other degenerative changes

These are frequently met with in old leucomata or anterior staphylomata consisting of hyaline infiltration, lipoid changes and calcification. Such scars are liable to undergo a serious form of ulceration called an 'atheromatous ulcer'.

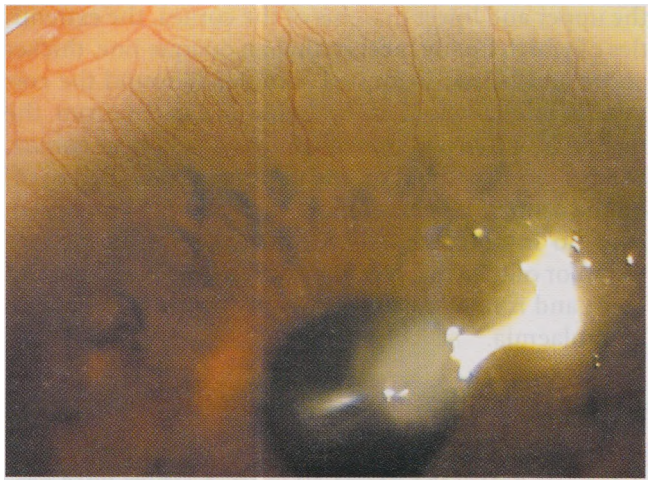


Fig. 15.31 Salzmann nodular degeneration.

ECTATIC CONDITIONS

It has already been stated that ectatic conditions of the cornea may result from inflammation, as in keratectasia and anterior staphyloma *(see* p. 196). Three forms of ectasia of non-inflammatory origin are known—keratoconus, keratoglobus and pellucid marginal degeneration. All three are sometimes classified as ectatic corneal dystrophies.

Keratoconus (conical cornea)

This is frequently due to a congenital weakness of the cornea, though it only manifests itself after puberty. However, it can also occur secondarily following trauma in which case it is unilateral, or in patients with vernal keratoconjunctivitis or Down syndrome due to repeated rubbing of the eye. The cornea thins near the centre and progressively bulges forwards, with the apex of the cone always being slightly below the centre of the cornea. The cornea is at first transparent and the vision is impaired due to myopic astigmatism. If the condition is marked, the conical shape is easily recognized in profile, particularly by the acute bulge given to the lower lid when the patient looks down (Munsen sign). In less advanced cases, distortion of the corneal reflex is the chief guide, a change best seen with a Placido disc or corneal topography (Fig. 15.32) or when the cornea is examined with a keratometer or other instruments for mapping the corneal topography. The keratometer mires are malformed, malaligned and malfocussed.

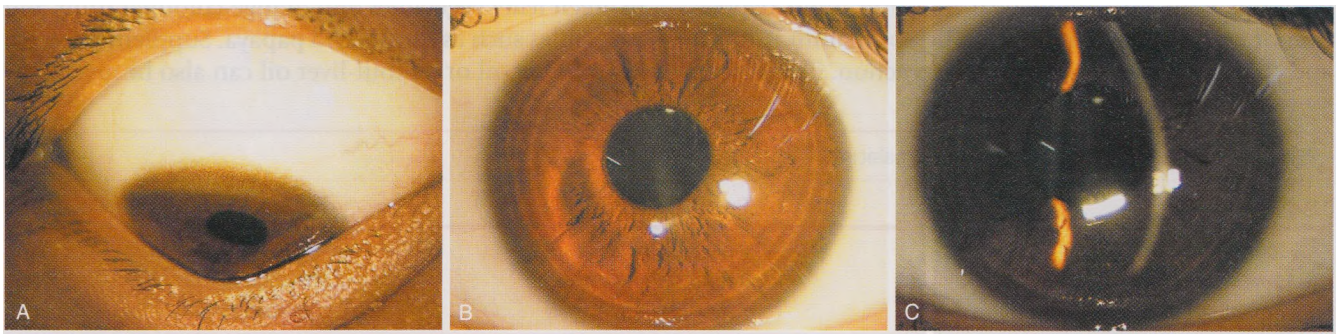
In the early stages the condition is diagnosed with corneal topography, which demonstrates the cone and typical astigmatic pattern. Corneal thinness can also be measured with ultrasonic pachymetry or the Orbscan II corneal topography system. With the ophthalmoscope or plane mirror at a distance of 1 m a ring of shadow, concentric with the margin, is seen in the red reflex (resembling a droplet of oil), altering its position on moving the mirror. It is due to a zone through which a few rays pass into the observer's eye, as the emergent rays in the centre are convergent while those on the periphery are divergent.

The patient becomes myopic, but the error of refraction cannot be satisfactorily corrected with ordinary glasses owing to the parabolic nature of the curvature which leads to irregular astigmatism in the later stages. The condition is almost invariably bilateral, though frequently more advanced on one side than the other. It may be slight and progress very slowly, or the reverse. In the later stages the apex shows fine, more or less parallel striae *(Vogt striae)* best seen with the slit-lamp, and also discrete opacities which become confluent. A brownish ring, probably due to haemosiderin, may form in the epithelium encircling the cone *(Fleischer ring).* Sometimes ruptures develop in Descemet's membrane in which case the stroma becomes suddenly oedematous and opaque *(acute hydrops).*

Treatment: In the early stages, vision may be improved with spectacles but contact lenses are more beneficial as they eliminate the irregular corneal curvature, and are said to have a supporting effect.

Corneal collagen cross-linking is a new modality of treatment introduced as an interim measure to tract progression. Riboflavin (0.1%) eye drops are instilled every 3 minutes or so for 30 minutes after removing the patient's epithelium. Once the cornea is adequately saturated with riboflavin, it is exposed to a quantitative dose (3mW/cm^2) of UVA radiation followed by insertion of a bandage soft contact lens to permit the epithelium to heal. Riboflavin acts as a photosensitizing agent that triggers increased cross-linking of the corneal collagen fibrils by the formation of intrafibrillar and interfibrillar covalent bonds by photosensitized oxidation to stabilize the comeal stroma, delay progression and improve contact lens tolerance.

If despite all measures the disease progresses or the cone becomes hydrated due to a sudden tear of the Descemet's membrane (acute hydrops), the most satisfactory treatment is corneal transplantation (keratoplasty). Keratoplasty is particularly successful in this condition and should be considered in progressive cases and whenever visual loss is considerable. Though penetrating keratoplasty is the



Fig, 15.32 Keratoconus. (A) Munsen sign; (B) ectasia and (C) thinning of the cornea.

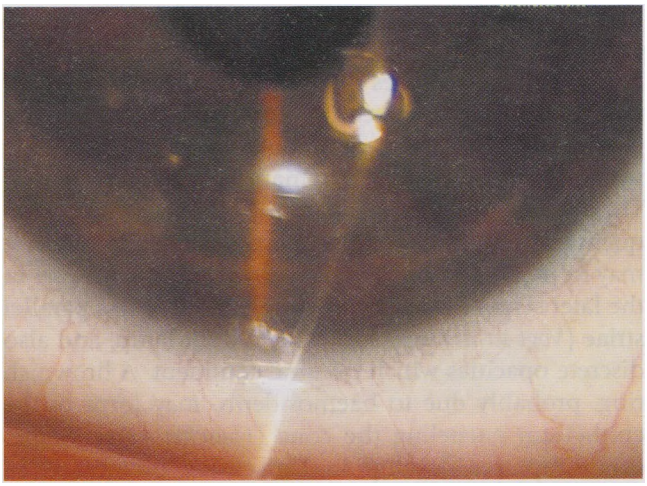


Fig. 15.33 Pellucid marginal degeneration. (By courtesy of RB Vajpayee)

most common surgical treatment, lamellar keratoplasty has also been shown to be very successful. Deep anterior lamellar keratoplasty (DALK) is currently fast becoming the procedure of choice, if the Descemet's membrane and endothelium remain uninvolved as it removes the entire corneal stroma sparing the host Descemet's membrane and endothelium with the dual benefit of reducing the risk of rejection and permitting use of donor corneal tissue with a relatively low endothelial count or older age.

Keratoglobus

This is a congenital anomaly in which there is a hemispherical protrusion of the whole cornea, occurring bilaterally. It is familial and hereditary. It differs from buphthalmos in that the intraocular pressure is normal, the cornea clear, refractive errors are 'with-the-rule', the angle of the anterior chamber normal, and there is no cupping of the optic disc.

Pellucid marginal degeneration

This is a painless bilateral corneal thinning affecting the inferior cornea (Fig. 15.33), usually from 4 to 8 o'clock positions with no conjunctival injection, lipid deposition or corneal vascularization. The epithelium is intact and there is no anterior chamber reaction. The cornea above the area of thinning becomes ectatic, with myopic 'against-the-rule' astigmatism. The thinning may slowly progress and rarely be associated with acute hydrops. Pellucid marginal degeneration may occasionally occur in conjunction with keratoconus.

MISCELLANEOUS CONDITIONS

Nutritional deficiency

Keratomalacia

This is common in developing countries and affects poorly nourished children who are deficient in vitamin A, often early in the first year of life; the condition is usually bilateral. The cornea becomes dull and insensitive, hazy and yellow infiltrates form until finally the whole tissue undergoes necrosis and seems to melt away (*keratomalacia)* within a few hours. A characteristic feature is the absence of inflammatory reaction. Keratomalacia is often precipitated by an acute systemic illness such as measles, pneumonia or severe diarrhoea. The children are usually extremely ill and very frequently die of other systemic diseases. Owing to their apathetic condition they do not close the lids, the cornea is continually exposed, and secondary bacterial infection can occur and complicate the clinical picture.

Treatment: Keratomalacia must be treated as an ophthalmic emergency and the child hospitalized. Vitamin A is administered in three doses, as outlined in Table 15.3. The first is to be given at diagnosis, the second after 24 hours and the third after 2 weeks.

Modes of administration: Oral oil-based preparations are preferred but if the child is suffering from persistent vomiting or profuse diarrhoea then an intramuscular injection of water-miscible vitamin A (retinyl palmitate) may be given at half these dosages as a substitute.

Since keratomalacia is potentially a bilaterally blinding condition, attention must be directed towards prevention. The general health should be improved and vitamin A given in an adequate quantity with a diet rich in green leafy vegetables and orange-coloured fruits and vegetables such as carrots and papaya. Supplements such as cod-liver oil or halibut-liver oil can also be given.

Table 15.3 Treatment schedule for keratomalacia*

Age	Preparation	Dose
<6 months	Retinyl palmitate orally	50 000 IU
6–12 months or weight <8 kg	Retinyl palmitate orally	100 000 IU
>12 months and weight >8 kg	Retinyl palmitate orally	200 000 IU

*A total of three doses are administered.

Exposure keratopathy

This occurs in eyes insufficiently covered by the lids. The epithelium of the exposed cornea becomes desiccated and the substantia propria hazy. Owing to the drying, the epithelium is cast off and the cornea falls prey to infective organisms.

The condition is due to any cause which may produce exposure of the cornea due to incomplete closure of the eyelids (lagophthalmos), such as extreme proptosis as in exophthalmic ophthalmoplegia or orbital tumour, paralysis of the orbicularis (neuroparalytic keratopathy), etc. The absence of reflex blinking and defective closure of the lids during sleep are important factors, so that extremely ill patients are liable to get this form of keratitis.

Treatment: This consists of keeping the cornea well covered. In mild cases it is sufficient to bandage the eyes at night. If possible the cause of the exposure must be removed, but in the meantime it may be necessary to perform a tarsorrhaphy by suturing the lids together.

Neurotrophic keratopathy

This occurs in some cases in which the ^ trigeminal nerve is paralysed, typically as a result of radical treatment for k trigeminal neuralgia. It does not occur in all cases of peripheral lesions of the trigeminal nerve; thus, if the Gasserian ganglion is removed or the trigeminal nerve injected with alcohol for trigeminal neuralgia with proper precautions, only a few cases develop neurotrophic keratitis, the tendency being decreased if there is an adequate tear film.

The characteristic feature of neurotrophic keratopathy is the desquamation of the corneal epithelium. The surface of the cornea becomes dull and the epithelium is thrown off, [first at the centre fthen over the whole surface except a narrow rimjjt the periphery: the entire epithelium may thus peel off intact. The substantia propria then becomes cloudy and finally yellow, breaking down into a large ulcer which is usually accompanied by a hypopyon. There is no pain, owing to the anaesthesia, but ciliary InjectionJs marked. ^Rehpsesjire therukj the hea I ecfscar q LI i ckTyTxeaki n g down again and the whole process being repeated.

Treatment: The ordinary treatment of a comeal ulcer should be tried initially, special care being devoted to the protection of the eye with a shield. Improvement is often marked, but in some cases, as soon as the shield is relinquished the ulceration starts anew. Closure of the lacrimal puncta to conserve moisture by abolishing the drainage of tears is sometimes of great value. If, however, relapses occur, it is best to suture the lids together (tarsorrhaphy, *see* Chapter 28) for up to at least 1 year. In the operation of lateral tarsorrhaphy after removal or blockage of the; Gasserian ganglu>iiJ7ioTmaesthetic Is npressarv since sensation is lost in theconjunctiva and lids. The beneficial effect of this procedure is very striking, as it invariably succeeds in arresting the process.

Neuroparalytic keratopathy

This is seen in facial nerve palsy as occurs in Bell's palsy, leprosy or neurological disorders leading to ectropion, lagophthalmos and exposure keratopathy (*see* Chapter 31). The inferior part of the cornea is most affected. Treatment is with lubricants, ointment with an eye shield at night and lateral tarsorrhaphy in severe cases.

Superior limbic keratoconjunctivitis

This is characterized by inflammation of the superior tarsal and bulbar conjunctiva and oedema of the corneoscleral limbal conjunctiva; corneal filaments are frequently present. Fine punctate fluorescein and Rose bengal staining of the superior cornea, limbus and conjunctiva are commonly found. Fine papillae may be seen on the superior palpebral conjunctiva and a superior corneal pannus may develop. The condition is usually bilateral, occurs frequently in females and follows a chronic course with remissions and exacerbations. The prognosis is excellent as eventual resolution usually occurs.

There is a strong association with thyroid disease. Hence thyroid function tests and clinical evaluation for thyroid dysfunction should be performed.

Treatment is symptomatic, with the liberal use of topical ocular lubricants and temporary punctal occlusion with collagen punctal plugs, if required. Any concurrent blepharitis should be treated with antibiotic ointment such as erythromycin or chloramphenicol applied four times daily for 1 week. If corneal filaments and mucus strands are present in excessive amounts, then acetylcysteine 10% drops are added three to five times a day.

Vernal keratopathy

Corneal involvement in patients with vernal keratoconjunctivitis includes punctuate epithelial erosions, commonly in the upper cornea, a 'shield' ulcer manifesting as a circumscribed, oval, painless ulcer in the upper cornea with a plaque of mucus and sometimes exudate in the base. Other features include pseudogerontoxon (pseudo arcus senilis) and signs consistent with the 'dry eye' syndrome. Most of these manifestations are due to extensive papillary hyperplasia of the upper tarsal conjunctiva, unstable tear film and dry eye.

Aphakic and pseudophakic bullous keratopathy

Often incorrectly called 'secondary Fuchs dystrophy', aphakic and pseudophakic bullous keratopathy is a condition akin to primary Fuchs dystrophy in its being due to endothelial damage. It is known to occur after complicated cataract surgery during which there is damage to the

comeal endothelium leading to functional decompensation and consequent corneal oedema. It is estimated that an endothelial cell density of approximately 500 cells/mm² is required to maintain normal transparency of the cornea and the average loss of cells after routine cataract surgery varies from 2 to 10%. However, following complicated cataract surgery, a cell loss of 16-20% is possible. If the patient has an unhealthy endothelium to begin with, as in Fuchs endothelial dystrophy or following an attack of acute glaucoma, the counts may be low and the cell loss induced by surgery—which might have had little effect on a healthy cornea—may lead to corneal oedema postoperatively. Measures to minimize cell damage during surgery include adequate anaesthesia, hypotension and the use of good quality viscoelastic and physiological solutions.

Treatment is difficult unless the primary cause of the oedema can be eliminated. Some comfort may be obtained by the application of a bandage contact lens and the frequent instillation of a concentrated saline solution (5%) or an ointment containing 6% sodium chloride. An alternative which is frequently effective is to strip off the entire epithelium and to replace it by a thin flap of the conjunctiva. Visual improvement depends on full-thickness keratoplasty.

Photophthalmia

Photophthalmia is caused by ultraviolet rays, especially from 311 to 290 nm, and is characterized by extreme burning pain, lacrimation, photophobia, blepharospasm and swelling of the palpebral conjunctiva and retrotarsal folds. It is due to desquamation of the epithelium leading to multiple erosions. There is a latent period of 4 or 5 hours between exposure and the onset of symptoms. The condition is generally caused by the bright flash of a short circuit or exposure to a naked arc light, as in industrial welding or cinema studios. It is rarely due to exposure to enclosed arc lights since the glass globe absorbs the most deleterious rays. In *snow blindness* the cause and symptoms are similar, for the ultraviolet rays are reflected from snow surfaces.

Prophylaxis consists of wearing dark glasses when such exposure is anticipated, made particularly of materials such as Crookes glass which cuts off nearly all the infrared and ultraviolet rays.

The *treatment* is by cold compresses and lubricant drops. Comfort will be obtained by bandaging both eyes for 24 hours to allow the epithelium to regenerate.

Deposition of materials in the cornea

These are rare. A primary lipid infiltration of obscure origin may occur; it is characteristic of *gargoylism.* Equally rare are primary *calcareous degeneration* and *dystrophia urica* in which urate crystals form yellow opacities in the cornea. Similarly, deposits of *cystine* may be associated with a generalized cystinosis, renal dwarfism and osteoporosis (*Fanconi syndrome).* Copper may be deposited in Descemet's membrane in *Wilson disease.* The corneal involvement is diagnosed based on the appearance of a golden-brown or greenish-tinged arc along the limbus at the level of Descemet's membrane when seen with a slit-lamp (Kayser-Fleischer ring, Fig. 15.34). If viewed in cobalt blue light the ring appears dark, almost black. The condition is reversible with time if the systemic disease is treated.

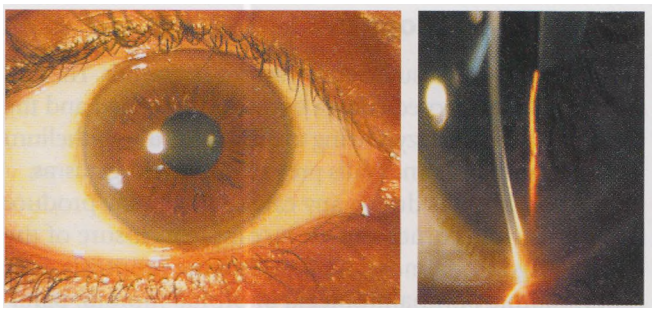


Fig. 15.34 Kayser–Fleischer ring.

Cornea verticillata

This is a whorl-like opacity in the corneal epithelium seen in patients on long-term treatment with medication such as amiodarone, chloroquine, phenothiazines and indomethacin. It is also seen in patients with Fabry disease and its carrier state. The condition is generally asymptomatic, harmless and reversible on stopping the drug. The whorl-like pattern shows the direction of migration of corneal epithelial cells. Occasionally the condition has been known to cause glare and surface discomfort which responds to topical lubricants.

Congenital opacities of the cornea

Congenital opacities of various kinds are sometimes encountered as developmental anomalies; others are due to injury received at birth. The latter are often temporary and diffuse, due to oedema caused by rupture of Descemet's membrane. Causes include sclerocornea, trauma, ulcer, mucopolysaccharidosis, Peter anomaly, congenital hereditary endothelial dystrophy (remembered by the mnemonic STUMPED).

Pigmentation of the cornea

Pigmentation may occur from the prolonged topical use of silver nitrate *(argyrosis).* As in the conjunctiva it is due to the permanent impregnation of the elastic fibres, particularly Descemet's membrane, with metallic silver.

A similar deposit of copper forms a grey-green or golden-brown pigmented ring round the periphery of the cornea in the region of Descemet's membrane and the deeper layers of the stroma when a copper foreign body is retained within the eye (*chalcosis*, *see* Chapter 24) and in hepatolenticular degeneration (Wilson disease, the *Kayser-Fleischer ring*, Fig. 15.34; *see* also Chapter 32).

Blood in the cornea is rare. It may occur as a bright red spot or streak superficially at the margin, or as a greenish or rusty stain throughout the whole tissue (blood staining). In the latter case it is derived from blood in the anterior chamber, usually associated with high tension and endothelial damage—a relatively infrequent complication following contusions.

Tumours of the cornea

These have been discussed with those of the conjunctiva *(see* Chapter 14).

SURGERY FOR CORNEAL DISEASES

Keratoplasty or corneal grafting

Like any other organ transplantation, the diseased cornea is removed and replaced with a healthy donor cornea. Donor corneas are harvested from cadaveric donors within 6 hours after death, sometimes up to 12 hours after death in countries with cold climates. They can be transplanted immediately or preserved in an eye bank by various preservation techniques for varying intervals. Short-term preservation requires the cornea to be used within 48-72 (maximum 96) hours. Intermediate-term preservation by organ culture methods extends this to 30 days and long-term preservation is up to 1 year by cryopreservation.

Depending on the underlying disease, the primary aim of the corneal grafting could be to (i) provide a clear visual axis and restore good vision (optical keratoplasty), (ii) restore the integrity of the globe in corneal diseases such as descemetocele, corneal fistulae, severe irreparable corneal perforation with tissue loss, etc., or (iii) primarily to remove infected tissue unresponsive to conservative treatment as in a sloughing corneal ulcer involving the whole cornea (therapeutic graft).

The cornea is an immunologically privileged organ because of its non-vascular nature and hence corneal graft rejection is less common than that of other organs such as the heart, liver, kidneys and bone marrow where careful donor-recipient matching and extensive immunosuppressive medication is required.

Corneal allografts can be of various types (Fig. 15.35): (i) full-thickness or penetrating keratoplasty; (ii) partial-thickness or lamellar keratoplasty and (iii) small patch grafts, which again can be full thickness or partial thickness. Rotational *autografting* is a variant of keratoplasty where, in the presence of a small scar impinging on the visual axis with a surrounding clear cornea, the patient's own cornea is trephined and rotated to transfer the opacity to a peripheral location and resutured. In this type of graft the risk of rejection is eliminated.

Steps of keratoplasty: After measuring the size of the opacity or the diameter of the cone in keratoconus in the host cornea, an appropriately sized trephine (a circular blade available in different diameters) is chosen. The size of the donor cornea is 0.5 mm larger than that of the host in most cases, though there are exceptions (0.25 mm oversizing is preferred in keratoconus and a 1.0 mm oversized donor graft is preferred in aphakia, and by some surgeons for children and for eyes with adherent corneoiridic scars). The advantages of an oversized donor button are better apposition, a deeper anterior chamber, less chances of development of peripheral anterior synechiae, less post-keratoplasty glaucoma and slightly myopic refraction.

The donor cornea is prepared by trephining the preserved cornea from the endothelial side and covering it with viscoelastic material to protect the endothelium. The host cornea is trephined to make a deep cut and the excision completed with scissors, taking care not to damage the underlying iris and lens. After injecting viscoelastic material to fill the anterior chamber, the donor

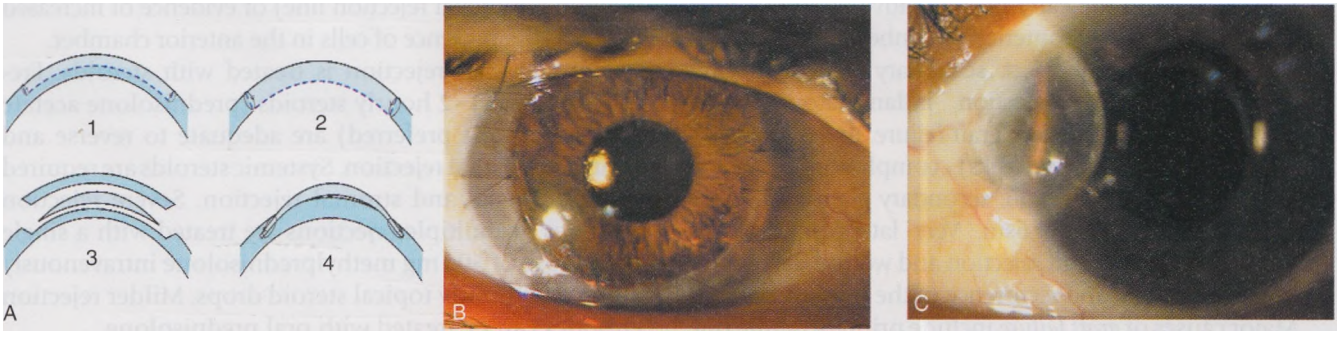


Fig. 15.35 Types of corneal grafts. (A) Schematic diagrams: 1, inlay lamellar; 2, penetrating; 3, keratomileusis; 4, onlay lamellar graft; (B) penetrating or 'full-thickness' corneal graft and (C) lamellar or 'partial thickness' corneal patch graft.

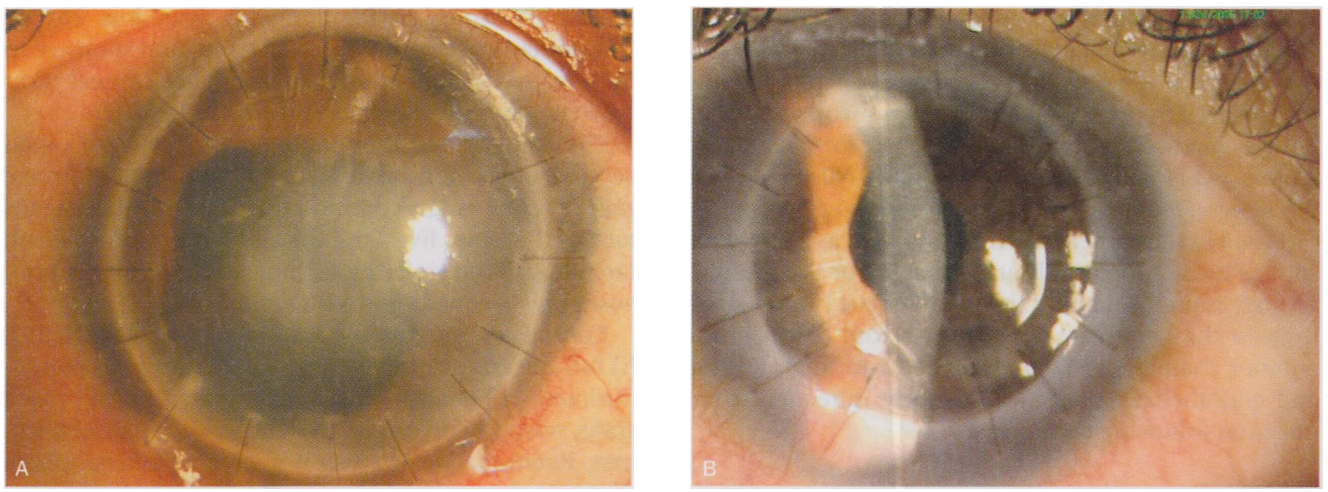


Fig. 15.36 (A) Corneal graft rejection showing a corneal graft with intact sutures. (B) Graft oedema with Descemet's folds and keratic precipitates on the endothelium are all indicative of endothelial rejection.

cornea is placed in the host bed and sutured in place using 16 interrupted sutures or a combination of interrupted and continuous sutures of 10-0 nylon.

A subconjunctival injection of antibiotic and steroid is administered and an eye pad with a shield or bandage applied.

Postoperatively the donor epithelium is shed off leading to an early postoperative epithelial defect which is then replaced with host epithelium and heals in the next 3-5 days. The patient is treated with topical tear substitutes, antibiotic-steroid combination therapy and antiglaucoma medication, if required. In the early postoperative period (initial 3 weeks) the frequency of instillation of steroid drops is 2-4 hourly and subsequently reduced to 6 hourly. Steroids are useful for their anti-inflammatory and immunosuppressive effect and continue to be used in reducing frequency and strength up to 1 year postoperatively or longer.

Visual recovery could be immediate or take a few months due to initial graft oedema and astigmatism. Follow-up is weekly or fortnightly for the first 3 months and then monthly till 6 months, every 2 months for 1 year and yearly thereafter.

Complications in the early postoperative period include wound leak, shallow anterior chamber, persistent or non-healing epithelial defect, secondary glaucoma, graft oedema, uveitis, graft infection, inflammatory 'sterile' suture infiltrates and primary graft failure. In the late postoperative period (after 3 weeks), complications include graft rejection, graft infection, secondary glaucoma, loose sutures and high astigmatism. Very late complications (after 1 year) include graft rejection and wound dehiscence from minor trauma and recurrence of the primary disease.

Major causes of *graft failure* include primary failure due to poor donor endothelium, graft infection, graft rejection and recurrence of the primary disease in the graft.

Corneal graft rejection, though its incidence is less than other organ transplants, can occur as early as 2 weeks and up to several years after keratoplasty. Graft rejection is more common in heavily vascularized corneas (particularly those with deep vascularization in two or more quadrants) and in regrafts, but can occur in all grafts except rotational autografts. Rejection could be epithelial, stromal or endothelial, or a combination of all three. Endothelial rejection is the commonest and the most liable to lead to graft failure.

Patients are warned about the signs of rejection following keratoplasty and asked to report immediately if these occur, as early treatment can lead to reversal of the rejection process.

Symptoms of diminution of vision, photophobia, mild pain and redness several weeks to years after a prior corneal transplant are indicative of acute graft rejection unless proven otherwise. Confirmatory signs include the presence of circumcomeal congestion, fresh keratic precipitates (Fig. 15.36) or a linear deposition of white blood cells on the comeal endothelium (endothelial rejection line), cellular infiltration or oedema in the stroma, epithelial oedema, subepithelial infiltrates, an irregular elevated line in the epithelium (epithelial rejection line) or evidence of increased flare and the presence of cells in the anterior chamber.

Corneal graft rejection is treated with steroids. Frequent topical 1-2 hourly steroids (prednisolone acetate 1% is the most preferred) are adequate to reverse and control epithelial rejection. Systemic steroids are required for endothelial and stromal rejection. Severe rejection episodes or multiple rejections are treated with a single pulse dose of 500 mg methylprednisolone intravenously along with hourly topical steroid drops. Milder rejection episodes can be treated with oral prednisolone.

Treatment, if administered immediately, maximizes the chances of graft survival. Patients are re-examined

every 3-7 days and once improvement is confirmed, steroids are tapered gradually and either discontinued or reduced to a minimum over several months. Intraocular pressure must be measured regularly to ensure early detection of steroid-induced glaucoma.

Phototherapeutic keratectomy

The excimer laser (198nm) can be used to ablate the superficial layers of the cornea to remove superficial opacities in conditions such as band-shaped keratopathy, superficial scars, oil droplet keratopathy, Reis-Buckler dystrophy and Salzmann nodular degeneration. Only superficial lesions (100|xm depth) can be thus treated. Contraindications include excessively thin corneas, dry eyes and deeper opacities. Side effects of therapy are hypermetropia and a faint corneal haze. Complications include a persistent epithelial defect, secondary infection, surgically induced hypermetropic refractive error, and secondary keratectasia.

Refractive surgery

See Chapter 8, p. 74 and 82.

Keratoprosthesis

A keratoprosthesis is a device designed to replace the cornea. Unfortunately, an ideal keratoprosthesis has not yet been devised. Implantation of a keratoprosthesis is considered only as a last resort where penetrating keratoplasty is not possible or has repeatedly failed. Implantation of a keratoprosthesis is reserved for bilaterally blind patients suffering from severe ocular surface disorders such as following chemical burns, Stevens-Johnson syndrome, severe dry eyes and recurrent graft rejections. Pre-operative pre-requisites include a minimum vision of light perception and absence of gross posterior segment disorders as evaluated by ultrasonography.

The basic design of a keratoprosthesis includes a central optical cylinder made of polymethylmethacrylate (PMMA) with a surrounding fixation device which is of different designs in terms of shape, size and material. Some of the materials used for the latter include methacrylate, teflon, dacron mesh, polycarbon, tooth and bone (osteo-odonto-keratoprosthesis), cartilage (chondro-keratoprosthesis) or nail (onycho-keratoprosthesis).

Complications include extrusion, glaucoma, retroprosthetic membrane formation, uveitis and retinal detachment.

SUMMARY

Transmission of light in 400-700 nm band of wavelength, refraction of light, reduction of peripheral oblique and spherical optical aberrations, and protection against physical, chemical and infective agents are the important functions of the cornea which is composed of 78% water, 18% collagen and 4% mucopolysaccharides and is normally transparent in appearance.

Diseases of the cornea are usually vision threatening. Corneal ulcers need to be recognized and treated promptly. Diseases like trauma, keratomalacia and chemical burns are preventable. Corneal scars can be treated by refractive correction if mild, but require corneal transplantation if severe. Donor corneas are obtained by consent of the legal next of kin after death and must be harvested within 6 hours of death.

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16

Diseases of the Sclera

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ANATOMY AND PHYSIOLOGY

The sclera is the tough white coloured opaque outer covering of the eyeball and is composed of collagen and elastin. It is 1 mm thick posteriorly, 0.66 mm at the insertions of the rectus muscles, 0.33 mm beneath the rectus muscles and is thinnest just behind their insertions. The sclera consists of three ill-defined layers, namely, the sclera proper with the episclera on the outside and the lamina fusca interiorly. It is pierced by the anterior ciliary arteries and episcleral veins anteriorly; and the vortex veins, posterior ciliary nerves and vessels and the optic nerve posteriorly. The fibres of the optic nerve pass through the lamina cribrosa of the sclera.

The avascularity of the sclera and the lack of reaction of its dense fibrous tissues to insult, whether traumatic or infective, make diseases of this tissue relatively rare; and when they do occur, they tend to be chronic and slow to respond to treatment.

INFLAMMATION

Two forms of inflammation of the sclera are described: superficial or episcleritis, and deep or scleritis. They might equally well be considered as mild and severe forms of the same disease, but the distinction is convenient since they differ in their evolution.

Episcleritis

This is a benign inflammatory affectation of the deep subconjunctival connective tissues, including the superficial scleral lamellae, and frequently affects both eyes, though their involvement may not be simultaneous. Anatomically, dense lymphocytic infiltration of the subconjunctival and episcleral tissues is found. It is often regarded as an allergic reaction to an endogenous toxin. The condition falls within the vague category of collagenous diseases. A history of rheumatoid arthritis is commonly obtained.

Patients—usually young adults and commonly females—present with an acute onset of redness, mild or no pain in one or both eyes, with no discharge. A history of recurrent episodes is common. Clinically, two types of presentations may occur: (i) simple or diffuse episcleritis; and (ii) nodular episcleritis. On examination, patients with simple or diffuse episcleritis have a sectoral or diffuse redness of one or both eyes mostly due to the

engorgement of the large episcleral vessels which run in a radial direction beneath the conjunctiva (Fig. 16.1). There is mild-to-moderate tenderness over the area of episcleral injection. In nodular episcleritis a circumscribed nodule of dense leucocytic infiltration, which may be as large as a lentil, appears usually 2 or 3 mm from the limbus. It is hard, tender and immovable (or at most can be moved slightly over the underlying sclera, with the conjunctiva moving freely over it). It is traversed by the deeper episcleral vessels so that it looks purple, not bright red. There may be little or no pain, but usually there is a feeling of discomfort and tenderness on pressure, and sometimes severe neuralgia. Nodular episcleritis tends to be more symptomatic and takes longer to resolve. In the worst cases the disease extends into the deeper parts of the sclera and thus passes almost imperceptibly into scleritis. The involvement of the eye is nearly always temporal in location. It is usually transient lasting several days or some weeks but has a strong tendency to recur; thus the disease may drag on for months. Occasionally the attacks are fleeting but frequently repeated *(episcleritis periodica fugax).* On the other hand, the disease may be extremely chronic, but never ulcerates and eventually the inflammation resolves, sometimes completely, but more frequently it leaves a slate coloured scar to which the conjunctiva is adherent. The cornea and uveal tract rarely participate in the inflammation.

Treatment

This is difficult and often unrewarding. If mild, the disease can be treated with lubricants alone. If moderate to severe, a mild topical steroid (e.g. fluorometholone) prescribed four times a day relieves the discomfort and inflammation. Rarely, more frequent and potent steroids are required. In cases where topical treatment is unsuccessful, oral non-steroidal anti-inflammatory drugs (NSAIDs) may help (ibuprofen 400 mg orally 3-4 times a day, aspirin or indomethacin taken with food or antacids). Some prefer topical and systemic NSAIDs to topical steroids as initial therapy. Patients on lubricants can be seen after several weeks, but those on topical steroids must be reviewed weekly to evaluate the clinical response and check for steroid-induced complications, especially any rise in intraocular pressure. Corticosteroids or NSAIDs administered topically as drops or ointment are of temporary benefit. Even in patients in whom no history of rheumatism can be elicited, salicylates may prove helpful, and should be tried. Prolonged remissions may be induced by ibuprofen 200-400 mg 3-4 times a day or aspirin 325-650 mg orally 3-4 times a day, 600 mg daily for 4-5 days and then reduced to lower doses.

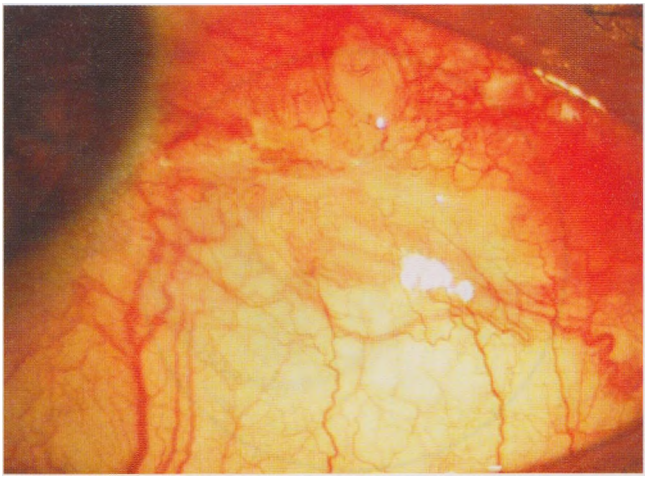


Fig. 16.1 Diffuse episcleritis.

Scleritis

Pathologically, scleritis resembles episcleritis, but extends more deeply, the essential difference being a dense lymphocytic infiltration deep within the sclera tissue.

Scleritis is usually a bilateral disease, rarer than episcleritis and occurs most frequently in women (Fig. 16.2A). It is associated with connective tissue disease in 50% of cases and a thorough investigation is required to eliminate active systemic disease such as polyarteritis nodosa, systemic lupus erythematosus, rheumatoid arthritis (Fig. 16.2B), Reiter syndrome, ankylosing spondylitis, non-specific arteritis, Wegener granulomatosis (Fig. 16.3A), dermatomyositis, polychondritis and gout. Other known associations include acute or previous attacks of herpes zoster ophthalmicus, syphilis and recent ocular surgery such as cataract extraction and retinal detachment surgery.

The clinical presentation may be classified as outlined in Table 16.1. One or more nodules may appear but the area affected is less circumscribed than in episcleritis. The swelling is at first dark red or bluish and later becomes purple and semitransparent like porcelain. It may extend entirely around the cornea, forming a very serious condition known as *annular scleritis.* In the diffuse type, hard whitish nodules, the size of a pin's head, may develop in the inflamed zone; they disappear without disintegrating. Scleritis differs from episcleritis in that the cornea and uveal tract are involved, there is some iritis but more

Table 16.1 Clinical classification of scleritis

I. Anterior scleritis
- Nodular
- Diffuse
- Necrotizing
  - With inflammation
  - Without inflammation

II. Posterior scleritis

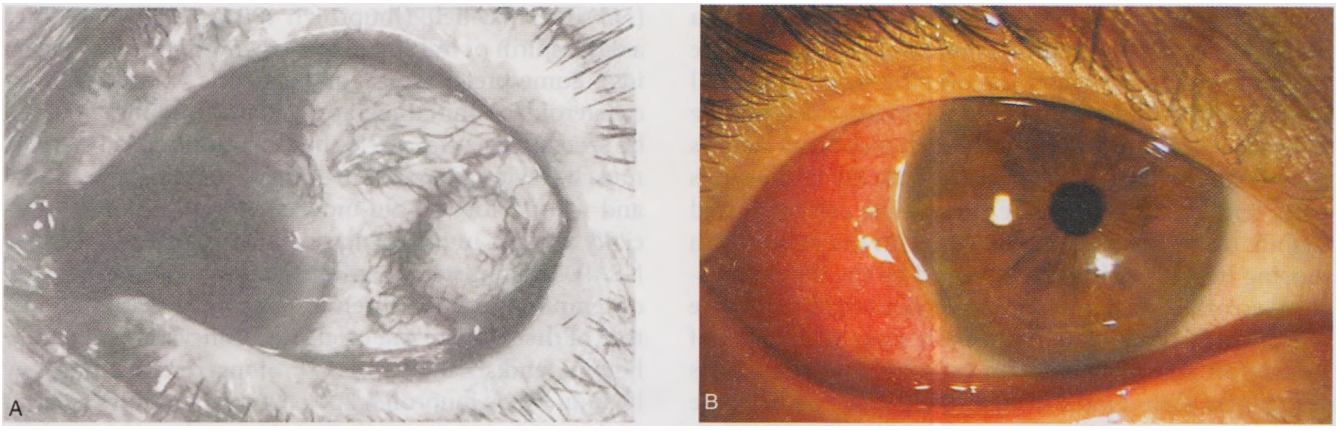


Fig. 16.2 (A) Nodular anterior scleritis. A discrete scleral nodule with displacement of the deep vessels over the nodule and surrounding inflammation overlying the unaffected sclera (By courtesy of P. Watson). (B) Anterior scleritis in a 42-year-old woman with rheumatoid.

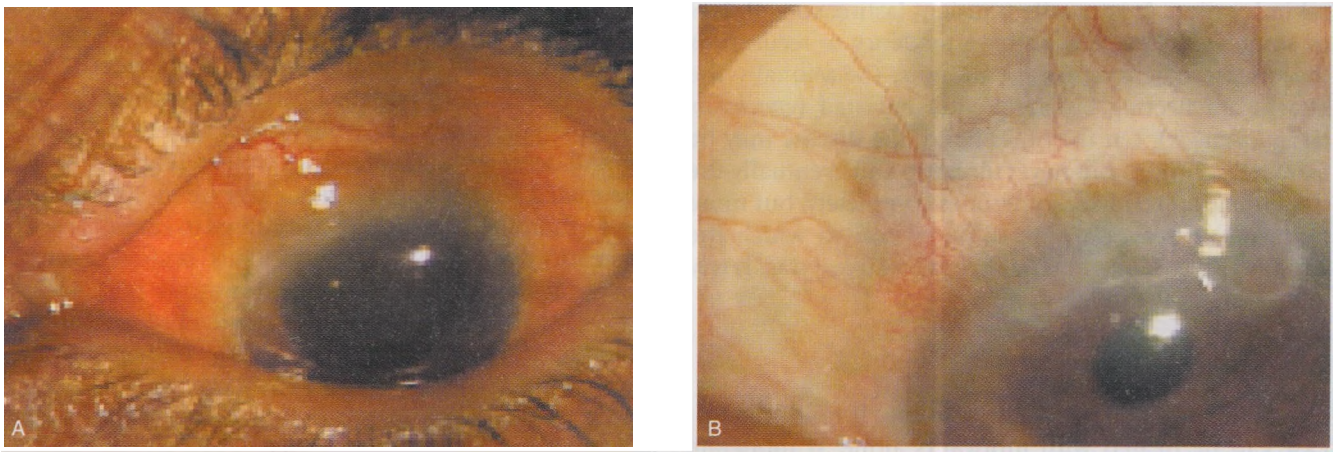


Fig. 16.3 (A) Diffuse anterior scleritis in a 45-year-old man with Wegener granulomatosis; (B) shows thinning of the sclera after treatment.

often cyclitis and anterior choroiditis are present. There is no ulceration, but the sclera is thinned and a dark purple cicatrix is formed, which occasionally becomes too weak to withstand the intraocular pressure, so that ectasia follows *(ciliary staphyloma).* Secondary glaucoma is a common sequel.

Besides causing intraocular complications, scleritis may sometimes extend to the cornea resulting in *sclerosing keratitis* (Fig. 16.4). An opacity develops at the margin of the cornea near the affected scleral area; it is approximately triangular or tongue-shaped, the rounded apex being towards the centre of the cornea. There is little or no corneal vascularization, and ulceration does not occur. Some clearing occurs from the centre towards the periphery and near the corneal limbus, but the densest parts usually persist as bluish clouds. The whole margin of the cornea may become opaque like the sclera and occasionally guttered, but the pupillary area almost invariably escapes. The most serious corneal complication is keratolysis in which the stroma melts away.

Necrotizing scleritis is associated with scleral necrosis, severe thinning and melting in severe cases. Two types are seen: either with inflammation or without inflammation.

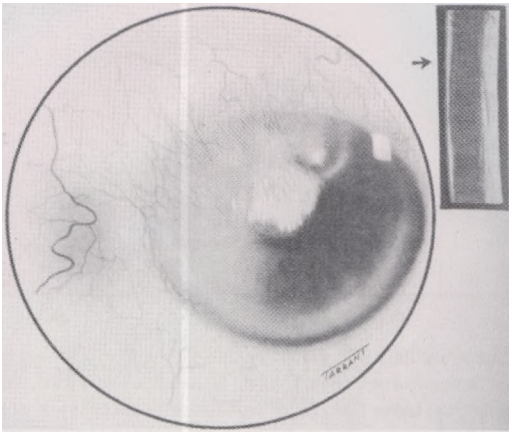


Fig. 16.4 Corneal involvement in scleritis.

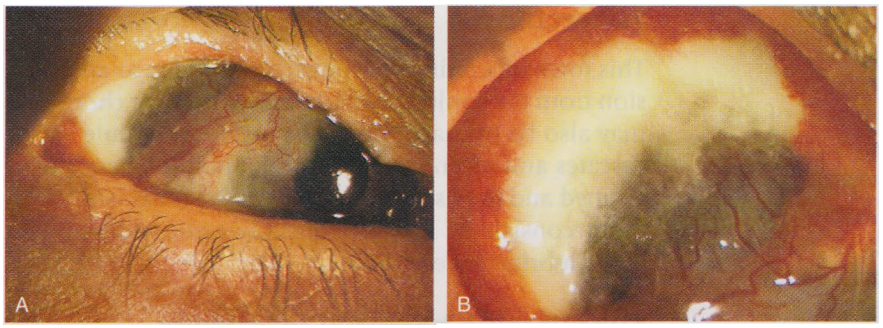


Fig. 16.5 (A and B) Necrotizing scleritis with inflammation; (B) magnified view.



Fig. 16.6 Necrotizing scleritis without inflammation.

Necrotizing scleritis with inflammation (Fig. 16.5) presents with a red, painful eye and progressive worsening of symptoms. It may be associated with anterior uveitis and is usually a part of a systemic autoimmune disease. Vascular sludging and occlusion, scleral thinning and complications such as glaucoma, cataract, sclerosing keratitis and peripheral corneal melting are common. The 5-year mortality from associated systemic disease is 25%.

Necrotizing scleritis without inflammation is called *scleromalacia perforans* (Fig. 16.6) and occurs in patients suffering from seropositive rheumatoid arthritis. There is painless scleral thinning with melting in severe cases and the underlying cause is believed to be ischaemia.

Posterior scleritis

This is an inflammation with thickening of the posterior sclera which may start primarily posteriorly or may be an extension of anterior scleritis. It is usually not associated with any systemic disease. The clinical presentation is varied and the diagnosis is easily missed, particularly in cases with no pain or no anterior segment involvement. Clinical features include decreased vision, with or without pain, proptosis or restricted ocular movements. Posterior vitiates, disc oedema, macular oedema, choroidal folds, choroidal detachment, uveal effusion syndrome and exudative retinal detachment may be present in varying degrees and combinations. B-scan ultrasonography and CT scanning may be helpful in diagnosis by demonstrating a thickened sclera.

Diagnosis

The patient who presents with episcleritis or scleritis should have a careful history taken, thorough systemic examination and, based on clinical judgement, the following investigations should be performed: full blood count, rheumatoid arthritis latex agglutination test (rheumatoid factor (RF)), Mantoux test, antinuclear antibody (ANA), antineutrophil cytoplasmic antibody (ANCA), VDRL, acid fluorescent treponemal antibody absorption (FTA-ABS) test, serum uric acid estimation, the *Treponema pallidum* immobilization (TPI) test for syphilis, X-rays of the chest and sacroiliac joints and, in certain patients, a full immunological survey for tissue antibodies. Soluble immune complexes, complement, lupus erythematosus (LE) cells and antinuclear factor (ANF) should also be assessed.

Treatment

In patients with diffuse or nodular scleritis, one or more of the following drugs is recommended: oral NSAIDs, oral prednisolone 1 mg/kg as a single dose in the morning for one week which can then be tapered to 20 mg per day over the subsequent 2-3 weeks, or immunosuppressive agents such as cyclophosphamide, methotrexate, cyclosporin or azathioprine. Immunosuppressive therapy is best given in conjunction with an internist or rheumatologist. Concurrent therapy with antacids or H_2-receptor blockers such as ranitidine 150 mg given twice daily orally or famotidine 20 mg twice daily orally is advisable.

In patients with necrotizing scleritis, systemic steroids and immunosuppressives are recommended. Abundant lubricants are important in scleromalacia perforans. Scleral patch grafting may be necessary if there is any significant risk of perforation.

In posterior scleritis, therapy includes systemic NSAIDs, steroids or immunosuppressive therapy. Intravenous methylprednisolone administered as pulse therapy is also effective and helps in reducing the side-effects of prolonged oral steroid intake.

Local steroids tend to be ineffective and subconjunctival injections of steroids should never be given for fear of rupture of the globe. Likewise, biopsy is dangerous as well as uninformative.

Infectious causes, if identified, are treated with appropriate topical and systemic antimicrobial agents. Panophthalmitis, if severe, will warrant intravenous antibiotics in the doses given for meningitis.

Specific inflammatory diseases

Collagen vascular diseases

Scleral involvement is common in this group of disorders, particularly in rheumatoid arthritis.

The serological feature of rheumatoid arthritis is the presence of circulating antibodies to immunoglobulin molecules, which are known as RFs. A majority of patients (70-90%) with rheumatoid arthritis are seropositive for classical RF.

The lesions of rheumatoid arthritis may be caused by the deposition of a globulin-antiglobulin complex whereby complexes of modified IgG and locally formed RF in the synovium result in the activation of complement. This provokes the release of hydrolytic enzymes and subsequent erosion of adjacent articular surfaces. It is likely that the scleral nodules in rheumatoid arthritis represent a granulomatous response to focal deposits of antigen-antibody complexes. The primary event of rheumatoid arthritis is possibly cryptogenic bacterial or viral infection in susceptible individuals, provoking an inappropriate immunological response.

Histologically, the typical scleral lesion assumes the characteristic combination of a proliferative infiltration by chronic inflammatory cells surrounding a central area of fibrinoid necrosis, as generally occurs in rheumatoid nodules. In the sclera the clinical manifestations take several forms. *Episcleral rheumatoid nodules* may appear and disappear, waxing and waning with the vagaries of the systemic disease. A more serious condition is *necrotizing nodular scleritis* in which a violent and painful anterior scleritis, often circumferential in its extent, characterized by extensive swelling and the appearance of one or more yellow nodules, usually proceeds to necrosis leading eventually to disintegration of the sclera and exposure of the underlying uvea (Fig. 16.5). In scleromalacia perforans a similar necrosis of the sclera occurs with exposure of the uvea but without painful symptoms (Fig. 16.6). Finally, in *massive granuloma of the sclera,* proliferative changes are predominant. A 'brawny scleritis' results, in which the sclera may become so thickened as to simulate an intraocular or orbital tumour. In all these cases, serious and often destructive extension occurs into the uveal tract, and the general prognosis is poor. Systemic treatment by corticosteroids offers the only known method of amelioration.

INFECTIONS

Gumma

This used to be seen in tertiary syphilis but is now uncommon.

Tuberculosis

This form of scleritis may be secondary, due to an extension from the conjunctiva, iris, ciliary body or choroid. It may also be primary, forming a localized nodule which caseates and ulcerates. The nodule should be excised or scraped and the tissue examined for the organism. Treatment consists of systemic antituberculous drugs with local, lubricating eye drops.

Suppurative bacterial infections

Virulent organisms such as *Pseudomonas* causing an endophthalmitis may spread to infect the sclera and episcleral tissue, leading to a panophthalmitis including a scleritis. Extension of such infection is clinically diagnosed by the development of painful eye movements due to inflammation involving the muscle sheaths at the point where they are inserted onto the sclera. Treatment consists of high doses of intravenous broad-spectrum antibiotics and a careful watch for further spread into the orbit and subsequent cavernous sinus thrombosis. Surgical measures include intravitreal injection of antibiotics, vitrectomy and, finally, evisceration of the globe if the eye has no light perception and all measures to contain the infection fail.

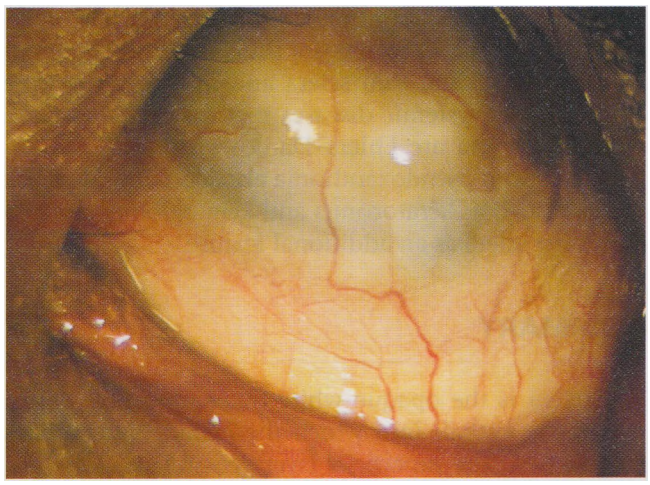
STAPHYLOMA

A staphyloma is a clinical condition characterized by an ectasia of the outer coats (cornea, or sclera or both) of the eye with an incarceration of the uveal tissue. The basic underlying pathology is a weakening of the eye wall, which can be caused by many inflammatory or degenerative diseases involving these structures. Most commonly the diseases causing a weakening of the globe are accompanied by a raised intraocular pressure and both contribute to the development of the staphyloma.

Depending on the site affected, staphyloma can be classified as (i) anterior, (ii) intercalary, (iii) ciliary, (iv) equatorial and (v) posterior.

Anterior staphyloma

This can be partial or total, depending on whether part or whole of the cornea is affected. The most common cause is a sloughing corneal ulcer which perforates and heals with the formation of a pseudocornea by the organization of exudates and laying down of fibrous tissue. It is lined internally by the iris and externally by newly formed epithelium. The anterior chamber is flat and later secondary glaucoma may supervene. Gradually the weak anterior surface of the eye protrudes outward leading to an anterior staphyloma (Fig. 16.7).



Fig, 16.7 Anterior staphyloma.

Intercalary staphyloma

This is located at the limbus and is lined by the root of the iris and the anteriormost part of the ciliary body. It is seen externally from the limbus to up to 2 mm behind the limbus. The usual causes are lesions that produce weakening of the globe in this region such as perforating injuries of the peripheral cornea, marginal corneal ulcer, anterior scleritis, scleromalacia perforans, complicated cataract surgery with poor wound apposition and secondary glaucoma.

Ciliary staphyloma

This affects the ciliary zone that includes the region up to 8 mm behind the limbus. Here the ciliary body is incarcerated in the region of scleral ectasia and has a bluish colour with a lobulated surface. Developmental glaucoma, end-stage primary or secondary glaucoma, scleritis and trauma to the ciliary region of the eye are some of the conditions that lead to a ciliary staphyloma.

Equatorial staphyloma

This occurs at the equatorial region of the eye with incarceration of the choroid. The equatorial region is approximately 14 mm behind the limbus and is inherently relatively weak owing to the passage of the venae vorticosae. Scleritis, degenerative myopia and chronic uncontrolled glaucoma are conditions that may lead to equatorial staphyloma.

Posterior staphyloma

This affects the posterior pole of the eye and is lined by the choroid. Degenerative high axial myopia is the most common cause. The ectatic portion is not visible externally but can be detected by fundoscopy and B-scan ultrasonography. Indirect ophthalmoscopy shows a posterior outward curvature of the globe detected as a crescentic shadow in the macular region. The retinal vessels are seen to change direction, dipping down into the region. The staphylomatous region may appear pale due to degenerative changes in the retina, retinal pigment epithelium and sometimes choroid.

Treatment

Inflammatory diseases which affect the outer coats of the eye such as scleritis, corneal ulcer and keratomalacia from vitamin A deficiency or rheumatoid arthritis with prevention of secondary glaucoma should be promptly treated to prevent the formation of staphylomas. Local excision and repair with a corneal and scleral patch graft can be performed. Large, unsightly blind eyes can be treated with staphylectomy and keratoplasty, or enucleated and replaced with an implant, depending on the extent of involvement and degree of cosmetic disfigurement.

TUMOURS

Choristomas

These are benign tumour-like lesions owing to the presence of normal tissue in an abnormal location. These lesions involve the episclera more commonly than the sclera and are usually congenital but may increase in size and prominence with age.

Limbal and epibulbar dermoids (see Fig. 14.14, p. 177) are choristomas which contain structures such as hair follicles, sebaceous glands and keratin of epidermal and mesodermal origin. They are most commonly located at the inferotemporal limbus, are often associated with Goldenhar syndrome (Fig. 16.8), and may need to be excised if they cause excessive astigmatism, encroach on the pupillary area or are cosmetically disfiguring.

Another variety is episcleral osseous choristomas that occur in the superotemporal quadrant, are adherent to the underlying sclera and are composed of mature compact bone.



Fig. 16.8 Goldenhar syndrome limbal dermoid and ear anomalies.

Malignant tumours

Primary tumours of the sclera are rare, but the sclera can be secondarily involved by tumours, such as retinoblastoma and malignant melanoma, which extend from within the eyeball. Tumours originating from structures outside the eyeball (such as squamous cell carcinoma and malignant melanoma from the conjunctiva or lids) and malignant lacrimal gland tumours may also invade the sclera. Clinically, a thorough local and systemic examination should be done for preauricular and cervical lymph nodes. Malignant lacrimal gland tumours are usually treated with exenteration of the orbit.

CONGENITAL ABNORMALITIES

Blue sclera

The sclera is bluish in babies, but the effect reduces with age. A much more pronounced blue coloration is sometimes seen in several members of the same family as a hereditary condition that persists throughout life. This disease is known as osteogenesis imperfecta and is characterized by frequent bone fractures (*fragilitas ossium*), blue sclera and deafness. Both sexes are equally involved; only those affected can transmit the disease. Histologically, the sclera and cornea are thin. The uveal pigment shines through the thin sclera and produces the blue colour. Other systemic diseases that may be associated with blue sclera are Ehlers-Danlos syndrome, Marfan syndrome and pseudoxanthoma elasticum. Local ocular diseases such as keratoconus and keratoglobus can also have blue sclera as an additional feature.

SUMMARY

The sclera is the opaque white outer protective covering of the eyeball into which the extraocular muscles are inserted. The superficial layer gets inflamed in episcleritis which is a benign self-limited condition which may occasionally be associated with systemic disease. The sclera proper is involved in scleritis which is less common but a more serious condition than episcleritis and is more often associated with systemic diseases like collagen vascular disorders, Behcet's syndrome, herpes zoster ophthalmicus, sarcoidosis, gout and gastroenteropathies. Scleritis is classified as posterior and anterior and the latter may be necrotizing (with or without inflammation) or non-necrotizing (nodular or diffuse).

17

Diseases of the Uveal Tract

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ANATOMY AND PHYSIOLOGY

The uvea is a highly vascular layer that lines the sclera and its principal function is to provide nutrition to the eye. TheJris is responsible for metabolism of the anterior segment, bv diffusion of metabolites through the aqueous. The ciliary body secretes aqueous which bathes the avascular structures of the anterior segment and the choroid, and provides nutrition to the outer retina. Its vascularity unfortunately allows the frequent involvement of the uveal tract in systemic vascular, immune and infectious diseases.

Although topographically apparently separate, the iris, ciliary body and choroid are so closely related as to form a continuous whole; th£cliseasf^^ tion which often affect the other reRions.

INFLAMMATION (UVEITIS)

The term *uveitis* emphasizes the close relationship between the anatomically distinct parts of the uveal tract, for inflammatory processes tend to involve the uvea as a whole and are generally not limited to a single part.

This feature is particularly well exemplified in inflammation of the iris and ciliary body; iritis never occurs

Table 17.1 Classification of uveitis		
Based on predominant anatomical site affected'		
Anterior uveitis	*Intermediate uveitis*	*Posterior uveitis Panuveitis*
Iritis	Posterior cyclitis	Choroiditis (focal/multifocal/diffuse)
Anterior cyclitis	Pars planitis	Chorioretinitis
Iridocyclitis	Hyalitis	Retinochoroiditis
	Basal retinochoroiditis	Neuro-uveitis
Based on aetiology		
Idiopathic, infective, immune-related, neoplastic, traumatic		

*The International Uveitis Study Group has recommended that the classification based on anatomical location be followed. (Bloch-Michel E, Nussenblatt RB. International Uveitis Study Group recommendations for the evaluation of intraocular inflammatory disease. *Am J Ophthalmol* 1987;103:234-5)

without some cyclitis, nor cyclitis without some iritis. The terms Jrife and *cyclitis are* used according to whether the iris or ciliary body appears clinically to be the more affected. The same disposition is also seen with regard to the choroid, although in a lesser degree, for the ciliary body is often involved in many cases of choroiditis. The classification used today *is (anterior) intermediate*j and *[posterior) uveitis. Generalized uveitis* or *panuveitis* is the commonest among chriyiic types of inflammation (Table 17.1).

Apart from the classifications based on the anatomical site of involvement, uveitis can also be categorized by clinical course as *acute,* chronic, *recurrent* and by pathology, which can be of two types—*granulomatous* and *non-granulomatous.*

Granulomatous iridocyclitis is characterized by the presence of large, greasy 'mutton fat' keratic precipitates (Fig. 17.1 A and B), which are deposits of white blood cells (mainly lymphocytes) derived from the aqueous, on the corneal endothelium and dense posterior synechiae with clusters of inflammatory cells on the pupillary bardej fKoeppe nodules! (Figs 17.2 and 17.3) or on the peripheral part of the anterior surface of the iris (Busacca nodules}.

Granulomatous uveitis is usually due to the invasion of the eye [by living organisms^ but can also be of an [julohnmune aetiologv.| A type iV/nypersensitivity reaction is common. In the absence of allergic sensitivity of the tissues, the inflammation tends to be insidious in onset with a chronic course and a minimum inflammatory reaction. Such chronic inflammations due to direct organismal infection are typically characterized by dense nodular infiltration of the tissues (Figs 17.2 and 17.3) rather than by diffuse exudative phenomena. In the absence of immunity these lesions show a slow and gradual extension; if immunity is present they tend to be circumscribed and relapse if the resistance falls. If hypersensitivity develops, a further organismal invasion leads to necrosis and caseation. The clinical picture varies considerably with the type of organism concerned; the important manifestations of each will be described later.

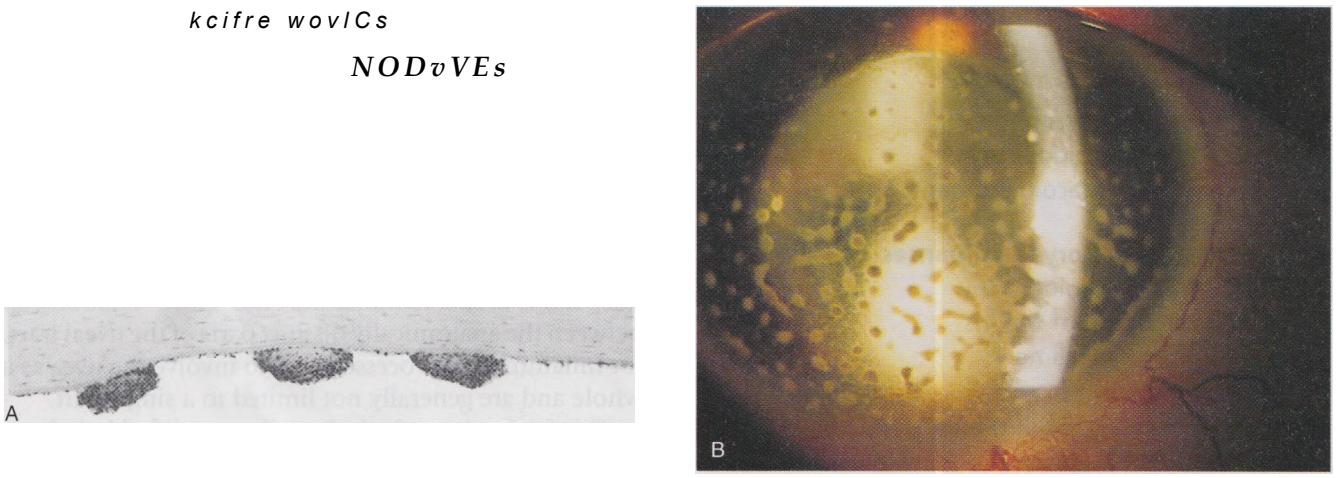


Fig. 17.1 (A) 'Mutton fat' keratic precipitates; (B) 'mutton fat' keratic precipitates.

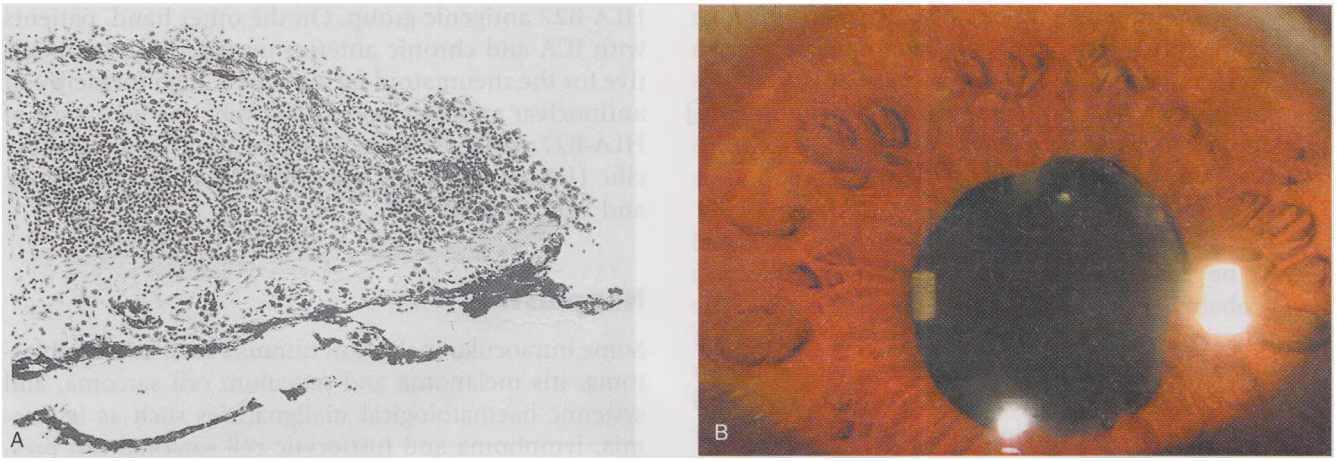


Fig. 17.2 (A) Granulomatous iridocyclitis (in brucellosis). A nodule of lymphoid cells is seen near the sphincter of the iris (By courtesy of AC Woods). (B) Posterior synechiae.

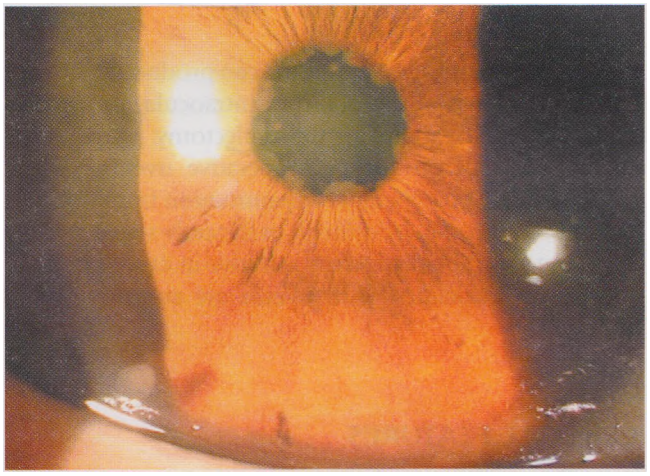


Fig. 17.3 Granulomatous uveitis with Koeppe nodules at the pupillary margin.

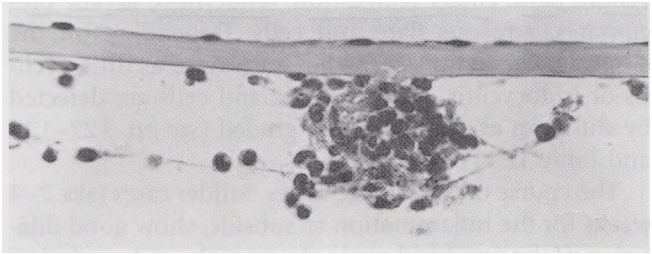


Fig. 17.4 Keratic precipitates in herpes.

Non-granulomatous uveitis is characterized by the presence of Tine keratic precipitates. More commonly seen allergic (or exudative) type of reaction in non-granulomatous uveitis tends to be of acute onset and short *duration,* diffuse in extension and without focal lesions m the iris. There is a considerable flare in the anterior chamber and the keratic precipitates, ifpresent, are few and composed of lymphoid cells arid polymorphs (Figs 17.4 and 11.12B).

AETIOPATHOGEIMESIS OF UVEITIS

Uveitis is said to be *acute* if it lasts less than 3 weeks, *chronic* if more than 3 weeks, *recurrent* if it recurs.

Inflammatory

Determining the aetiology of inflammation of the uveal tract is one of the most difficult problems in ophthalmology. In some cases the aetiology is obvious and several infections have distinguishing clinical features; but in most cases with a non-descript clinical picture, a definitive diagnosis is difficult. It seems probable that most of these are not due to direct infection but are immunogenic in origin. The foreign antigen is usually an infectious agent and the uveitis occurs late in the course of the predisposing disease, once hypersensitivity mechanisms have been established. The following classification may prove useful:

1. *Infective exogenous infections,* due to the introduction into the eye of organisms through a perforating wound or ulcer. This results usually in an acute iridocyclitis, often of a suppurative type, and sometimes in a panophthalmitis in which the whole interior of the eye is involved and inflammation extends into the sclera and episclera as well.
2. *Secondary infections,* in which the inflammation of the uveal tract is due to its spread from one or other of the ocular tissues—the cornea, sclera or retina.
3. *Endogenous infections,* in which organisms, primarily lodged in some *other* organ of the body, reach the eye through the blood stream. These comprise bacterial infections such as tuberculosis, syphilis, gonorrhoea, brucellosis viral infections

such as mumps, smallpox or influenza in which an iridocyclitis occurs; and protozoal infections such as toxoplasmosis. The same mechanism causes the violent .panophth^Imdtis seen in St'pticaenija} due to *Streptococcus*, *Staphylococcus*, *Meningococcus* or *Pneumococcus;* in these the inflammation is suppurative^

4. *Immune-related inflmnmn.t.inns* are generally considered to be common. A primary source of infection probably exists somewhere in the body. The infection is generalized due to the escape of organisms into the blood stream when the ocular tissues become sensitized to them. Later, a renewal of activity in the original focus leads to a further dissemination of the organisms or their'proteins which, meeting the sensitized ocular tissues, excite an immune respoiise~ in them and lead to the 'deposition of ^immune complexes. Alternatively, the immune-mediated inflammation could be part of an underlying autoimmune disorder.

Acute iridocyclitis may be comparable to the simple act of antibody formation in a lymph node but it is possible that immunological thymus dependent 'memory cells' may be implanted in the eye without direct local exposure to the antigen. These cells proliferate on contact with the antigen, should it reappear in the blood stream, and differentiate to become cytotoxic lymphocytes. This could explain the non-specific focal reaction that may occur in eyes with chronic inflammatory disease after the removal of infected teethor areas ofTocal infection.

Uveitis can also represent a response to antigenic stimuli in other parts of the eye. The uvea may retain sensitized lymphocytes after the initial reaction, which provide an immediate response should the cause of the inflammation recur. Iridocyclitis occurs commonly with severe corneal infections and choroiditis with retinal inflammation.

Uveitis may represent hypersensitivity to autologous tissue components. It is found in association with Still disease in children, sj^emiclupusCTjjhematosus, Wegener granulomatosis, prooi^osis, ankyfesing^spondyhusTTSlterdisease, relapsing polychondritis, Behcet syndrome and rheumatoid arthritis, all of which have an autoimmune component in their aetiology.

A number of diseases associated with uveitis occur much more frequently in persons with certain specific HLA antigens. Thus, in patients with ankylosing spondylitis 90% belong to the'HLA-B27 ftntigenic group in contrast to approximately 8% of the normal population. There is also a disproportionately high percentage of patients of the HLA-B27 antigenic group in adult patients with^ acute anterior uveitis. Patients suffering from juvenile chronic arthritis flCAl with acute anterior uveitis are usually negative for the rheumatoid factor and for antinuclear antibodies but belong to the HLA-B27 antigenic group. On the other hand, patients with JCA and chronic anterior uveitis, although negative for the rheumatoid factor, have a high incidence of antinuclear antibody and a relatively low incidence of HLA-B27 antigens. Other diseases associated with specific HLA antigens are Vogt-Koyanagi-Harada disease and Behcet syndrome.

Neoplastic

Some intraocular malignant tumours such as retinoblastoma, iris melanoma and reticulum cell sarcoma, and systemic haematological malignancies such as leukaemia, lymphoma and histiocytic cell sarcoma can present with features of uveitis and are termed/masquerade7 syndromes *(see* p. 246 and Chapter 23).

Traumatic

Blunt or penetrating ocular trauma can produce features of iridocyclitis. Surgical trauma from intraocular procedures such as cataract extraction, trabeculectomy, vitreoretinal surgery, etc. can produce postoperative uveitis. Distinguishing sterile postoperative inflammation from infective endophthalmitis can be difficult in the early stages and the condition should be treated as infective in case of doubt.

Diseases associated with uveitis are summarized in Table 17.2.

CLINICAL FEATURES

Anterior uveitis

This is typically characterized by photophobia, blurred vision, pain, ciliary congestion, tenderness, keratic precipitates, aqueous flare and cells. Depending on the clinical presentation, it can be categorized as iritis, cyclitis or iridocyclitis. Aqueous flare and cells are detected by slit-lamp examination and graded *(see* pp. 122-123 and Table 11.1)

The course of the disease varies. Milder cases take 2-4 weeks for the inflammation to subside, show good dilatation of the pupil with cycloplegics and rapid resolution of redness and pain after starting treatment. In chronic cases, the ciliary body is always seriously involved and the inflammatory signs may be less. Complete resolution may occur in mild cases treated early and suitably, particularly if early dilatation of the pupil has forestalled the development of posterior synechiae. In all cases, a characteristic feature is the tendency to relapse. Each fresh attack runs a similar course, although usually less severe, often leaving further traces and increased impairment of vision.

Table 17.2 Diseases associated with uveitis

Non-granulomatous uveitis

Acute

- Idiopathic
- Infectious diseases such as mumps, influenza, adenoviral, measles, chlamydial, Lyme disease, leptospirosis, Kawasaki disease and rickettsial diseases
- HLA-B27-associated (ankylosing spondylitis, Reiter syndrome, and isolated HLA-B27 positivity without systemic disease)
- Behget disease
- Psoriatic arthritis
- Inflammatory bowel disease
- Lens-induced uveitis (phacolytic, phacoanaphylactic, phacotoxic)
- UGH syndrome (uveitis-glaucoma-hyphaema)
- Corneal graft rejection
- Glaucomatocyclitic crisis (Posner-Schlossman syndrome)
- Trauma
- Anterior segment ischaemia
- Secondary syphilis

Chronic

- Juvenile chronic arthritis
- Chronic iridocyclitis of children
- Fuchs heterochromic iridocyclitis

Granulomatous uveitis

Acute

- Rare

Chronic

- Sarcoidosis
- Herpes simplex, herpes zoster, varicella
- Syphilis
- Tuberculosis
- Leprosy
- Brucellosis
- Phacoanaphylactic

Iritis

To thoroughly understand iritis and its complications it is necessary to remember the anatomy and the pathological changes that occur in the iris. It is practically a diaphragm of blood vessels and unstriped muscle fibres held together by a loose, spongy stroma. Inlts perpetual movement the pupil [alyTnargin slides to - a n d - fro over the lens capsule. The more the pupil is constricted the more of the posterior surface of the iris is in contact with the lens capsule; when fully dilated the iris may not touch the lens.

Inflammation of the iris has fundamentally the same characteristics as in other connective tissues. Dilatation of the blood vessels occurs with impairment of the capillary walls and exudation of a protein-rich fluid into the tissue spaces with leuco- or lymphocytosis. Owing to the extreme vascularity of the iris, the peculiar distribution of the vessels and the looseness of the stroma, hyperaemia tends to cause the pupil to contract mechanically on account of the radial disposition of the vessels. An unusually large amount of exudation and swelling causes the iris to virtually become a water-logged sponge full of sticky fluid so that its movement is impaired, and the normal pupillary reactions become sluggish or abolished. The extravasated fluid also contains substances which act as irritants causing the muscle fibres to contract, and since the sphincter overcomes the action of the dilator muscle, constriction of the pupil results. It follows that in iritis the pupil is constricted, its reactions are sluggish, and the delicate pattern of the iris, instead of being clear and sharply defined, becomes blurred and indistinct ('muddy' iris). The colour undergoes considerable change; blue irides become bluish or yellowish green; brown irides show less difference, but become greyish or yellowish brown. A comparison of the colour of the two irides will usually reveal some difference, for iritis is generally unilateral during an acute attack.

The hyperaemia also manifests itself in circumcorneal ciliary congestion, most marked if the ciliary body is seriously involved. Since the iris is richly supplied with sensory nerves from the ophthalmic division of the trigeminal nerve, pain, typically worse at night, is a prominent symptom of acute iritis. It is not confined to the eye, although severe neuralgic pain is felt here, but is also referred to other branches of the nerve, especially to the forehead and scalp, to the cheeks and malar bone, and sometimes to the nose and teeth.

Albuminous exudates escape into the anterior chamber and, particularly if the ciliary body is involved, the/ aqueous becomes plasmoid *(see* p. 122) containing leucocytes and minute flakes of coagulated protein, or even fibrinous networks in severe cases. It therefore becomes hazy, forming a milky 'flare' in the beam of the slit-lamp which, as it traverses the anterior chamber, should be invisible *(see* Fig. 11.8). This turbidity interferes with a clear view of the iris and is easily mistaken for haziness of the cornea. In very intense cases, polymorphonuclear leucocytes are poured out and sink to the bottom of the anterior chamber to form a hypopyon. Hyphaema, or blood in the anterior chamber, rarely occurs.

At the same time, the nutrition of the corneal endothelium becomes affected so that the cells become sticky and may desquamate in places. The exudates tend to stick there, forming *keratic precipitates.* These are seldom present in simple iritis, but form an important feature of cyclitis and iridocyclitis.

The exudates poured out by the iris and ciliary body also cover the surface of the iris as a thin film and spread into, and sometimes completely over, the pupillary area. When these are profuse the ifitis is termed *plastic.* The pupil may thus get 'blocked', a^ondition which seriously impairs the sight. Moreoveft fhe iris sticks to the lens capsule because of the exudates and becomes fixed. If atropine is instilled at an early stage the iris may be freed and the pupil once again becomes dilated and circular.
In such cases, spots of exudate or pigment derived from the posterior layer of the iris may be left permanently X,

upon the anterior capsule of the lens, forming valuable evidence of previous iritis.

If, however, the adhesions are allowed to become organized they are converted into fibrous bands which the atropine is unable to rupture. Such firm adhesions of the pupillary margin to the lens capsule are called *posterior synechiae;* they show some predilection for the lower part of the pupil in the early stages, probably due to gravitation of the plastic exudates. When they are localized and a mydriatic causes the intervening portions of the circle of the pupil to dilate, the pupil assumes a festooned appearance (Fig. 17.5). Such an irregular pupil is a sign of present or past iritis. Owing to the contraction of organizing exudates upon the iris the pigment epithelium on its posterior surface may be pulled around the pupillary margin so that patches of pigment may be seen on the anterior surface of the iris (*ectropion of the uveal pigment).* Thus, in severe cases of plastic iritis or after recurrent attacks, the whole circle of the pupillary margin may become tied down to the lens capsule. The condition is called *annular* or *ring synechiae* or *seclusio pupillae;* it is of great danger to the eye, since, if unrelieved, it inevitably leads to a secondary angle-closure glaucoma. The aqueous, unable to pass forwards into the anterior chamber, collects behind the iris, which becomes bowed forwards like a sail—a condition which is called *iris bombe.* The anterior chamber from the front is seen to be funnel-shaped, deepest in the centre and shallowest at the periphery. The filtration angle is thus obliterated by the apposition of the iris to the cornea at the periphery where adhesions may eventually form *(peripheral anterior synechiae).* The circulation of the aqueous is therefore obstructed and the ocular tension rises (*see* p. 294).

When the exudate has been more extensive, it may organize across the entire pupillary area, which ultimately becomes filled by a film of opaque fibrous tissue—this condition is called a blocked pupil, or *occlusio pupillae.* If there has been much cyclitis the posterior chamber also fills with exudates which may organize, tying down the iris to the lens capsule; this condition of *total posterior synechia* leads to retraction of the peripheral part of the iris, so that the anterior chamber becomes abnormally deep at the periphery, sometimes deeper than in the centre.

In the worst *cases* of *plastic iridocyclitis,* a cyclitic membrane may form behind the lens. In young children the condition forms a type of *pseudoglioma [see* Chapter 23). In the later stages, the degenerative changes in the ciliary body prevent it from fulfilling its functions of supplying the eye with intraocular fluid and nutrition. First the vitreous becomes fluid and later the lens becomes opaque. Finally the eye shrinks (*phthisis bulbi,* Fig. 17.6)

During the course of any type of disease affecting the uveal tract, the *intraocular pressure* may be affected. Most frequently a rise of *tension* is seen in the active stages which is determined firstly by the height of the pressure in the widely dilated capillaries and, secondly, by the difficulty *experienced* by the sticky albuminous aqueous in escaping through the filtration channels at the angle of the anterior chamber (*hypertensive iridocyclitis).* In the later stages, when the pupil has been bound down blocking the flow of aqueous from the posterior to the anterior chamber resulting in an iris bomba, a secondary glaucoma may also follow. Finally, if the ciliary body region becomes atrophic, interference with the secretion of aqueous may lead to lowering of the ocular tension and the development of a soft eye, which is an ominous sign.

Repeated attacks of iritis lead to atrophy of the iris, which assumes a dirty grey or brown colour like felt or blotting paper. Red streaks often mark the site of permanently dilated vessels, usual ly newly formed, and therefore not necessarily radial in direction. The pupillary margin is thin and frayed, and the reactions are diminished.

The diagnosis of acute iridocyclitis: Iritis is most frequently mistaken either for conjunctivitis or acute glaucoma. The error of mistaking iritis for acute glaucoma is very

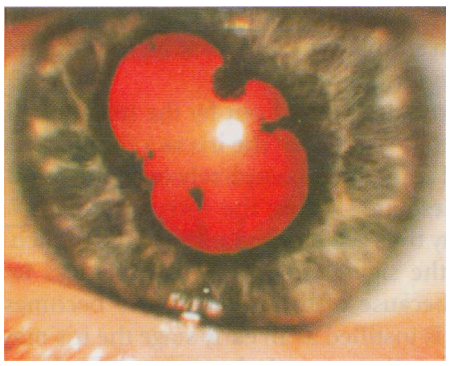


Fig. 17.5 Posterior synechiae with festooned appearance of the pupil on dilatation.

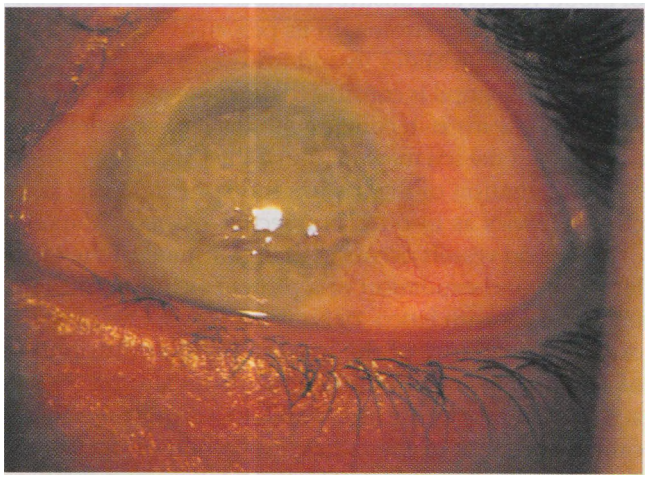


Fig. 17.6 Phthisis bulbi.

serious, particularly because the treatment of the two conditions is diametrically opposite. Dilatation of the pupil, which is urgently necessary in iritis, is the worst possible treatment in acute angle-dosure glaucoma.

Cyclitis

In cyclitis, exudates from the ciliary body pass into the anterior chamber directly from the part which forms a boundary of the chamber (*see* Fig. 1.3), and indirectly by passing forwards through the pupil. The deposition of keratic precipitates on the back of the cornea is a prominent feature, while clouds of dust-like opacities appear in the vitreous. When the exudates organize they not only cause total posterior synechia but also surround the lens and extend throughout the vitreous. Behind the lens they form a transverse or *cyclitic membrane.* Strands of fibrous tissue are formed in the vitreous, which become anchored to the retina in various places, and their subsequent contraction may lead to tractional retinal detachment. The exudates that organize upon the surface of the ciliary body cause destruction of the ciliary processes, diminishing or abolishing the secretion of aqueous. Hence the intraocular pressure falls (*hypotony*) and the eye may even become shrunken and quadrilateral in shape owing to pressure by the rectus muscles—*phthisis bulbi;* thereafter, degenerative changes supervene.

Chronic iridocyclitis deserves special mention because of its insidiousness and the difficulty in its diagnosis. It is an extremely chronic disease characterized by diminution of vision with few physical signs. In severe cases, there is some ciliary congestion, tenderness on pressure over the ciliary region, a deep anterior chamber, keratic precipitates behind the cornea and dust-like opacities in the vitreous. The keratic precipitates, which may be the only obvious evidence of the disease, are sometimes scattered over a triangular area in the lower pan of the cornea (Arlt triangle), due to convection currents in the aqueous and gravitation of the particles towards the bottom of the anterior chamber *(see* Fig. 15.16B). These are more commonly scattered irregularly over the lower part of the cornea as few isolated deposits *(see* Fig. 11.12B). They require detailed careful examination for their discovery and their importance cannot be overestimated. The smaller spots sometimes coalesce forming small plaques, which gradually become translucent. A change in the colour of the iris due to atrophy is an important sign since it may aura a attention immediately especially if the normal eye has a brown iris; it indicates, however, a late stage of the disease.

The vitreous opacities are mainly wandering leucocytes, but many are coagulated fibrin and particles of albuminous exudate. Their mobility in the vitreous shows that this gel has become fluid.

The disease is generally very chronic and liable to exacerbations with the gradual and insidious formation of posterior synechiae. Vision is diminished during the more acute phases and recovers considerably in the intervals, but each recurrent attack leaves a more permanent defect. After many years, the eye may finally become soft and tender and enter into the condition of phthisis bulbi.

An important and not uncommon complication is a rise of intraocular pressure in the course of the disease to constitute the clinical syndrome of *hypertensive iridocyclitic crisis* (of Posner and Schlossman). In this condition the eye may appear normal, but periodically acute or subacute recurrent attacks of raised intraocular pressure occur associated with the presence of an aqueous flare and keratic precipitates. The latter are often so few and unobtrusive as to be seen only on careful examination with the slit-lamp and are of relatively short duration. These attacks, accompanied by the diminution of vision and appearance of halos around lights with headaches, resemble attacks of angle-closure glaucoma so closely that a mistake in diagnosis is often made. The condition is probably due to an accompanying trabeculitis. The diagnosis may depend solely on the detection of one or two keratic precipitates, but its establishment is of utmost importance since, in this condition, treatment with cycloplegics such as atropine and topical corticosteroids rapidly resolves the attack.

Intermediate uveitis

Intermediate uveitis, also known as *chronic posterior cyclitis* or *pars planitis,* essentially affects the pars plana of the ciliary body and the periphery of the choroid. It occurs particularly in children and young adults. Females are more commonly affected than males. Both eyes are affected in 80% of cases. Retinal phlebitis with extravascular leakage into the vitreous and the late development of exudates in the vitreous near the ora serrata is seen. The inflammation is non-specific; the cause is usually unknown.

The onset is insidious and the patient usually presents with complaints of floaters and a deterioration of vision, which occurs due to opacities in the anterior vitreous. Clinical signs include a minimal aqueous flare with occasional keratic precipitates (sometimes termed a 'spill-over' anterior uveitis), anterior vitritis, white snowball-like exudates near the ora serrata, coalescent exudates giving the appearance of a 'snowbank' and mild peripheral periphlebitis. Other features include macular oedema, papillitis or disc oedema, retrolenticular cyclitic membranes, vitreous haemorrhage and, rarely, tractional retinal detachment. The differential diagnosis includes toxoplasmosis, peripheral toxocariasis, syphilis, multiple sclerosis and sarcoidosis. The disease could either resolve spontaneously or have a prolonged course.

However, most cases (80%) do not need any treatment. In chronic cases therapy is disappointing though corticosteroids have a place. Immunosuppressants should only be used in severe cases where steroids have previously failed.

Posterior uveitis

Inflammations of the posterior uvea exhibit the general characteristics of those affecting the anterior part of the uveal tract. They may appear either in the form of isolated foci of inflammation or they may be diffuse. If they are diffuse, the anterior uvea is always involved. It is important to remember that the outer layers of the retina depend upon the choroid for nutrition so that an inflammation of the choroid always involves the former secondarily.

The typical symptoms of posterior uveitis include the presence of 'floaters' with or without a diminution of vision, which is often painless but occasionally accompanied by pain, photophobia and some redness if there is associated involvement of the anterior segment. Signs include detectable inflammatory cells and opacities in the vitreous (vitritis), exudates or infiltration in the retina or choroid, oedema of the retina and choroid, and sheathing of vessels. Other less frequent features include disc oedema, retinal haemorrhages, associated signs of anterior segment inflammation such as posterior synechiae, anterior aqueous flare and cells, i.e. 'spill-over' uveitis. Late changes such as a complicated cataract, glaucoma, retinal detachment or choroidal neovascularization may occur.

Choroiditis, which may be focal, multifocal or diffuse in location, may occur in two clinical forms. As with iridocyclitis, a *granulomatous* form is usually associated with direct organismal infection, the essential feature of which is the occurrence of localized accumulations of chronic inflammatory cells (lymphocytes, plasma cells, etc.) and a non-granulomatous or exudative form. *Non-granulomatous* or exudative choroiditis is a non-specific plastic inflammatory response characterized initially by more acute cellular infiltration (predominantly leucocytes) and much exudation, the aetiology of which is exactly comparable with the similar type of non-granulomatous iridocyclitis.

A recent focus of choroiditis is seen ophthalmoscopically as a yellowish area, and when near a retinal vessel, it is seen to lie at a level deeper than the vessel. This appearance is due to infiltration of the choroid, and the presence of exudates hiding the choroidal vessels which cause the normal red reflex. In the early stages, the membrane of Bruch is intact, and only fluid can pass through it, but this suffices to make the overlying retina cloudy and grey so that the edges are hazy and ill defined. The exudates not only pass into but also through the retina, so that punctate or diffuse opacities are seen in the vitreous.

In the later stages the membrane of Bruch may be destroyed, allowing leucocytes to pass through it into the retina and vitreous. A marked vitreous haze usually indicates ciliary body involvement; while the presence of keratic precipitates on the back of the cornea and inconspicuous posterior synechiae proves that in many cases of apparently localized choroiditis the whole uveal tract is implicated (panuveitis).

Owing to the fibroblastic activity of the choroidal stroma, exudates become organized, and the fibrous tissue formed destroys the normal structures and fuses the choroid and retina firmly together. The colour of the spots gradually changes to white, due partly to the fibrous tissue deposited and partly to thinning and atrophy; thus permitting the white reflex from the sclera to shine through.

The pigment of the retinal pigmentary epithelium is extremely resistant, even though the cells which contain it are destroyed. It tends to heap up into masses, both intra- and extracellular, while the neighbouring pigment cells are stimulated to proliferate. Isolated masses of black pigment are thus formed in the white areas, especially at the edges, so that in the atrophic stage the white areas are surrounded by a black zone of pigment. The process has then reached its natural termination, and these sharply defined areas remain permanently unaltered.

Symptoms in the early stages are mainly defects of vision due to lesions of the retina and clouding of the vitreous. Symptoms are marked when the lesion is in the central area and usually escape observation when in the periphery. The inflamed area is slightly raised, so that the contour of the retina is altered, causing distortion of images and giving rise to an apparent change in the size of the objects seen—*metamorphopsia.* Thus, straight lines appear to be wavy, objects appear smaller than they are—*micropsia;* sometimes larger—*macropsia,* due to separation or crowding together, respectively, of the rods and cones. Subjective flashes of light due to retinal irritability *(photopsia)* are also seen. These subjective symptoms are often accompanied by the perception of a 'black spot' in front of the eye, corresponding to the lesion—a *positive scotoma.*

In the later stages, the affected areas are incapable of giving rise to visual impulses so that *negative scotomata* are present in the field of vision. There is a hiatus in the field of vision similar to the normal blind spot. The importance of negative scotomata depends upon their location. Peripheral scotomata may pass unnoticed, but a central scotoma destroys vision; though peripheral vision still permits the patient to get about, all fine work is impossible.

The disease is chronic and organization of the exudates takes several weeks. The occurrence of fresh spots may extend the acute stage over a period of months, and the ultimate defects are permanent. The condition is often bilateral.

Choroiditis is usually classified according to the number and location of the areas involved.

Disseminated or diffuse choroiditis: It is diagnosed when small areas of inflammation are scattered over a greater part of the fundus behind the equator. In milder cases, only a few spots are formed and the exudates in the vitreous become absorbed. In more severe cases, the spots are numerous, fresh foci arising and passing through the stages described above, until finally the entire fundus may be covered with atrophic areas. Vitreous changes increase, and finally the nutrition of the lens suffers and a complicated cataract results. Owing to the transience of the acute stage the atrophic stage is seen more frequently under observation. Such a condition may be due to syphilis, but in many cases the cause is obscure.

Multifocal choroiditis: It has fewer and more discrete foci. When confined to the peripheral part of the fundus, it may also be termed as anterior choroiditis. It is frequently symptomless and discovered only on routine examination. Late atrophic changes should be clearly distinguished from those found in high myopes and in old people as a part of senile degeneration.

Central choroiditis: This affects the posterior pole or macular region. It may occur as part of disseminated choroiditis, or can occur alone.

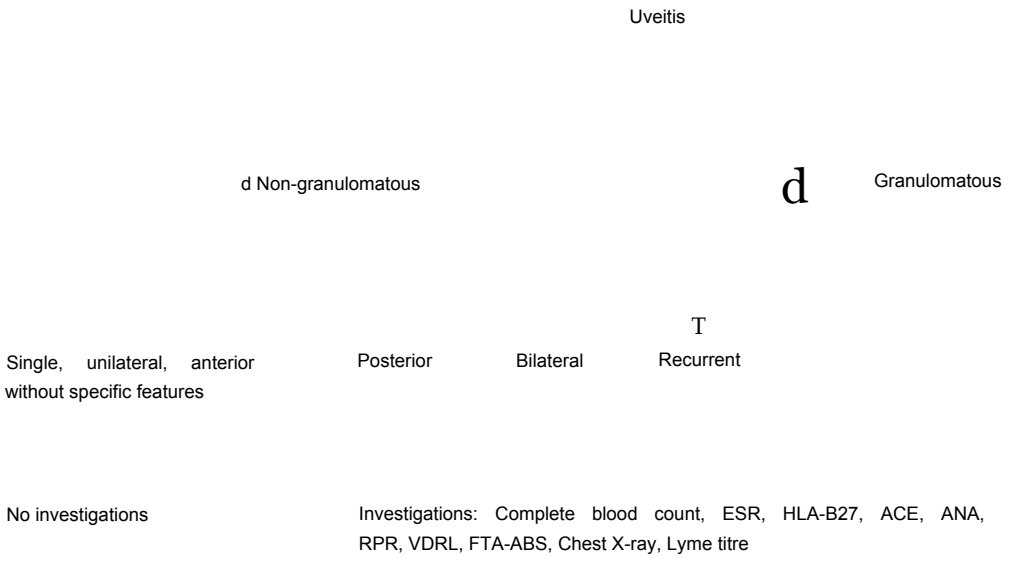
Juxtapapillary choroiditis (of Jensen): Usually oval in shape, this type occurs in young persons as an exudation close to and about the same size as the disc. The exudates may cover the retinal vessels, and there are vitreous opacities and sometimes keratic precipitates. There is generally a sector-shaped defect in the field of vision. The cause is usually obscure. The inflammation slowly subsides, leaving a patch of atrophy, but recurrence may take place.

ROUTINE INVESTIGATION OF UVEITIS

A limited number of known aetiological factors account for a considerable proportion of cases of uveitis and the problem frequently arises as to which initial investigations in conjunction with the clinical findings are justifiable and likely to help in making a definitive diagnosis. A careful history and detailed ocular examination is important; these include checking of the intraocular pressure and examination of the fundus after dilating the pupils. The generally accepted approach for ordering investigations is detailed in Flowchart 17.1. Essentially, the investigations are tailored according to the disease suspected on clinical examination (Table 17.3).

The general treatment of uveitis

In *anterior uveitis,* dilatation of the pupil and relaxation of the ciliary muscle with cycloplegics such as atropine 1% drops or ointment twice or thrice daily, warm compresses, and the control of the acute phases of inflammation with steroids, are the essentials of local treatment. In milder cases weaker, short-acting agents such as cyclopentolate 1% thrice daily or homatropine 2% thrice daily may be used.



Flowchart 17.1 Investigations in a case of uveitis based on clinical presentation.

Table 17.3 Investigations of patients with different types of uveitis

Type of uveitis	Possible aetiology	Investigations
Acute anterior	Idiopathic	
	Seronegative spondyloarthropathies (ankylosing spondylitis, Reiter disease)	Urine for WBCs, X-ray of sacroiliac joints. ESR, C-reactive protein, HLA-typing
	Sarcoidosis	Chest X-ray, Mantoux test, serum ACE
	Secondary syphilis	Serological tests
Chronic anterior	Heterochromic uveitis	Gonioscopy
	Juvenile chronic arthritis	Antinuclear antibody
Acute posterior	Toxoplasmosis	Serology if appearance is equivocal
Chronic posterior	Pars planitis	None of value
	Toxocariasis	Eosinophil count, skin test, serum IgE

ACE, angiotensin-converting enzyme; ESR, erythrocyte sedimentation rate.

1. Cycloplegics act in three ways: (i) by keeping the iris and ciliary body at rest; (ii) by diminishing hyperaemia and (iii) by preventing the formation of posterior synechiae and breaking any that have already formed. When the pupil is well dilated, the frequency of instillation is reduced over 10-14 days and then discontinued. A very powerful mydriatic effect is also obtained by the subconjunctival injection of 0.3 ml of mydricaine, a mixture of atropine, procaine and adrenaline.
2. Corticosteroids (*see* p. 151), usually administered topically as drops or ointment or as subconjunctival injections, are of great value in controlling the inflammation in the acute phase. Potent corticosteroids such as betamethasone, dexamethasone and prednisolone are used in full strength initially. As the inflammation subsides they can be given in a 1:10 dilution or with fluorometholone or medrysone drops, which are less likely to raise the intraocular pressure. If the uveitis is severe and is not responding well to frequent topical steroids then periocular repository steroids (e.g. 40-80 mg methylprednisolone or triamcinolone) can be injected in the sub-Tenon space. Ideally, before injecting depot steroids periocularly, it is wise to use full strength topical steroids for 6 weeks to ensure that the patient is not a steroid responder (i.e. develops a substantial elevation of intraocular pressure following topical steroid use). Occasionally the results are dramatic and the eye becomes white with great rapidity but sometimes improvement is slow and systemic steroid therapy is required.

   Common indications for systemic steroid therapy include a severe uveitis, or where there is no improvement on maximal topical and repository steroids. The systemic administration of corticosteroids cuts short an attack and hastens healing.
3. Hot applications are extremely soothing to the patient and help to reduce the pain. They are of therapeutic value in increasing the circulation.
4. Aspirin is very useful in relieving pain, but if the pain is intense, stronger preparations may be indicated. In the convalescent stage, dark glasses should be worn.
5. Systemic immunosuppressives or immune-modulating agents such as methotrexate, cyclophosphamide and cyclosporin may be needed in some cases which do not respond to conventional steroid therapy. These agents should be administered in conjunction with an internist or rheumatologist.
6. Specific treatment directed to the underlying disease needs to be added in cases where the exact aetiology is identified. For example, in Reiter syndrome if urethritis is present, the patient and sexual partners are treated for chlamydial infection (tetracycline 250-500 mg 6 hourly, doxycycline 100 mg 12 hourly or erythromycin 250-500 mg 6 hourly for 3 - 6 weeks). Lens-induced uveitis requires removal of the lens. Behcet syndrome often needs systemic steroids and immunosuppressives, and responds well to chlorambucil. Syphilis is treated with penicillin and tuberculosis with standard antitubercular therapy (isoniazid, rifampicin, ethambutol and pyrazinamide).

The treatment of *choroiditis* is unsatisfactory since the retina is grossly damaged before the condition can be controlled.

Treatment of sequelae and complications

Secondary glaucoma is one of the serious complications of iridocyclitis. If it develops before posterior or peripheral synechiae form, the most effective treatment is to intensify atropinization and use corticosteroids to allay the

inflammatory congestion. Corticosteroids, aqueous suppressants such as beta-blockers administered topically, and acetazolamide given systemically are frequently very useful in such cases. Pilocarpine and latanoprost are contraindicated as uveitis maybe exacerbated.

A laser iridotomy is essential in all cases with annular synechiae to restore communication between the posterior and anterior chambers and thus avoid the supervention of secondary glaucoma. All such procedures, however, must be avoided during an acute attack of iritis since the traumatic iritis set up will frustrate the aim of the operation by filling the opening with exudates. It is best, if possible, to forestall a ring synechia by performing the iridectomy, during a quiescent interval, before the adhesion extends round the entire circle.

Other complications include cataract, band keratopathy and cystoid macular oedema. Cataract can be removed surgically after the uveitis has been quiescent for at least 2-3 months. Band keratopathy can be treated with excimer laser photoablation (phototherapeutic keratectomy or PTK) or removed mechanically by chelating with sodium EDTA. Cystoid macular oedema resolves spontaneously but recovery can be hastened by treatment with oral prednisolone and acetazolamide (Diamox).

PURULENT UVEITIS, ENDOPHTHALMITIS AND PANOPHTHALMITIS

Exogenous

Purulent exogenous uveitis is generally caused by infected wounds, whether accidental or the result of operations (such as cataract or glaucoma surgery) or corneal ulcers. In the case of ulcers and when the penetrating wound is corneal, the inflammation may remain as an anterior uveitis if the infection is not virulent or if it is controlled by treatment, but the usual tendency is for the whole eye to be eventually involved in a *panophthalmitis.* In deeper injuries the vitreous is usually affected first (*endophthalmitis*); organisms grow readily in it as in a culture medium, and purulent cyclitis, retinitis and choroiditis develop. Endophthalmitis is defined as an intraocular inflammation which predominantly affects the inner spaces of the eye and their contents, i.e. the vitreous and/or the anterior chamber.

Organisms responsible for bacterial endophthalmitis include pneumococci, staphylococci (both S. *aureus* and *S. epidermidis),* streptococci, *Escherichia coli, Pseudomonas pyocyanea, Bacillus cereus* and *subtilis,* and *Clostridium welchii* (Table 17.4). The anaerobe *Propionibacterium acnes* should not be overlooked as a cause. *Fungal endophthalmitis* may occur after intraocular surgery or injury with vegetable matter such as a thorn or wooden stick. Fungal endophthalmitis has an incubation period of several weeks and predominantly affects the anterior vitreous and anterior uvea with the formation of a hypopyon. The vitreous becomes a granuloma and the pupils become occluded with inflammatory material.

Table 17.4 Common organisms causing endophthalmitis

Exogenous endophthalmitis
Acute postoperative (one to several days after surgery)
Staphylococcus epidermidis
Staphylococcus aureus, Streptococcus spp.
Gram-negative bacteria *(Pseudomonas* spp., *Proteus* spp., *Haemophilus influenzae, Klebsiella* spp., *Escherichia coli, Bacillus* spp., *Enterobacter* spp.) and anaerobes
Delayed-onset postoperative (a week to a month or more after surgery)
Fungi: *Aspergillus, Fusarium, Candida, Cephalosporium, Penicillium*
Bacteria: *Propionibacterium acnes,* and any bacteria infecting a thin filtering bleb (often streptococci), vitreous wick or after partial suppression with antibiotics during or after surgery
Post-traumatic
Bacillus spp., *S. epidermidis,* fungi (often *Fusarium), streptococcus* spp. and others. Mixed flora are common.
Endogenous endophthalmitis
Bacillus cereus (especially in intravenous drug abusers), streptococci, *Neisseria meningitides, Staphylococcus aureus, Haemophilus influenzae)* among bacteria, *Mucor* and *Candida* among fungi

Delayed onset exogenous endophthalmitis can occur after cataract surgery or glaucoma-filtering surgery with thin filtering blebs following use of antifibroblastic agents. Fungal infection and *Propionibacterium acnes* are the most likely organisms in endophthalmitis occurring several weeks or months after cataract surgery.

Endogenous

The endogenous form of purulent uveitis is metastatic in origin. Such cases are seen as a complication of the exanthematous illnesses such as meningococcal septicaemia and in immunosuppressed patients such as those receiving corticosteroids or immunosuppressives, or those with acquired immune deficiency syndrome. The infection may be bacterial, fungal or viral. Mucormycosis extends directly from the nasopharynx in debilitated individuals with diabetic ketoacidosis.

Clinical features

The cardinal features of *endophthalmitis* are pain, swelling of the lid and decrease in vision. A high index of suspicion, particularly in postoperative cases, is important. In differentiating endophthalmitis from postoperative 'sterile' inflammation, pain and a marked diminution of vision favour the possibility of infection. In case of doubt, careful observation over the next 6-8 hours will show rapid worsening if infection is the cause.

In both endogenous and exogenous endophthalmitis there may be a rise in temperature, headache and sometimes vomiting, but fever is more common with endogenous infection. Systemic features appear late in the course of exogenous infection and are usually indicative of the infection spreading outside the eyeball, i.e. a panophthalmitis, possibly even progressing to an orbital cellulitis. In the exogenous form, the edges of the wound become yellow and necrotic, a hypopyon appears (Fig. 17.7), there is severe chemosis with intense ciliary and conjunctival congestion, and the lids are swollen and red. There is severe pain in the eye. The vitreous becomes purulent (endophthalmitis), as shown by a yellow reflex with oblique illumination. The anterior chamber soon becomes full of pus and the cornea cloudy and yellow; ring infiltration and corneal melting may occur. There may be proptosis and painful limitation of movement of the globe due to extension of the inflammation to Tenon's capsule (panophthalmitis). If not adequately treated in time, the infection may spread further leading to orbital cellulitis and subsequently even cavernous sinus thrombosis.

In metastatic cases, ophthalmoscopic examination shows that the media are hazy, the yellow oedematous retina is only dimly seen; and there is a yellow reflex. There is formation of a hypopyon and rapid failure of vision.

In severe cases the inflammation gives rise to the widespread formation of cyclitic membranes, destruction of the ciliary processes and a fall in the ocular pressure resulting in shrinkage of the globe. In the most severe cases and when the infection is allowed to take its natural course, the pus bursts through the walls of the globe, usually just behind the limbus; thereupon the pain subsides and after prolonged suppuration the eyeball shrinks. The condition is not likely to set up sympathetic ophthalmitis.

A detailed history, ocular examination and ultrasonography are required to confirm the clinical diagnosis by demonstrating exudates in the vitreous in patients with very hazy media. A vitreous tap or biopsy needs to be performed and the aspirate examined by Gram and Giemsa staining of smears, and specimens sent for bacterial and fungal cultures. A complete and differential blood count with assessment of fasting blood glucose and serum electrolytes may also be considered before starting systemic antibiotics.

Anterior chamber and vitreous taps should be performed at once and samples inoculated directly onto blood and chocolate agar plates, Sabouraud medium for fungi and thioglycolate for anaerobes. After a vitreous tap, a single injection of antibiotics with or without dexamethasone is given into the vitreous cavity.

Treatment

To achieve the best results it is essential to treat all cases empirically on the basis of smear examination with a suitable combination of broad spectrum antibiotics and corticosteroids from the beginning. In the majority of cases exact bacteriological diagnosis is not possible and treatment must be empirical. The cardinal prerequisite to successful therapy is a suitable selection of antibiotics, which cover all eventualities. Every possible route of administration should be used to maintain a high intraocular concentration of antibiotics throughout treatment. Cephalosporins or vancomycin with gentamicin or amikacin are recommended.



Fig. 17.7 Endophthalmitis.

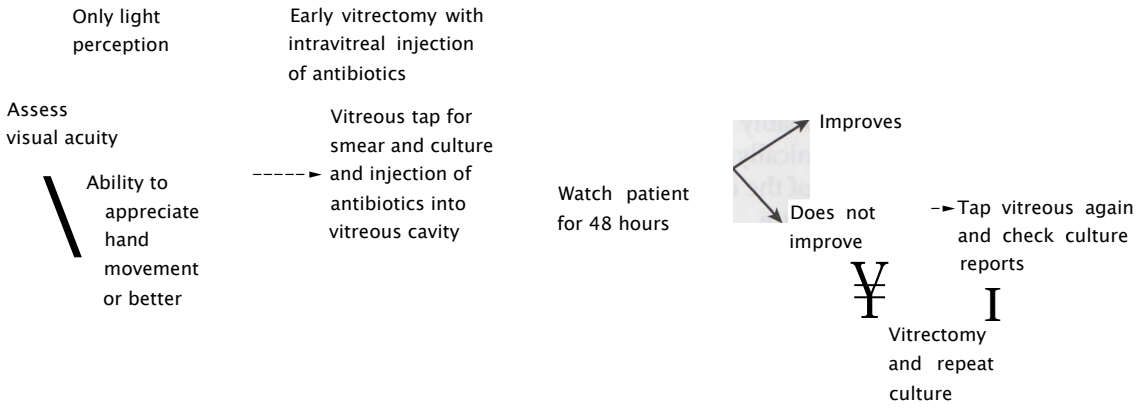
Some authorities recommend the combined use of corticosteroids from the outset (unless there is a strong clinical suspicion of a fungal aetiology in which case steroids should be withheld), while others prefer to wait for a confirmed positive clinical response to antibiotic therapy before administering steroids over the next 24-48 hours. The rationale for corticosteroid therapy derives from its anti-inflammatory effects, especially control of the polymorphonuclear reaction leading to preservation of the ocular structures.

Therapeutic regimen

Commonly used *topical antibiotics* are fortified cefazolin (5%) or vancomycin (5%) with gentamicin or amikacin (1.3%) 1 hourly, alternating every half hour *(seep.* 197, Table 15.2 for preparation of fortified antibiotics).

Cycloplegia is achieved initially with topical atropine 1 % twice a day substituted by short-acting agents after 3-4 days.

Intravitreal antibiotics are the treatment of choice and are injected after taking a 0.2-0.3 ml vitreous aspirate for preparing smears and obtaining cultures. A combination of amikacin (0.4 mg in 0.1 ml) or gentamicin (0.4 mg in 0.1 ml) and ceftriaxone (2 mg in 0.1 ml) or vancomycin (1.0 mg in 0.1ml) is generally recommended. Simultaneous injection of dexamethasone 0.4 mg in 0.1 ml is optional.



Flowchart 17.2 Approach to management of a case of endophthalmitis.

Based on the results of the Endophthalmitis Vitrectomy Study (EVS) Group. Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis (*Arch Ophthalmol* 1995; 113:1479–96).

The subconjunctival route of administration of antibiotics is controversial and not frequently used, as adequate intraocular levels are achieved with intensive fortified topical antibiotics administered round-the-clock if required. The dosages are: amikacin 25 mg in 0.5 ml, ceftriaxone 100 mg in 0.5 ml, vancomycin 25 mg in 0.5 ml and dexamethasone 6 mg in 0.25 ml (*see* p. 147).

Immediate *pars plana vitrectomy* is beneficial if the visual acuity on presentation is light perception or worse, or if the patient does not respond to intravitreal antibiotics within 48hours (Flowchart 17.2).

Recovery from bacterial and fungal endophthalmitis is hastened by the removal of infected vitreous (vitrectomy) and the introduction of intravitreal antibiotics. The optimum time for vitrectomy is 24 hours after intravitreal injection of antibiotics if there is no improvement. However, if there is a vitreous abscess seen on initial examination or a fungal infection is suspected, vitrectomy should be undertaken immediately.

Monitoring the clinical course: Patients need to be reviewed every 4-8 hours. The antibiotic regimen is modified according to the patient's response and the culture and sensitivity reports. If the patient responds well to treatment, the frequency of topical fortified antibiotics may be slowly tapered off after 48 hours. The visual outcome in such cases is influenced by the duraucn\ between. tbe omet of infection and institution of therapy, and the nature of the infecting organism.

Cases suspected to be of fungal aetiology should have intravitreal injection of amphotericin B (5 (xg in 0.1 ml) without the use of any adjunctive steroids. Systemic (intravenous) and topical fortified antibiotics are given; but a vitrectomy is often required. If positive cultures are obtained, additional oral antifungal agents (fluconazole, ketoconazole or amphotericin B) should be given.

As soon as it is evident that the eye cannot be saved and is completely blind with no light perception, it should be eviscerated, especially if signs suggestive of panophthalmitis develop (*see* p. 235). In most cases a *frill excision,* whereby a collar of sclera is left around the optic nerve, can be carried out. This allows more rapid healing than an evisceration and also prevents the spread of infection up the optic nerve sheath which might give rise to meningitis.

SPECIFIC TYPES OF UVEITIS

The more *important* types of uveitis associated with specific infections are discussed below.

Bacterial uveitis

Tuberculosis

Tuberculosis may affect any part of the uveal tract. T-cell activity is of significance in *tuberculous* infection. The ingestion of bacilli by macrophages is a major factor in limiting the spread of infection. However, in patients who have had a previous tuberculous infection, the cell-mediated response is also associated with tissue damage due to the direct effect of sensitized T lymphocytes on cells containing the **invested bacilli.**

Tuberculous iritis: The metastatic *granulomatous type* occurs in a miliary and a conglomerate or solitary form. In the *miliary type* there is a small yellowish-white nodule surrounded by numerous smaller *satellites,* usually situated near the pupillary or ciliary margin. This syndrome develops in severely debilitated patients with impaired immunological responsiveness and if there has been massive dissemination of bacilli. In the *conglomerate*

form there is a larger yellowish-white tumour, although smaller satellites may be present; the nodules contain giant cells.

An *exudative non-granulomatous type of iritis* may also occur in tuberculosis, which is probably allergic or immuno-inflammatory in nature. Clinically there is little to distinguish it from other forms of the disease. It is usually recurrent or very chronic in nature.

Tuberculous choroiditis occurs in acute miliary and chronic forms of the disease. It can either manifest as choroidal tubercles (approximately 0.3-3.Omm) or as tuberculomas which appear as a single large subretin al choroidal mass, often more than two disc diameters in size. Miliary tubercles are found in acute miliary tuberculosis, especially tuberculous meningitis, usually as a late event. Ophthalmoscopically, they appear as three or four round, pale yellow spots, usually near the disc, although any part of the choroid may be affected. They afford the most important diagnostic evidence of tuberculosis in cases of meningitis and obscure general disease. Microscopically, they consist of typical giant cell systems, containing a variable number of tubercle bacilli. Until the introduction of chemotherapy, miliary tuberculosis of the choroid was usually a prelude to death, whereas now recovery is common.

The differential diagnosis includes sarcoidosis, Behget syndrome, leprosy, syphilis, cat-scratch disease, leptospirosis and brucellosis.

The Mantoux dermal reaction is generally used for diagnosis. A positive result is of some value in children, but does not prove that the ocular condition is tuberculous. A negative result, however, makes the diagnosis of allergic tuberculosis unlikely. Anergy to tuberculoprotein occurs in patients suffering from sarcoidosis, Hodgkin disease and other immune deficiency states. The Mantoux test is, however, only a presumptive test, as are a chest X-ray and therapeutic trial with isoniazid. Definitive diagnostic tests are direct demonstration of *M. tuberculosis* on histopathological examination, cultures or polymerase chain reaction (PCR) on samples obtained from the ocular tissues.

Treatment: Rifampicin with isoniazid, ethambutol and pyrazinamide, i.e. a four-drug regimen is prescribed. Ethambutol and pyrazinamide are stopped after 2 months and the other drugs are continued for 6 months. Ethambutol may impair vision leading to a decrease in visual acuity, blurring and red-green colour blindness. Patients should be warned about possible visual symptoms and, if any are noticed, ocular examination should be undertaken. Visual symptoms or optic neuropathy are rare if the dosage of ethambutol is less than 15 mg/kg/day and more likely if the dose exceeds 25 mg/kg/day. As soon as symptoms of toxic optic neuropathy develop, the drug should be stopped; vision generally returns slowly.

Leprosy

Leprosy (Hansen disease) is caused by the acid-fast bacillus *Mycobacterium leprae,* similar to the agent that causes tuberculosis. There are about 11 million cases throughout the world, and about one-third have complications relating to the eye. The infection predominantly involves the skin, superficial nerves, nose and throat. It occurs as two principal types: (i) the lepromatous (cutaneous) type, with depressed cellular immunity and frequently with direct ocular involvement; and (ii) the tuberculoid (neural) type, with systemic resistance and good cell-mediated immunity. Ocular involvement is indirect, caused by complications resulting from neuroparalytic and neurotrophic keratopathy (*see* p. 213). The eyes can also be involved in the lepra reactions (Types I and II).

The eyes are usually involved late in the lepromatous type of disease. There may be an initial superficial infection with conjunctivitis, episcleritis, or keratitis followed by uveitis. Visual loss arises because of corneal and lens opacities associated with small, non-reacting pupils and atrophy of the iris. In patients with lepromatous leprosy the tissues are laden with leprosy bacilli. Skin papules containing antigen-antibody complexes, to which the term erythema nodosum leprosum has been given, are formed and the iridocyclitis present may be another manifestation of immune complex deposition.

In contrast to the lepromatous form, uveitis is rare in tuberculoid leprosy and, when it occurs, it may represent an extension of the more frequent corneal involvement or due to the spread of infection along the ciliary nerves. Bacilli are scanty, antibody formation inconspicuous and the tissue lesions are characterized by multiple granulomata, which may develop around peripheral nerves producing neuroparalytic lagophthalmos and severe exposure keratopathy because of involvement of the facial nerve. Neurotrophic keratopathy may develop in a cornea that has lost its protective mechanisms through involvement of the trigeminal nerve.

In the treatment of leprosy in adults, dapsone, a member of the sulphone group, in a daily dose of 50-100 mg is the drug of choice. Rifampicin, ofloxacin, clofazimine and minocycline are used in various regimens in combination with dapsone.

Brucellosis

Also called Lyme disease; undulant fever; Malta fever; melitensis, infection by *Brucella* (*abortus, suis* or *melitensis)* is widespread throughout the world and the eye is one of the many sites that may be affected. Initially there is an acute phase of generalized systemic infection followed by a chronic phase characterized by intermittent bouts of low fever, during which ocular manifestations occur late. Keratitis and optic neuritis are rare, while a uveitis of a chronic granulomatous nature is more common. The disease is

prone to relapse and diagnosis can only be suggested following the exclusion of other forms of chronic iridocyclitis or choroiditis by an agglutination test, a cutaneous test, or an opsonocytophagic test. Treatment, apart from the usual measures, is by the sulphonamides or chlortetracycline.

Whipple disease

This is a rare disease worth mentioning, as specific treatment is available if it is correctly diagnosed. It is caused by infection by a bacterial organism which has been demonstrated histologically in all tissues of the body with the exception of bone, but has not yet been cultured, and an underlying inherent inability of the host's immune defence system to eliminate the infection. The disease is characterized by recurrent episodes of inflammation affecting any system of the body with leucocytosis and clinical response to antibiotics. Ocular inflammation can manifest as corneal infiltrates, anterior uveitis, vitritis with characteristic whitish opacities in the vitreous shaped like mulberries, vasculitis, retinitis and disc oedema. Supportive evidence is in the form of elevated white blood cell counts and a thickened jejunal mucosa on radiological investigation. Definitive diagnosis is by jejunal biopsy.

Spirochaetal uveitis

Syphilis

Syphilis may attack any part of the uveal tract. The clinical manifestations of the infection are protean and are partly due to direct organismal invasion and partly due to modulation of the immune system of the host, mainly cell-mediated immunity and possibly humoral immunity as well. The eyes can be affected in any stage of syphilis in various ways affecting the conjunctiva, cornea, sclera, uvea, optic nerve and central nervous system *(see* Chapter 31) and the disease has been recognized to be a great 'masquerader'. Penicillin did control the rampant prevalence of this infection in the past, but the incidence of the disease has shown a dramatic increase in recent years in concurrence with human immunodeficiency virus (HIV) infection. Not only is it recommended that tests for both HIV and syphilis be performed if either is found to be positive, but it is also recommended that a high index of suspicion be maintained in high-risk cases because unusual clinical signs are noticed in those with concurrent HIV infection; the disease has a more fulminant course and is slower to respond to treatment.

Syphilitic iritis: This manifests itself in two forms. A non-specific *iritis* or *iridocyclitis*, which can be granulomatous or non-granulomatous, occurs typically in the secondary stage of the disease, soon after the skin eruptions, usually within the first year after infection, but not before the third month. In light-coloured irides, prominently dilated iris vessels termed *roseola*, possibly due to treponemal emboli causing local vascular obstruction, dilatation and tortuosity have been noted to be a distinctive feature. Posterior synechiae form between the iris and the lens. The iritis lasts for 2-8 weeks and does not usually recur. In the absence of early antisyphilitic treatment it is seen in at least 3-4% of syphilitics, usually males, and is generally unilateral, but the fellow eye may become affected later. *Treponema pallidum* has been found in the aqueous.

A 'plastic' iritis also occurs in congenital syphilis, usually as an accompaniment of interstitial keratitis *(see* p. 205). It also occurs in very young babies with congenital syphilis without any corneal complication, but usually with large nodules or gummata on the iris.

Finally, an acute 'plastic' iritis may occur as a *Jarisch-Herxheimer reaction* 24-48 hours after the first therapeutic dose of penicillin, probably due to the flooding of the system with treponemal toxins.

Gummatous iritis: occurs late in the secondary or rarely during the tertiary stage, and is characterized by the formation of yellowish-red, heavily vascularized nodules near the pupillary and ciliary borders of the iris, but not in the intermediate region; they are usually multiple, vary in size from that of a pinhead upwards and are generally associated with much exudation and broad synechiae.

Syphilitic choroiditis and chorioretinitis: This may occur as disseminated choroiditis, peripheral choroiditis, diffuse chorioretinitis, pseudoretinitis pigmentosa, neuroretinitis, big blind spot syndrome, exudative maculopathy, uveal effusion, vasculitis, central retinal vein occlusion, retinal necrosis and, in HIV-infected individuals, lesions resembling placoid pigment epitheliopathy and atypical serpiginous choroidopathy. Vitritis is common and severe.

The *differential diagnosis* of syphilitic uveitis is tuberculosis, sarcoidosis, autoimmune uveitis, serpiginous choroidopathy and acute posterior placoid pigment epitheliopathy.

The diagnosis of syphilis can be established either by (i) direct demonstration of the organism with darkfield microscopy or using direct fluorescent antibody with high specificity but low sensitivity or (ii) serological tests. For ocular lesions the former are cumbersome and impractical and serological tests are mainly used. The serological tests are also classified into two broad categories based on whether they detect antibody to lecithin or cardiolipin which is a cholesterol antigen and are hence non-treponemal [such as the Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests], or whether they detect antibodies specifically against treponemal *antigens* [such as fluorescent treponemal antibody absorption (FTA-ABS) tests and treponemal haemagglutination (THA) tests]. The non-treponemal tests have lower specificity, but are useful as screening tests and to monitor response to treatment. They are not known to be useful in detecting late latent

and tertiary syphilis, as false-negative results are common. The treponemal tests are more specific and are used to confirm the diagnosis after a positive screening test result and to detect late latent and tertiary syphilis. It is mandatory in any case of ocular syphilis with a positive serological test to look for evidence of neurosyphilis by CSF examination. CSF leucocytosis with elevated protein concentration and a positive CSF-VDRL test are considered confirmatory evidence of neurosyphilis. Patients with concurrent HIV infection can be a diagnostic challenge as, in such cases, both types of serological tests can be unreliable.

Treatment: Penicillin is used to treat all stages of syphilis. Those with early syphilis, i.e. primary, secondary or latent syphilis of less than 1-year duration are treated with a single intramuscular injection of benzathine penicillin G or benzyl penicillin. Immunocompetent individuals with syphilis of more than 1-year duration are treated with intramuscular injections of benzathine penicillin G weekly for 3 weeks. All patients with ocular syphilis should be investigated for neurosyphilis and, if affected, must be treated with neurosyphilitic therapeutic doses, i.e. intravenous aqueous penicillin G 2-3 mega units every 4hours for 14 days. Congenital syphilis is treated with aqueous penicillin G or procaine penicillin G for 14 days. It must be remembered that syphilitic infection is more severe and has a faster progression in patients known to be HIV infected.

Leptospirosis

Infection with the spirochaete *Leptospira* occurs by contact or ingestion of water contaminated with the urine of infected domestic and wild animals such as cattle, pigs, dogs and rodents, which are the natural hosts; human beings act as accidental hosts. People in developing countries who swim, bathe or work in contaminated water, veterinarians and farmers are at high risk for contracting this infection.

Non-specific constitutional symptoms of headache, fever and malaise are common. Uveitis occurs in up to 10% of cases and is often associated with a hypopyon. Diagnosis is by antileptospira antibody tests on blood and culture of live organisms. Treatment is with topical steroids and cycloplegics in conjunction with intravenous penicillin in severe infections and oral doxycycline in milder cases.

Viral uveitis

Important viral infections that cause chorioretinitis or retinitis include cytomegalovirus, herpesviruses, rubeola, rubella, influenza A, Epstein-Barr, and herpes B virus from monkey bites or scratches.

Acute retinal necrosis

Acute retinal necrosis (ARN) is a severe posterior uveitis caused by infection with the varicella zoster virus or herpes simplex viruses (both I and II). *Progressive outer retinal necrosis* (PORN) is a specific clinical entity caused by the same viruses. It is seen in patients who are immunocompromised due to the acquired immune deficiency syndrome (AIDS) or those on immunosuppressive drugs. Herpes zoster has been demonstrated to be responsible, based on electron microscopy and polymerase chain reaction reports. The basic difference between the two is the propensity of PORN to affect the posterior pole and outer retinal layers, the presence of fewer intraocular inflammatory signs (vitritis, retinitis, vasculitis) and a tendency to demonstrate a more fulminant retinal destruction as compared to ARN. ARN tends to start in the periphery and then progresses over days or weeks to other areas and involves the full thickness of the retina leading to necrosis and rhegmatogenous retinal detachment. The condition is bilateral in 80% and in most cases fellow eye involvement occurs within 3 months. The main differential diagnoses include other infections causing retinitis such as cytomegalovirus, HIV, toxoplasmosis, syphilis, immunological disorders such as Behcet syndrome and malignancies such as ocular large cell lymphoma.

Diagnosis is mainly clinical. A definitive diagnosis can be made with isolation of the varicella zoster virus or herpes simplex virus, seroconversion, histopathological examination of biopsy specimens of the vitreous and retina and testing of ocular fluids such as the vitreous or aqueous by polymerase chain reaction.

Treatment with intravenous acyclovir can arrest the disease and prevent involvement of the fellow eye. Retinal detachment can be surgically corrected by vitreoretinal surgery with silicone oil tamponade.

Cytomegalovirus

Cytomegalovirus is an opportunistic pathogen in immunocompromised individuals and is the most common infection in AIDS. *Cytomegalovirus retinitis* is characterized by greyish patches or scattered white dots with irregular sheathing of adjacent blood vessels and vitreous clouding. There are superimposed haemorrhages followed by healing and retinal atrophy. Cytomegalic viraemia is also common in renal transplant patients but ocular infection, though rare, may produce an acute cytomegalic necrotizing retinitis with irreversible damage and loss of vision. The retina may already be compromised by vascular hypertension. Ganciclovir is effective in controlling this infection, but requires an indefinite maintenance therapy (*see* p. 150). The average rate of survival of AIDS patients after the initial diagnosis of cytomegalovirus retinitis is 6 months. Ganciclovir implants (slow-release) can be inserted into the eye by suturing the implant to the sclera and letting it lie suspended in the vitreous cavity.

In children, infantile cytomegalovirus disease may produce severe brain damage with mental deficiency. The ocular lesion varies from an isolated central retinal lesion to a chorioretinitis with much disorganization of the globe.

Acquired immune deficiency syndrome

This syndrome has protean manifestations which are detailed in Chapter 32 on ocular manifestations of systemic disorders.

Chronic iridocyclitis and anterior vitritis, which do not respond to steroid therapy in a drug abuser, should arouse suspicion of HIV infection, and investigation by paracentesis of the anterior chamber should be carried out. Opportunistic infections predominantly produce a retinitis with secondary involvement of the adjacent uveal tissue.

Measles

During the acute phase of infection with the measles virus, visual impairment may be noted with a residual pigmentary retinal disturbance following recovery.

In rare cases, following recovery children develop subacute sclerosing panencephalitis (SSPE) in which there is permanent loss of vision and pigmentary changes in the retina especially in the macular area. This presents as a central neuroretinitis or chorioretinitis several years after the initial attack of measles. It is possible that SSPE is a slow virus infection in which the acute phase of measles is followed by persistence of the virus in the brain and retina causing gradual destruction of the non-replicating neuronal cells.

Fungal uveitis

Exogenous fungal uveitis can be caused by a variety of fungi and is seen after penetrating trauma with vegetable matter or following intraocular surgery. Endogenous fungal uveitis also occurs by haematogenous spread from a focus elsewhere in the body; the clinically relevant varieties are briefly described here.

Fungal uveitis due to *Candida albicans* is an example of infection by an opportunistic non-pathogenic fungus found on the mucous membranes; infection occurs when the immunity is compromised. Chorioretinitis with infiltration into the vitreous may be produced by haematogenous spread from the alimentary tract, although involvement of the external eye is the predominant manifestation. Treatment is with intravenous and intravitreal amphotericin B and pars plana vitrectomy.

Coccidiodes immitis, endemic in Argentina, North Mexico and southern California can produce iridocyclitis and chorioretinitis in those living or travelling in these regions. Diagnosis is established by Papanicolaou staining of ocular fluid aspirates, cultures and serological tests. Treatment is with intravenous amphotericin B.

Histoplasma capsulatum can affect the eye of healthy individuals in a characteristic way termed as *ocular histoplasmosis syndrome* (OHS). In immunocompromised patients it causes either an isolated choroidal granuloma or an endophthalmitis. The diagnosis is made clinically, based on the features detailed below and by histopathological examination of biopsy specimens. Treatment of endophthalmitis or choroidal granuloma is with intravenous amphotericin B.

Ocular histoplasmosis syndrome is endemic in certain areas of North America, particularly the Ohio and Mississippi river basins, but similar lesions have been seen in other countries as well. Epidemiologically this syndrome has been related to *H. capsulatum* infection. Choroidal neovascular membranes or disciform lesions at the macula (Fig. 17.8A and B) accompanied

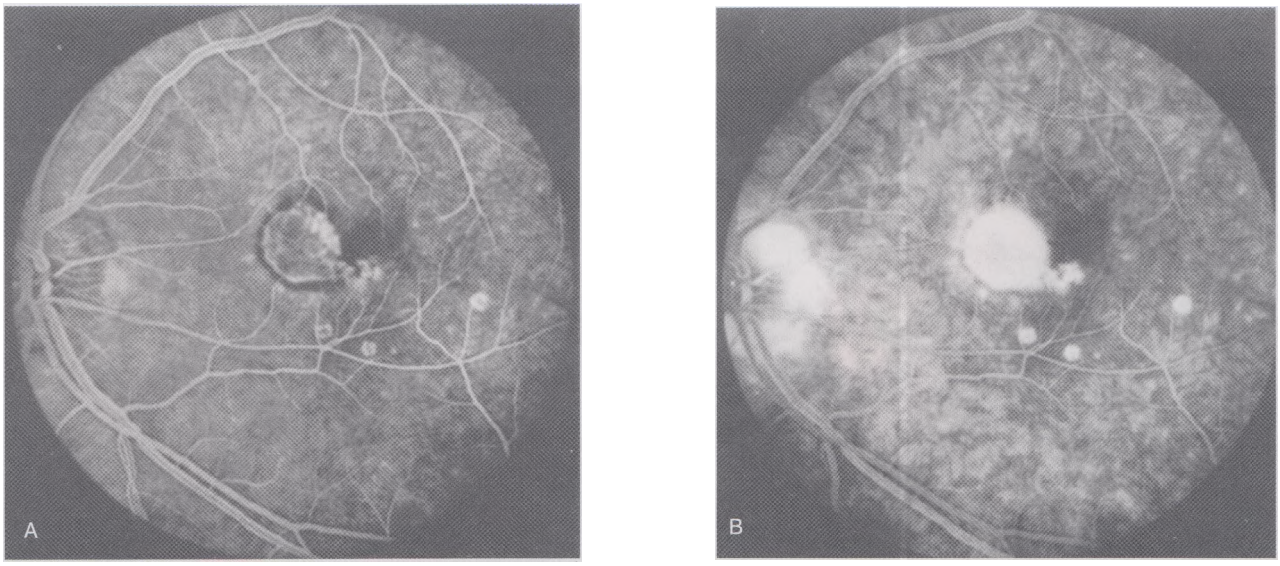


Fig. 17.8 Histoplasmosis of the macula. (A) Early fluorescein angiogram; (B) late fluorescein angiogram.

by well-circumscribed peripheral chorioretinal scars in the absence of inflammatory signs in the aqueous and vitreous, and associated with peripapillary pigment epithelial atrophy, form a characteristic picture. It occurs in the young and carries the risk of bilateral central visual loss.

Asymptomatic choroidal neovascularization membranes or those which do not threaten the peripapillary or macular region can be left to resolve spontaneously. If vision is threatened, argon green or krypton red laser photocoagulative ablation is useful. Treatment of extrafoveal neo-vascular membranes (those with an edge at least 200 away from the centre of the fovea) is most rewarding. Juxtafoveal (1-199 jjum from the foveal centre) membranes are also amenable to laser treatment, but subfoveal membranes have a poor prognosis.

Parasitic uveitis

Toxoplasmosis

This is a protozoan infection derived mainly from cats. The oocysts of *Toxoplasma* affect both the retina and choroid to produce a chorioretinitis. It is probable that in infants the primary site is most often the retina which is involved in association with the brain. As a cause of uveitis, toxoplasmosis probably accounts for 25% of all cases in the UK.

In infants, in whom the infection is acquired transplacentally, the ocular lesion is usually associated with encephalitis, and although almost every tissue of the body may be affected, the retinal picture is characteristic enough to suggest the diagnosis. There are bilateral and frequently multiple chorioretinal lesions in the fundus, the macular area being particularly involved. The entire thickness of the retina and choroid is destroyed in a necrotizing inflammation so that a punched-out, heavily pigmented scar remains. It is probable that this condition is often misdiagnosed as congenital 'colobomata'. This lesion is frequently associated with well-marked meningeal changes. Such infants are usually acutely ill with a history of convulsions and, if they survive, may show hydrocephalus, areas of calcification in the brain and mental retardation.

In adults, toxoplasmosis probably constitutes one of the more common causes of choroiditis (particularly in Europe). The lesion is usually widespread and characterized by severe, recurrent attacks, often at the edge of a previous scar, associated with exudation into the vitreous (Fig. 17.9A and B). Posterior uveitis can be fairly extensive with widespread retinochoroiditis which can be better demonstrated by indocyanine green angiography. Encysted trophozoites are insulated from the lymphoid system but periodic rupture of the cysts releases protozoa which provoke a secondary immunological response. It was earlier believed that all cases of ocular toxoplasmosis were possible examples of congenital infection, but it is now known that ocular infection can be acquired. Pathologically, the characteristic feature is a wide area of necrosis of the retina in which the parasites may be found, either free or encysted. Apart from demonstration of the parasite, diagnosis depends on serological tests [the Sabin-Feldman dye test with a titre greater than 1:16, the complement fixation (CF) test, the indirect haemagglutination (IHA) test and ELISA test for IgG and IgM], Corticosteroids are used in conjunction with sulphatriad (sulphadiazine, sulphathiazole and sulphamerazine) in a dosage of three 500 mg tablets every 6 hours; 100 mg of pyrimethamine is advised twice on the first day and 25 mg daily thereafter. A complete blood count and platelet count must be done once or twice each week. Citrovorum factor (3 mg) or folinic

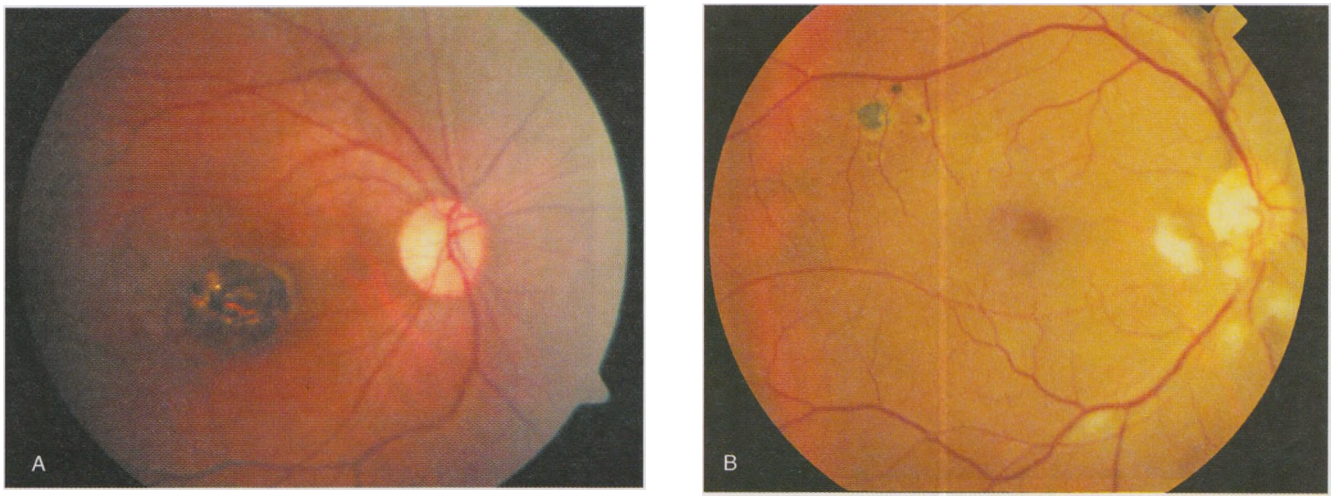


Fig. 17.9 (A) Toxoplasmosis. Central macular scar due to congenital toxoplasmosis. (B) Healed scar of toxoplasmosis with fresh lesions.

acid is necessary weekly. Treatment should be continued for 4-6 weeks.

Alternatively clindamycin and sulphadiazine act synergistically. Clindamycin is given for 4 weeks in oral doses of 300 mg 6 hourly along with sulphadiazine prescribed as an initial loading dose of 2 g followed by 1 g 6 hourly. Another alternative is a combination of trimethoprim/sulphamethoxazole (160 mg/800 mg) twice daily with or without clindamycin and prednisolone. Cycloplegics and topical steroids are used to control any anterior segment inflammation, if present. In any case with suspected toxoplasmosis, systemic corticosteroids should never be used alone without appropriate antimicrobial treatment.

If medical measures fail, photocoagulation may protect a threatened macula.

Onchocerciasis

Onchocerciasis is due to infestation with *Onchocerca volvulus,* a filarial nematode worm. The vector is the blood-sucking black fly *Simulium.* Microfilariae are mobile and may reach the eyes. When alive, they cause little or no reaction, but when dead, they produce focal inflammation with reactive destruction of the tissues.

Punctate or sclerosing keratitis with anterior uveitis is common. It has recently been proposed that an immunological response to the lipopolysaccharide of the cell wall of a bacterium present along with *Onchocerca volvulus* may be the key factor in producing this inflammation. Microfilariae may be seen in the anterior chamber. In the choroid the vessels become attenuated and there is perivascular sheathing. Optic atrophy may occur.

Excision of the worm-containing subcutaneous nodules may help to reduce the infestation, particularly if the nodules are close to the eye. Treatment used to be with diethylcarbamazine which is effective against microfilariae, and suramin, which is active against the adult worm. Patients, however, may suffer a severe adverse reaction if heavily infested and the treatment must last for 2-5 months. Continuous non-pulsed delivery of diethylcarbamazine at a critical low dosage may succeed in killing the microfilariae without exciting inflammatory reactions dangerous to the host. However, due to unacceptable side effects, these two drugs have been replaced with ivermectin. Transmission of *Onchocerca volvulus* may be reduced by efficient larvicidal measures to control the insect vector.

Cysticercosis infestation

Cysticercosis (seen in Africa, Central and South America and South Asia) is an infestation with the larval form of *Cysticercus cellulosae* of the pork tape worm *Taenia solium.* It can produce a violent uveitis presenting as endophthalmitis. The live cysticercus present in the vitreous cavity or located subretinally causes little reaction, but death of the organism releases toxins which produce the inflammation. There is a strong likelihood of accompanying cysticercus infection in the brain and a head CT or MRI scan should be performed.

There is no role for medical treatment of intraocular cysticercosis as violent inflammation following death of the cyst after drug therapy can lead to loss of the eye with phthisis bulbi. Surgical removal of intravitreal and subretinal cyst by vitrectomy is the treatment of choice.

Immunological uveitis

Ankylosing spondylitis and uveitis

Ankylosing spondylitis is a chronic, progressive, pauciarticular (involvement of four or less than four joints) disorder involving the sacroiliac and the posterior intervertebral joints. The onset is insidious with intermittent attacks of arthralgia. Males, in the third decade, are more frequently affected than females. There is a strong association with the HLA-B27 antigen.

Acute, recurrent iridocyclitis is part of the syndrome (25% of patients). The disease lasts 10-20 years and usually burns itself out. Evidence of axial skeletal involvement should be looked for in young males presenting with this ocular disorder.

Reiter disease and uveitis

This syndrome affects young males and is associated with a high incidence of the HLA-B27 antigen. Rheumatic manifestations (pauciarticular pattern usually affecting large joints) occur in 98% of patients, genitourinary in 74%, ophthalmic in 58% and mucocutaneous in 42%. It tends to affect patients who present with non-specific urethritis, postgonococcal urethritis or dysentery. *Chlamydia* have been isolated from the urethral discharge in about 50% of cases. There is an association with dysentery due to *Shigella flexneri* and it is possible that the Shigella antigen may produce an auto-hypersensitivity in patients who have the HLA-B27 antigen. The urethritis associated with Reiter disease requires administration of oral tetracycline in a dosage of 500 mg four times a day. It is also essential that all sexual partners be examined for genital infection.

Ophthalmic involvement is in the form of a recurrent acute iridocyclitis which responds to conventional treatment.

Juvenile chronic arthritis

Juvenile chronic arthritis (JCA, previously termed juvenile rheumatoid arthritis) is defined as chronic arthritis

beginning at below 16 years of age. It encompasses four different subsets of disease which differ in presentation and management, but all four are associated with uveitis in some form.

The subset of JCA which most resembles adult rheumatoid arthritis is in fact the least common. Adolescent females are affected with bilaterally symmetrical polyarticular involvement of the small joints of the hands and feet, associated with a positive rheumatoid factor (RF). Iritis *per se* is not common but is seen as a complication of scleritis, which is a known manifestation. Dry eye is another important ocular problem.

The pauciarticular subset of JCA involves mainly girls 2-6 years of age, who are positive for antinuclear antibody (ANA) and negative for RF. Ocular involvement is common (50% of patients), predominantly manifesting as a bilateral chronic uveitis of insidious onset, often with minimal signs such as mild pain and redness. The disease is chronic, often missed unless specifically looked for, and leads to complications such as glaucoma, cataract, posterior synechiae, pars planitis and band keratopathy.

Another pauciarticular form of JCA is a spondyloarthropathy affecting males over 12 years of age who are positive for the IILA-B27 antigen. This group is affected by an acute unilateral iritis of sudden onset, which is generally self-limited, resolving with treatment in few weeks.

The fourth subset of JCA is Still disease which affects adolescents, more commonly females, and presents with prominent systemic features of high fever, leucocytosis, skin rash, lymphadenopathy, hepatosplenomegaly, arthralgias and a raised ESR. Ocular involvement is uncommon but iritis has been reported to occur.

Behcet syndrome

This is a serious condition with an immunological basis in which severe iridocyclitis, usually characterized by a hypopyon, is associated with evidence of obliterative retinal vasculitis. It is accompanied by ulcerative lesions in the conjunctival, oral and genital mucosae, together with neurological and articular manifestations. It is seen particularly in young adults, and recurs periodically and persistently as extremely severe attacks leading to eventual serious impairment or complete loss of vision. This syndrome belongs to the broad category of connective tissue disorders but is probably of two types: the first associated with herpetiform ulcers in the mouth and the second with aphthous ulcers without evidence of an infective basis. Alternatively, the syndrome may be initiated by a viral infection and perpetuated by autoimmune phenomena. There is a significant association with the HLA-B5 antigen. No specific treatment is known and only non-specific measures are available such as systemic steroids or immunosuppressives, preferably oral administration of chlorambucil 6-8 mg daily for at least 1 year.

Sarcoidosis

Boeck sarcoid is a systemic disease manifested by infiltration of the affected tissue by non-caseating tuberculoid granulomata, which either resolve or are replaced by hyalinized scar tissue. It is frequently complicated by a granulomatous iridocyclitis. Uveitis may present as one of the following:

1. *Acute* iridocyclitis, which is often a presenting sign of sarcoidosis inassociationwithhilarlymphadenopathy and erythema nodosum.
2. *Chronic* iridocyclitis, where multiple discrete granulomata develop in the iris in older individuals; it has a chronic course and poor prognosis.
3. *Posterior uveitis* with choroidal involvement, occasionally associated with granulomata in the retina.
4. *Uveoparotid fever* or *Heerfordt's disease,* which is bilateral and characterized by a simultaneous involvement of the entire uveal tract, parotid gland and frequently the cranial nerves. It appears in young persons between 10 and 30 years of age, commencing with malaise and fever, sometimes accompanied by a skin rash resembling erythema nodosum. Approximately half the cases commence with a granulomatous iridocyclitis and half with a painful swelling of the parotid resembling that due to mumps; subsequently diplopia due to palsy of the ocular motor nerves or facial paralysis is prone to occur. The disease is self-limiting although the iridocyclitis may cause permanent visual damage. The parotid swellings last for 6 weeks to 2 years but ultimately subside.

Other features are sarcoid granulomata which are conjunctival nodules in the lower fornix, calcification of the cornea associated with hypercalcaemia and keratoconjunctivitis sicca.

The diagnosis is made by the presence of other systemic manifestations such as pulmonary changes and areas of rarefaction in the bones. Investigations include a chest X-ray, gallium scan of the head, neck and mediastinum for increased uptake, detection of raised levels of serum angiotensin-converting enzyme (ACE), estimation of serum lysozyme, serum electrophoresis for hypergammaglobulinaemia and biopsy of the skin or conjunctival nodules, palpebral lobe of the lacrimal gland if enlarged, lymph node or lung. Biopsy specimens should be stained with an acid fast as well as a methenamine-silver stain to rule out the differential diagnosis of tuberculosis and possible fungal infection. Patients with sarcoidosis often fail to react to an intradermal injection

of tuberculin indicating a disturbance of immune function. In the Kveim test, the skin of patients with sarcoidosis responds to an injection of a suspension of sarcoid tissue by developing a localized granuloma.

Uveitis associated with vitiligo, poliosis and deafness (Vogt-Koyanagi-Harada syndrome)

This is a rare bilateral condition in Caucasians, but commoner in pigmented races—Asians, Hispanics and Africans. It occurs in young adults. Originally separately categorized as Vogt-Koyanagi syndrome (poliosis, vitiligo, alopecia and chronic anterior uveitis) and Harada disease (bilateral posterior uveitis with exudative detachments and CSF abnormalities such as pleocytosis), the two are now clubbed together as the distinction in clinical pattern is not always present. There is a chronic granulomatous iridocyclitis, with an exudative choroiditis, which often leads to an exudative detachment of the retina. The ocular inflammation is accompanied by a patchy depigmentation of the skin and whitening of the hair, eyebrows and eyelashes (poliosis). The cause is unknown but may be an autoimmune response against melanocytes. Inflammation is controlled with high doses of systemic steroids and, once improvement occurs, gradually tapered over months to years. In case steroids fail to produce an adequate clinical response, or if the patient cannot tolerate their side effects, cytotoxic and immunosuppressive drugs such as cyclophosphamide and cyclosporin may be required.

Sympathetic ophthalmitis

See Chapter 24.

Heterochromic iridocyclitis of Fuchs

This is a low-grade chronic cyclitis, the only apparent features of which are a lightening of the colour of the affected iris and the presence of a few keratic precipitates on the cornea. The latter distinguish the condition from congenital heterochromia. The iris becomes atrophic, loses its markings and readily transilluminates in circumscribed areas, and a cataract frequently develops. The condition is usually said to be associated with some disturbance of the sympathetic nerve supply which controls the chromatophores, accounting for the depigmentation and the tone of the blood vessels. When the blood vessels are dilated, white cells escape and get deposited on the cornea as precipitates. The cataract has a good operative prognosis, but secondary glaucoma may develop *(see* p. 294). During cataract surgery, fine filiform haemorrhage from the opposite angle has been noticed to occur as soon as the anterior chamber is opened—this is referred to as *Amsler sign.*

Geographical choroidopathy

This is a distinct clinical entity of unknown aetiology in which there are acute, recurring, well-defined lesions affecting the pigment epithelium. Though a bilateral disorder, simultaneous onset in both eyes is rare. It is known to occur in all races between the ages of 30 and 70 years. The usual symptom is blurring of vision. The earliest changes consist of yellowish-grey areas at the level of the pigment epithelium associated with some swelling of the overlying retina but no inflammatory cells in the vitreous. During the several months of evolution of the lesion, there is no change in its shape or size. Acute lesions last weeks to months but the disease has a chronic, recurring course. It progresses over several years and is characterized by the occurrence of further acute lesions.

Fluorescein angiography reveals relative hypofluorescence corresponding with the grey lesion. Over the next 3 months, pigment epithelial and retinal swellings subside and the centre of the lesion takes on a grey appearance with a lighter coloured margin. Fluorescein angiography at this stage shows a relative hyperfluorescence at the margin of the lesion, while the centre of the lesion remains hypofluorescent. After 3 months, fluorescein studies show uniform hyperfluorescence of the lesion lasting throughout the angiogram. Old lesions show atrophy of the pigment epithelium and choriocapillaris but the larger choroidal vessels are not affected. The margin of the lesion is clearly defined, with regular hyperpigmentation. The differential diagnosis is choroidal sclerosis, placoid pigment epitheliopathy, pigment epithelitis and serpiginous choroidopathy. Electrophysiological testing can be useful, with the electro-oculogram (EOG) usually being normal and the electroretinogram (ERG) being abnormal.

Serpiginous choroiditis is a descriptive name for a variant of the same disease. There is some evidence of an immunological aetiology. The clinical picture resembles an insidiously disseminated choroiditis characterized by multiple, confluent foci of exudate and scar formation affecting mainly the superficial portion of the choroid. The macula is frequently involved with peripapillary and macular geographic lesions. Fluorescein angiography and histological studies reveal disappearance of the choriocapillaris and the pigment epithelium. Ophthalmoscopy shows small, greyish, disc-like or circular confluent lesions and choroidal scars with slight pigment dispersion, leading to depigmentation in a serpiginous configuration.

Therapy consists of prednisolone in combination with antitubercular drugs, if evidence suggests a tubercular aetiology. Antimetabolites such as cytosine arabinoside and azathioprine may be indicated in cases where the macula is threatened.

Acute retinal pigment epithelitis: This condition has a characteristic acute onset with a fairly rapid resolution over 6-12 weeks and ultimate recovery of normal vision. The typical lesion is a dark greyish spot which is well defined in the acute and later stages. It is surrounded by a pale halo-like area. The lesions form in two or four clusters in the macular area and may be unilateral or bilateral. The intervening retina is normal. Fluorescein angiographic findings are minimal in the acute stage but hyperfluorescence corresponding to the initial halo-like zone can eventually be seen.

Acute multifocal placoid pigment epitheliopathy

This disease affects both the eyes in healthy subjects of either sex between the ages of 20 and 30 years. Spontaneous resolution with good visual recovery is usual, although the syndrome is probably a manifestation of a diffuse systemic inflammatory condition.

The primary lesion appears to be an obstructive vasculitis at the level of the choriocapillaris resulting in ischaemic injury and focal swelling of the retinal pigment epithelial cells. This gives rise to the characteristic ophthalmoscopic appearance of cream-coloured placoid lesions over the posterior pole within the equatorial region. Fluorescein angiography shows patchy, irregular choroidal filling, gradually outlining these lesions which mask the background fluorescence. Each area is stained with fluorescein during the later stages without significant leakage of dye. Upper respiratory symptoms, altered sensitivity to drugs and increased levels of gamma globulin favour a viral or an immune complex mechanism. The differential diagnosis includes multifocal choroiditis, primary retinal pigment epithelial detachment and acute epithelitis. Rapid loss of central vision is commonly followed by prompt resolution of the lesions with significant visual improvement continuing several weeks after the apparent ophthalmoscopic improvement. The alteration in the retinal pigment epithelium is permanent but changes in the choriocapillaris are minimal.

Masquerade syndromes

These include a group of diseases which mimic anterior or posterior uveitis in their clinical features but the aetiopathogenesis is entirely different, being usually neoplastic or occasionally ischaemic. Acute leukaemia, iris melanoma, juvenile xanthogranuloma, small round cell malignancies, anterior segment ischaemia, reticulum cell sarcoma or large cell lymphoma are some of the conditions which can present in this manner. In addition to the investigations detailed in general uveitis, cytological and immunohistological studies of aqueous and vitreous specimens assist in establishing the diagnosis.

VASCULAR AND CIRCULATORY DISTURBANCES

The blood supply of the uveal tract is derived almost entirely from the posterior ciliary arteries. However, the peculiar distribution resulting in the formation of the major arterial circle of the iris causes involvement of both the iris and the ciliary body in pathological vascular conditions. On the other hand, the blood supply to the choroid, being essentially segmental, results in the formation of lesions restricted to isolated areas. The richness of anastomoses in the anterior part of the uveal tract precludes isolated vascular lesions. Massive expulsive haemorrhage may occur in the choroid in conditions with sclerosis of the walls of the choroidal vessels, which give way on sudden lowering of the intraocular pressure during surgery for cataract or glaucoma.

Central serous choroidopathy

This presents a characteristic clinical picture of an oedema limited to the macular area and is caused by exudation from the parafoveal or choroidal capillaries. The retinal pigment epithelium (RPE) functions as a pump that maintains a firm retinal pigment epithelium-photoreceptor adhesion and a dry subretinal space. It also acts as a barrier to physiological leakage from the choriocapillaris. Central serous choroidopathy (Fig. 17.10A and B) is a focal disease of the retinal pigment epithelium and the junction between the retinal pigment epithelium and Bruch's membrane.

This condition occurs preferentially in young males as a sudden blurring of vision accompanied by a positive scotoma and metamorphopsia. The visual acuity is correctable by the use of convex lenses. On examination, there is a circular swelling seen in the macular area usually about the size of the optic disc. The oedema may be superficial or deep to the retinal pigment epithelium, so that the affected area is raised above the level of the retina and is surrounded by a characteristic ring-shaped reflex. A few exudative dots can be seen behind the sensory detachment, on examination with a +78 D or +90 D lens. Intravenous fluorescein injections have shown that it is sometimes due to a leakage of fluid through a pinpoint defect in Bruch's membrane resulting in a smokestack or inkblot appearance in the late phases. A good prognosis in serous detachment of the pigment epithelium depends on age (under 55 years), a detachment less than 1 DD (disc diameter) in size and non-involvement of the fovea. The visual acuity returns to normal within 3-6 months in most cases but some subjective symptoms persist. Argon laser burns may be applied to coagulate the leak if the oedema has persisted for 3 months or longer. The aim of treatment is to produce

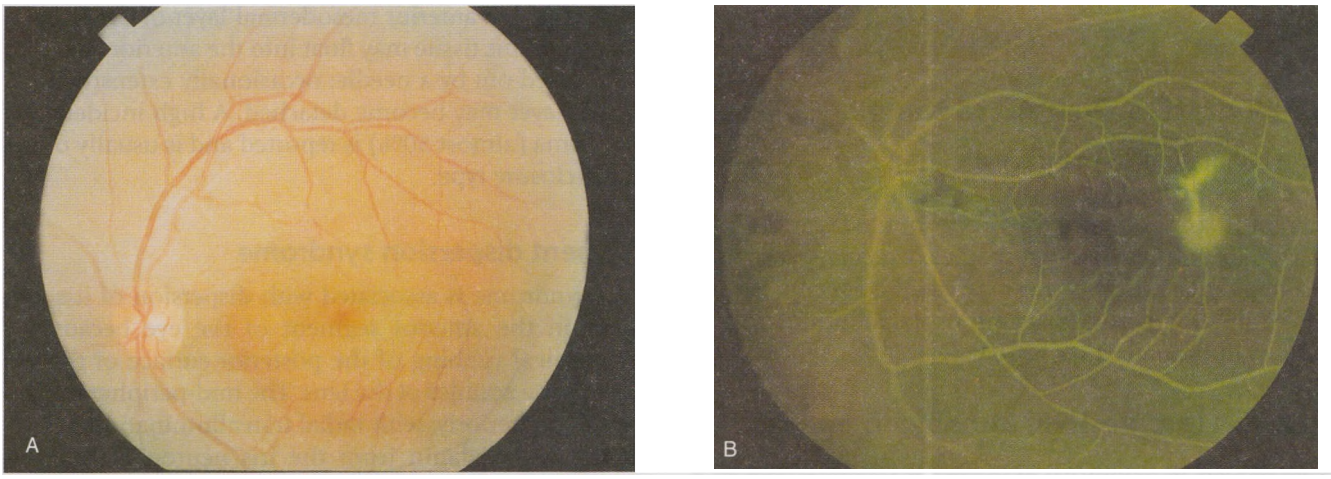


Fig. 17.10 Central serous retinopathy or choroidopathy: (A) photograph showing a central, circular, raised area of retina around the macula. Retinal blood vessels can be seen to change course at the edge of the lesion. (B) Fluorescein angiography shows a classical smokestack leak. (By courtesy of AH Paul)

a burn just sufficient to blanch the pigment epithelium if it is not too near the fovea. Serous detachment of the macula in young patients with a demonstrable leak flattens more rapidly after argon laser treatment but the prognosis for ultimate visual acuity is not improved.

Recurrences are frequent and produce extensive degeneration, which is called *retinal pigment epithelium decompensation.* Monochromatic argon green laser applied to the focal area of staining of the retinal pigment epithelium detected during late fluorescein transit stabilizes acuity in a large number of patients. Complications that can occur following central serous retinopathy are geographic atrophy of the pigment epithelium and choriocapillaris, invasion of the subpigment epithelial space by new vessels with progression to a fibrovascular scar and tearing of the retinal pigment epithelium. Such tears arise spontaneously or following krypton red photocoagulation.

Neovascularization of the iris

Neovascularization of the iris (NVI) or rubeosis iridis is a peculiar condition that occurs commonly in eyes having proliferative diabetic retinopathy or central retinal vein obstruction. It is characterized by the development of new, branching and enlarged vessels in the iris (Fig. 19.16), the neovascularization being frequently accentuated towards its root and in the angle of the anterior chamber. The new vessels leak protein and give rise to a turbid aqueous. NVI may be associated with signs of iritis. A rise in intraocular pressure occurs, initially with an open anterior chamber angle showing neovascularization, but later as fibrosis takes place the angle zips up, leading to an intractable neovascular glaucoma. Panretinal photocoagulation of an ischaemic retina prevents the development of neovascular glaucoma. Once NVI develops, panretinal photocoagulation can cause regression in the early stages by decreasing the production of vasculogenic factors from the ischaemic retina. If the ocular media are hazy, as frequently seen, anterior retinal cryopexy would be as effective. A trabeculectomy with adjuvant administration of mitomycin C or a drainage implant is used to control the raised intraocular pressure. The visual prognosis is poor.

Uveal effusion syndrome

A diagnosis of idiopathic uveal effusion syndrome is made after excluding all other inflammatory and hydrostatic causes of uveal effusion. The basic pathogenesis is a transudation of fluid from the vascular uvea with extravasation from the choriocapillaris into the suprachoroidal space and within the uveal tissues. The result is bilateral choroidal and ciliochoroidal effusion and subsequent detachment; in severe cases, a secondary serous retinal detachment occurs. Cells may be present in the vitreous and dilated episcleral vessels may be seen.

The differential diagnosis includes all disorders likely to produce the same effect, but with an identifiable cause, such as inflammatory diseases including scleritis, chronic uveitis, AIDS, and diseases which produce a hydrostatic effect due to obstruction of outflow. The latter include conditions such as arteriovenous fistula, nanophthalmos with a thickened sclera, and diseases with combined inflammatory and hydrostatic mechanisms such as tears of the retinal pigment epithelium, following cataract, glaucoma or retinal detachment surgery with inflammation and hypotony, excessive laser treatment or cryotherapy and supra-choroidal haemorrhage.

The condition is known to resolve spontaneously following which the retinal pigment epithelium shows patchy 'leopard spot' changes.

DEGENERATIVE CHANGES

Degenerative changes in the iris

Depigmentation of the iris with atrophy of the stroma is seen in old people. Depigmentation of the pupillary margin is common and may occur in the form of small triangular patches or radial fissures. Irregular lacunae in the pigmentary epithelium may often be seen with retroillumination with a slit-lamp or transillumination by contact illumination.

Essential (progressive) atrophy of the iris

This disease of unknown aetiology is characterized by a slowly progressive atrophic change in the tissues of the iris, which leads to the complete disappearance of large portions of this tissue. It forms part of the iridocorneal endothelial (ICE) syndromes. The disease usually starts insidiously in early adult life by the development of large areas of atrophy which coalesce and progress to form lacunae. Vision is eventually lost by the gradual onset of glaucoma due to downgrowth of an endothelial membrane over the tissues at the angle of the anterior chamber. Contraction of the membrane produces synechiae, corectopia, iris atrophy from ischaemia, ectropion uveae, dyscoria (abnormal shape of the pupil), polycoria (more than one pupil due to secondary holes in the iris) and nodules in the iris. The prognosis is poor, but fortunately the disease is usually unilateral (Fig. 17.11).

Iridoschisis

This rare condition occurs most commonly as a degenerative ageing senile phenomenon, though it may follow as a late result of severe trauma. Large dehiscences appear on the anterior mesodermal layer of the iris and strands of this tissue may float into the anterior chamber as if teased out by a needle; occasionally extensive areas of this layer may become detached. A high incidence of glaucoma (almost 50%) is reported and is usually of the angle-closure type.

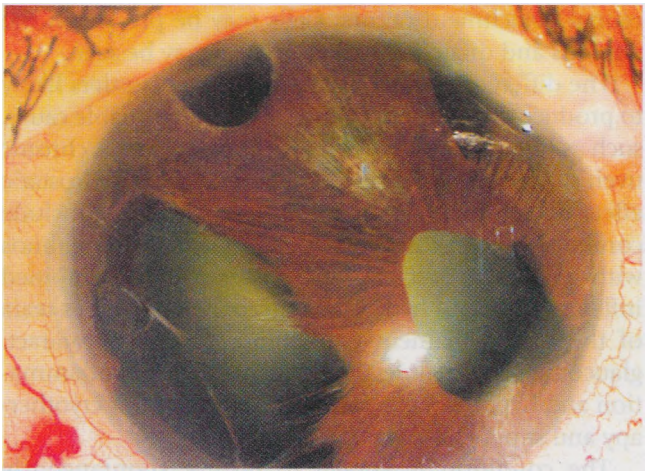


Fig. 17.11 Essential atrophy of the iris, a part of the iridocorneal endothelial syndrome.

Pigment dispersion syndrome

This syndrome is associated with dispersion of iris pigment in the anterior segment of the eye because of mechanical rubbing of the posterior surface of the iris against the zonules of the lens. The mid-peripheral iris is concave anteriorly, with radial transillumination defects in the iris. Melanin from the iris neuroepithelium is phagocytosed by the corneal endothelial cells, seen on slit-lamp examination as a vertical spindle (Krukenberg spindle). There is deposition of melanin pigment in the trabecular meshwork (Sampaolesi line) and glaucoma.

Degenerative changes in the choroid

Degenerative conditions are more frequent and important in the posterior than the anterior part of the uveal tract. They may be secondary (postinflammatory) or primary.

Secondary degenerations

Those following inflammatory lesions culminating in localized spots of complete atrophy have already been considered. The loss of nourishment to the retina causes atrophy of the outer layers and migration of pigment from the pigment epithelium into the more superficial parts of the retina. The pigment tends to get deposited in the perivascular spaces of the veins, so that the retinal veins may be mapped out here and there by pigment. More noticeable ophthalmoscopically are jet-black branched spots of pigment resembling bone corpuscles and standing out in sharp relief—an appearance seen in its most typical form in pigmentary retinal dystrophy (*see* p. 320). An almost identical picture, though usually without the characteristic distribution of the pigmented spots, may result from choroidal atrophy due to other causes such as syphilis.

Primary choroidal degenerations

These may be localized or general. The localized forms are usually central, although circumpapillary changes around the disc are not infrequent in myopia (*see below*) or the late stages of glaucoma.

Central choroidal atrophy is most commonly the result of myopia or obliterative vasosclerosis, essentially a change due to ageing.

Myopic choroidoretinal degeneration. Degenerative changes are common in pathological axial myopia; these are particularly marked around the optic disc and in the central

area of the fundus involving the choroid and retina. These changes are not due to the mechanical effects of stretching but are primary in nature and genetic factors play a prominent part in their incidence. They have been erroneously described as 'myopic choroiditis' but the condition is not inflammatory. They do not run parallel to the degree of myopia and tend to occur after mid-adult life, whereas the elongation of the eye is a phenomenon characteristic of the latter part of the first and second decades. They probably involve both the ectodermal (retinal) and mesodermal (choroidal and scleral) tissues; but as the atrophic changes in the retina are secondary to those in the choroid, the entire clinical picture will be considered here. This includes atrophic changes in the sclera around the disc, in the central area of the choroid and retina, and peripheral parts of the retina.

In the majority of cases of moderate myopia, there is a *myopic crescent* (Fig. 17.12). This is a white crescent at the temporal border of the disc; very rarely it may be nasal. In high degrees of myopia it may extend to the upper and lower borders, or form a complete ring around the disc.

The cause of the myopic crescent has given rise to much discussion; it may be absent in high myopia and is often present in low myopia, is essentially atrophic and not merely due to stretching. Anatomically there is considerable distortion of the disc. On the temporal side the pigment epithelium stops short at a variable distance from the disc and here the choroid is atrophic (Fig. 17.13). In other cases the retina, including the pigment epithelium, encroaches over the nasal edge of the disc (supertraction crescent).

Atrophic changes in the choroid in myopia occur mainly in the central area of the fundus. There is a gradual disappearance of the small vessels of the choroid with the development of lacunae forming irregular areas of atrophy, which may extend to the region of the disc, where they may eventually fuse with each other

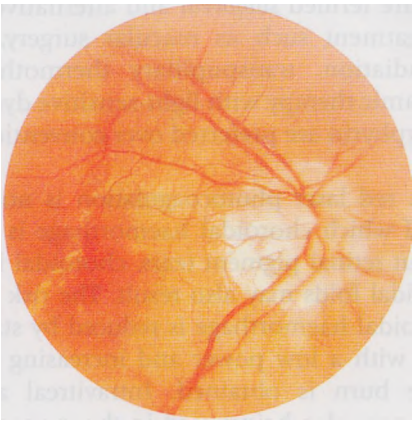


Fig. 17.12 Myopia with temporal crescent and early maculopathy.

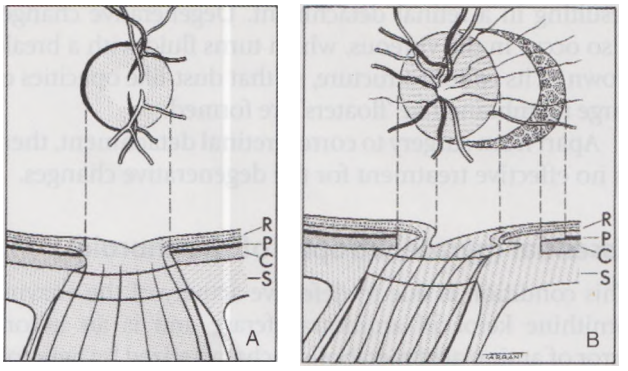


Fig. 17.13 (A) The normal configuration of the optic disc and (B) the myopic disc. R, retina; P, pigmentary epithelium; C, choroid S, sclera. On the temporal side the choroidal and scleral crescents are delineated. Note the oblique temporal direction of the optic nerve fibres and the overlapping on the nasal side resulting in supertraction.

and with the myopic crescent so as to form an irregular circumpapillary ring. Small haemorrhages and occasionally choroidal thromboses are not uncommon in the macular area. Choroidal thromboses may give rise to the sudden formation of a circular claret coloured or black spot at the fovea, which may persist (*Foster-Fuchs spot*, Fig. 17.14). These changes are associated with an atrophy of the overlying retina and involve considerable loss of visual acuity which tends to be progressive and may result in a central scotoma. At the same time, the retinal pigmentary epithelium becomes depigmented over most of the fundus so that the choroidal vessels are well seen. Linear breaks in Bruch's membrane (called *'lacquer cracks*') may be seen as fine lines.

Degenerative changes, typically those of cystoid and lattice degeneration, are also common at the periphery of the retina. These may lead to the formation of retinal holes

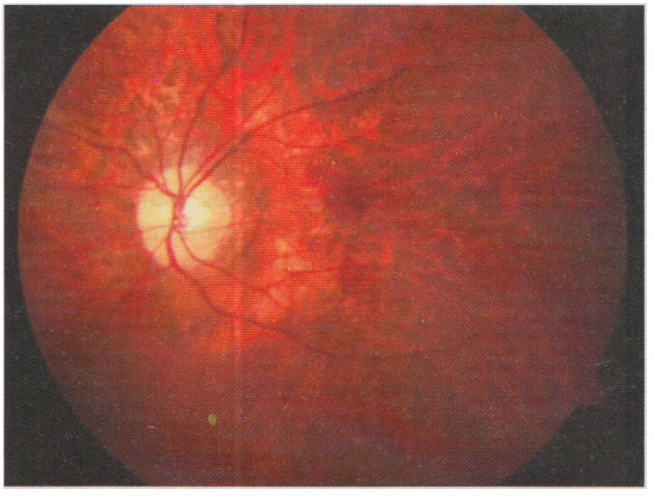


Fig. 17.14 Myopia with extensive retinal degeneration and a Foster-Fuchs spot in the macula.

resulting in a retinal detachment. Degenerative changes also occur in the vitreous, which turns fluid with a breakdown of its colloid structure, so that dust-like opacities or large membrane-like 'floaters' are formed.

Apart from surgery to correct retinal detachment, there is no effective treatment for the degenerative changes.

Essential (gyrate) atrophy of the choroid

This condition is due to defective activity of the enzyme ornithine ketoacid aminotransferase and is an inborn error of amino acid metabolism characterized by hyperornithinaemia and progressive atrophy of the choroid, the pigment epithelium and the retina. It starts usually with a patchy distribution in early adult life, at first in irregular areas which finally coalesce so that practically the entire fundus disappears, with preservation of only the macula.

Choroideraemia

This condition resembles the terminal stage of gyrate atrophy although it lacks the fine, dense, velvet-like pigmentation so typical of gyrate atrophy in the late stages. The condition is a hereditary degeneration and the most prominent symptoms are night-blindness and extreme concentric contraction of the visual fields.

Senile macular degeneration

Senile or *age-related macular degeneration (ARMD)* is a non-hereditary degeneration involving the choriocapillaris, Bruch's membrane, retinal pigment epithelium and photoreceptors. It is the most common cause of permanent central visual loss in the elderly.

A clinical distinction has been made between an *exudative* (wet) and a *non-exudative* (dry) macular degeneration based on the presence or absence of fluid. In certain patients these may not be two separate disease entities but may represent a continuum of a spectrum of clinical manifestations. The exudative or wet type of macular degeneration is due to leakage of fluid from a neovascular growth beneath the retina known as a subretinal neovascular membrane.

Drusen of Bruch's membrane are a thickening of the membrane due to dysfunction of the retinal pigment epithelium (*see* Fig. 20.24A) and are among the earliest findings in the macula, varying in size, shape and colour. Drusen need not result in visual loss, and visual impairment may occur associated with a generalized granularity and/or atrophy of the retinal pigment epithelium, photoreceptors and choriocapillaris. Such granularity may also occur in the absence of drusen, with a similar reduction in acuity. Macular degeneration is a bilateral disease although the fundus of the fellow eye may appear quite different. While non-exudative degeneration accounts for 90% of all cases of acquired macular degeneration, it results in visual loss at a level of legal blindness in only about 10%, and exudative 'wet' ARMD is the major blinding form of the disease.

Subretinal neovascular membranes outside the fovea (extrafoveal): Treatable neovascular membranes in aged patients should be diagnosed as early as possible—indicated by any acute loss of central vision, metamorphopsia or a change noted on the Amsler grid. A highly magnified stereo-examination of the macula is mandatory. The best method is slit-lamp biomicroscopy using a +90 D or +78 D lens.

Clinical signs of a neovascular subretinal membrane are a greyish pigmentation deep to the retina, a subretinal or retinal haemorrhage, hard exudates or subretinal fluid (Fig. 17.15). Fluorescein angiography delineates a membrane with a lace-like appearance, which fills early with the choroidal vasculature and leaks (Fig. 17.15). If the nearest edge of the membrane is 200 |im or more from the centre of the fovea, the entire subretinal membrane should be treated with heavy confluent argon green laser photocoagulation. The efficacy of this type of laser has been proved for extrafoveal choroidal neovascularization in ARMD, presumed ocular histoplasmosis syndrome and idiopathic choroidal neovascularization. Recent angiograms are necessary to confirm that the new vessels are completely destroyed. This must be followed by daily monitoring of the patient using an Amsler grid, and prompt treatment if distortion is noted.

Subretinal membranes that are located closer than 200 |xm from the centre of the foveal avascular zone are termed *juxtafoveal.* These should be treated carefully with laser energy because if it is absorbed by the retinal xanthophyll pigment present in the fovea, there will be considerable iatrogenic damage. Argon green laser or krypton red laser photocoagulation is effective in the treatment of subretinal neovascular membranes located within 250 |jim from the centre of the foveal avascular zone because of minimal absorption by the retinal xanthophyll pigment. Neovascular membranes beneath the fovea are termed *subfoveal* and alternative modalities of treatment such as macular surgery, external beam irradiation, transpupillary thermotherapy or photodynamic therapy with light-sensitive dyes such as vertepoporphyrin are preferred over conventional laser treatment.

Krypton red laser photocoagulation is not without hazards, of which choroidal haemorrhage is the commonest, but retinal pigment tears, choroidal ischaemia and choroidal folds may also result. The risk of immediate choroidal haemorrhage is reduced by starting the procedure with a low power and increasing it until a grey-white burn is obtained. Intravitreal anti-VEGF agents are now also being used in the management of subfoveal choroidal neovascular membranes.

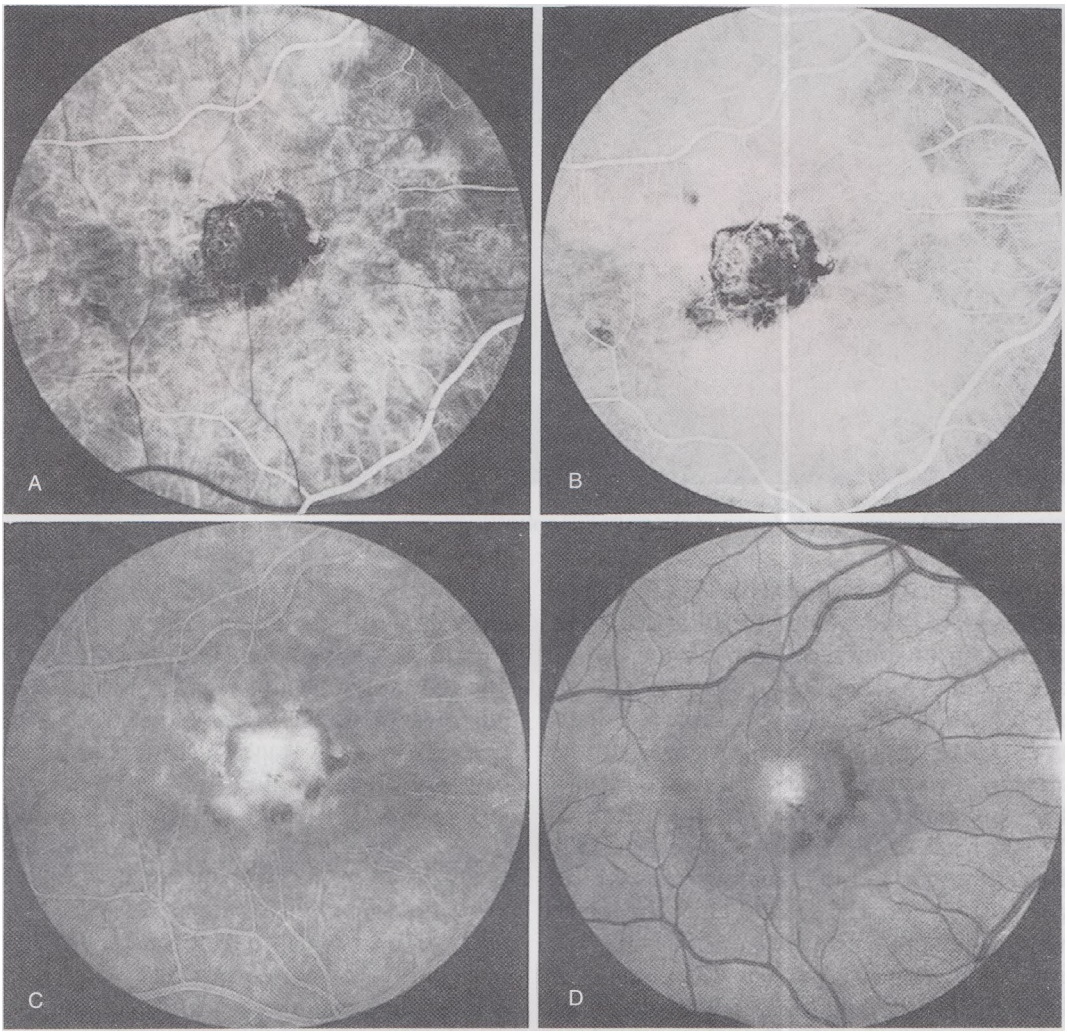


Fig. 17.15 Exudative 'wet' type of age-related macular degeneration showing a subretinal choroidal neovascular membrane. (A–C) are fluorescein angiograms and (D) is a fundus photograph.

Variants of ARMD have certain characteristic features, though they form a part of the broad spectrum of the disease. These variants are briefly described below.

Disciform degeneration at the macula (Junius-Kuhnt disease): In early disciform degeneration the pigment epithelium becomes separated from Bruch's membrane, and blood vessels grow into this space from the choriocapillaris through breaks in the membrane. Both the detachment of the pigment epithelium and the abnormal blood vessels can be identified by fluorescein angiography. The abnormal capillaries often bleed and the overlying neuroretina may show cystic macular oedema and serous detachment. Eventually the vascular complexes undergo fibrosis and give rise to the classical picture of senile disciform macular degeneration (Fig. 17.15).

The patient usually presents with visual loss in one eye due to an advanced stage of this disease. The vision in the fellow eye may be only slightly affected at the stage of pigment epithelial detachment or at the stage of development of new vessels, provided the latter have remained intact and not given rise to haemorrhage. Treatment by the argon laser is often effective by destroying the delicate neovascularization before haemorrhage ensues. This method allows exact localization and treatment by a beam of light with a diameter as small as 50 |xm.

Senile central choroidal atrophy: This assumes two chief forms, (i) In *central guttate choroidal atrophy* (Tay 'choroiditis') there are numerous minute yellowish-white spots in the macular region. They are usually round, but the larger spots may have crenated edges, thus showing signs of fusion. There may be indefinite signs of greyish pigmentation of their edges as the pigmentary epithelium is stretched over them. The spots are due to peculiar hyaline excrescences on the surface of the choroid, commonly known as *colloid bodies* or *drusen* (Fig. 17.16); they are of the same nature as Bruch's membrane, and like it are

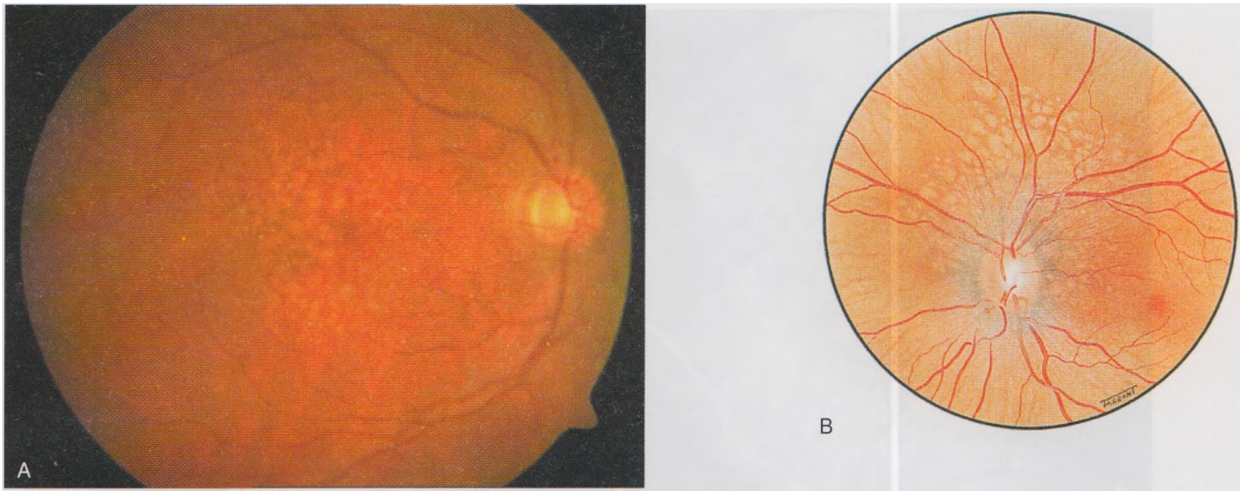


Fig. 17.16 Guttate choroidal atrophy with drusen of the posterior pole.

secreted by the pigmented epithelial cells. They resemble the drusen seen in ARMD and are a precursor of disciform macular degeneration in some eyes. Though the condition is bilateral, it causes little impairment of vision.

(ii) *Central areolar choroidal atrophy* (*sclerosis*): There appears a large circular or oval patch of degeneration in the macular region in which the choroidal vessels are visible owing to atrophy of the retinal pigment epithelium (Fig. 17.17). As a result of the atrophy of the choroid the sclera shines through and the patch appears white, although traversed by choroidal vessels. Only the larger choroidal vessels are seen, the smaller ones having disappeared; and even these may appear smaller than usual owing to degeneration of their walls when they may appear densely white and sclerotic. There is an absolute central scotoma. Occasionally the degeneration progresses slowly to involve most of the fundus. This form of central atrophy is genetically determined.

The *treatment* of these degenerative diseases is unsatisfactory. In those types of degeneration which involve a separation of the pigment epithelium and neovascularization, the argon laser may prove useful. The patient should be assured that peripheral vision will not be affected; although unable to read or do fine work, he will always be able to see sufficiently well to get about freely. In the early stages, reading is facilitated by the use of a magnifying reading aid.

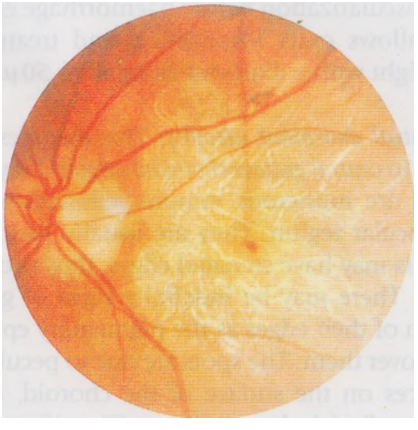


Fig. 17.17 Central areolar choroidal atrophy.

Detachment of the choroid

The choroid is often apparently detached from the sclera in eyes which have been lost by plastic iridocyclitis or glaucoma, and this may also result from severe haemorrhage or a new growth. The condition also commonly occurs soon after intraocular operations such as trabeculectomy with excessive filtration, owing to the increased vasodilatation and exudation into the outer lamellae of the choroid following the sudden lowering of intraocular pressure. The anterior chamber is shallow and on ophthalmoscopic examination the detached choroid is seen through the pupil as a dark mass; it may also be visible as a dark brown mass by oblique illumination. The prognosis is usually good, the choroid being replaced spontaneously and reattached and the anterior chamber re-established. Occasionally, however, the intraocular pressure of the eye remains low, and if the iris remains long in contact with the cornea at the angle of the anterior chamber, peripheral synechiae may form so that an obstructive glaucoma may eventually develop. In such circumstances it should be ensured that the wound or the conjunctival flap is not leaking; if it is, it should be reconstituted and repaired, if necessary by a conjunctival or scleral flap from above. In recalcitrant cases in which the choroidal detachment shows no evidence of subsiding, drainage of the subchoroidal fluid through the sclera is recommended and the anterior chamber re-established with a balanced salt solution.

CONGENITAL ABNORMALITIES

One iris may have a different colour from the other (*heterochromia iridium),* or parts of the same iris, usually a sector, may differ in colour from the remainder (*heterochromia iridis)* The blue iris is due to the absence of pigment in the iris stroma, the pigment in the retinal epithelium being seen through the translucent stroma.

The iris often shows patches of brown pigmentation; these *benign melanomata* are due to abnormal groups of pigmented cells lying in the posterior layers of the stroma.

The pupil is normally slightly to the inner side of the centre of the cornea. In some cases it is considerably displaced, usually also to the nasal side—*corectopia.* Rarely there are other holes in the iris besides the pupil—*polycoria.*

The iris may be apparently absent—*aniridia* or *irideremia*—a condition which is usually bilateral; however, a narrow rim exists at the ciliary border, but is hidden from view during life by the sclera. On examination, the ciliary processes and the suspensory ligament of the lens can be seen. There is a tendency for secondary glaucoma to develop due to the abnormal structure of the angle of the anterior chamber. It can also be associated with cataract, and dry eye with an ocular surface disorder.

Persistent pupillary membrane

This is due to the continued existence of part of the anterior vascular sheath of the lens; a fetal structure which normally disappears shortly before birth. Fine threads stretch across the pupil, or may be anchored down to the lens capsule. They can be distinguished from post-inflammatory synechiae as they always come from the anterior surface of the iris just outside the pupillary margin—from the position of the circulus iridis minor. Such tags occur frequently and are of no pathological importance. They are commonest in babies and probably undergo some absorption as age advances; but many persist permanently. Examination with a slit-lamp shows that minute remnants of the pupillary membrane are very common even in adults.

The fetal pupillary membrane consists of a network of small blood vessels supported by a very delicate stroma containing pigment cells. Sometimes the pigment is left on the lens surface and persists. It forms a stippling of very fine brown dots scattered over a circular area 5 or 6 mm in diameter in the centre of the pupil. These spots can be distinguished from the pigment spots left by posterior synechiae which have broken down as they are much smaller, stellate in shape when magnified under the slit-lamp, much more numerous and regularly arranged, and there are no concomitant signs of iritis. They do not usually interfere with vision.

Colobomata

Colobomata form one of the commonest congenital malformations of the eye (but are nevertheless rare), in which the tissues of the uvea and the associated retinal tissues or their prolongation onto the back of the iris are badly developed or deficient. As a rule they are due to defective closure of the embryonic cleft in which case they occur in the lower part of the eye (*typical colobomata)* (Fig. 17.18A). Colobomata of the iris found in other directions are called atypical (Fig. 17.18B). A coloboma *of the iris* may involve this tissue only, when it is usually pear shaped, the deficiency extending from the pupil towards, but not always as far as, the ciliary body, usually running downwards and slightly inwards. A coloboma of the iris may also be associated with a similar *coloboma of the lens, choroid and retina,* or the latter condition may occur alone. An inferiorly tapered cornea giving it a pear-like shape is a strong indicator of a defect in closure of the embryonic cleft giving rise to an iris and fundal coloboma.

A typical coloboma of the fundus appears as an oval or comet-shaped defect with the rounded apex towards

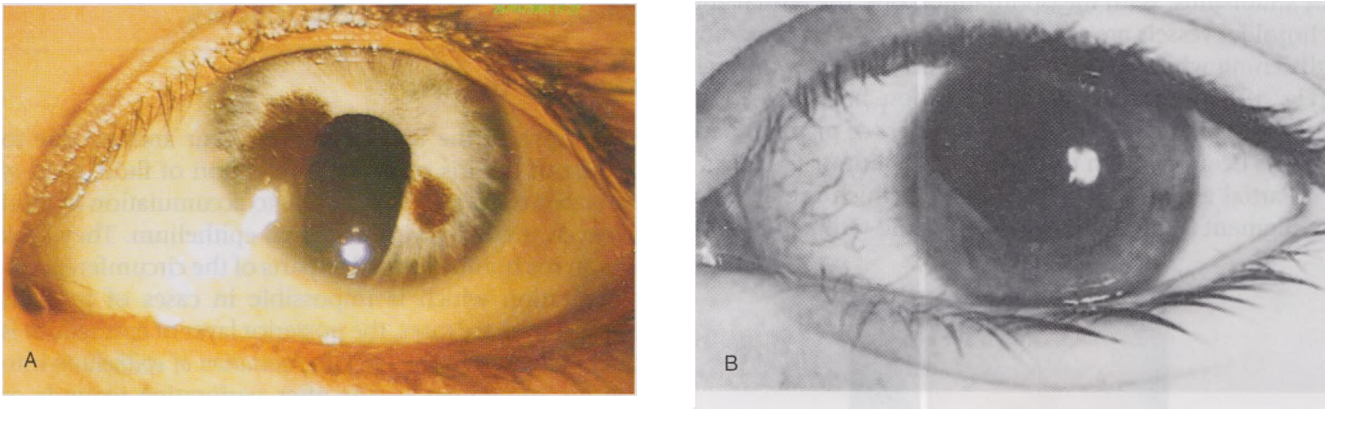
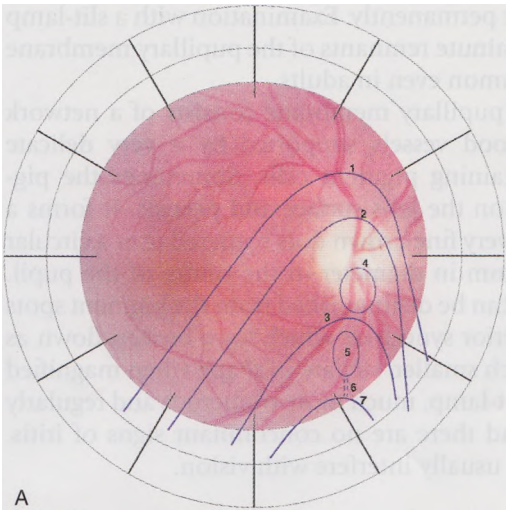
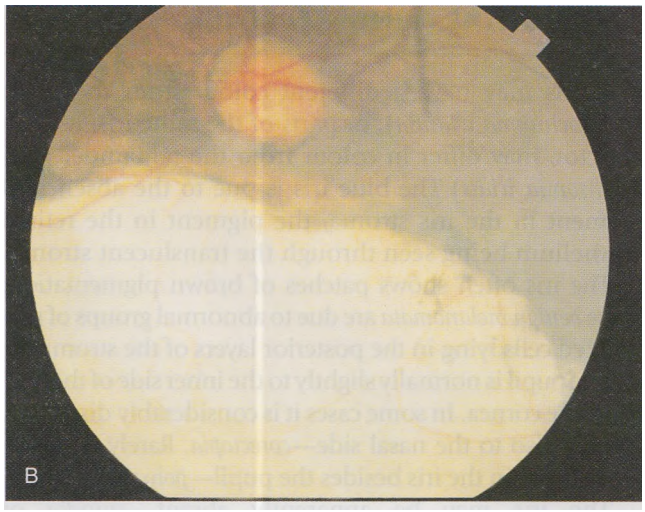


Fig. 17.18 (A) Typical coloboma of the iris located inferonasally, with heterochromia iridis. (B) Atypical coloboma of the iris located supranasally.





Fig, 17.19 Coloboma of the fundus (retina and choroid). (A) Ida Mann classification; (B) example of type II coloboma.

the disc, which may or may not be included (Fig. 17.19). A few vessels are seen over the surface, some retinal, others derived from the choroid at the edges. The surface is often irregularly depressed (ectatic coloboma). Central vision is generally poor, and there is a scotoma in the field corresponding more or less to the coloboma, although this usually contains some retinal elements near the edges. There is a high risk of retinal detachment, and prophylactic laser delimitation along the edges of the coloboma is sometimes advocated.

Albinism

This is a hereditary condition in which there is a defective development of pigment throughout the body. It is divided into ocular, oculocutaneous and cutaneous forms; the first being further subdivided on the basis of the tyrosinase test. Owing to the absence of pigment in the eye, the iris looks pink (Fig. 17.20) and the patients suffer from dazzling glare. Nystagmus, photophobia and defective vision are usually present and occasionally there may be strabismus. With the ophthalmoscope, the retinal and choroidal vessels are seen with great clarity, separated by glistening white spaces where the sclera shines through (Fig. 17.21). Microscopic examination has shown that total albinism is extremely rare, as traces of pigment have always been found in the retinal epithelium.

Partial albinism is commoner, in which the absence of pigment is limited to the choroid and retina, the irides being blue. The macular regions are pigmented and may therefore look normal.

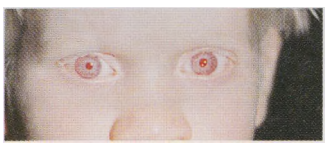


Fig. 17.20 Oculocutaneous albinism.

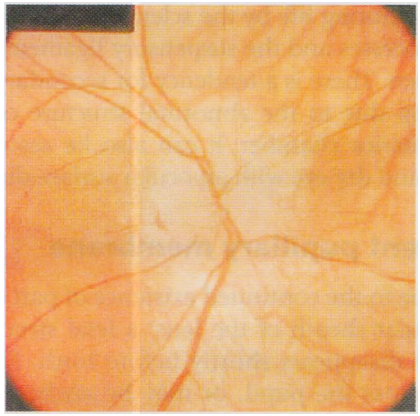


Fig. 17.21 Albinotic fundus.

Treatment consists in the use of tinted glasses as protection from glare.

MISCELLANEOUS CONDITIONS

Cysts of the iris

Serous cysts of the iris sometimes occur and are due to closure of the iris crypts with retention of fluid. *Cysts of the posterior epithelium* occur due to accumulation of fluid between the two layers of retinal epithelium. They look like an iris bombe limited to parts of the circumference—a limitation which is impossible in cases of true iris bombe. In these cases, the posterior layer of epithelium is often adherent to the lens. *Implantation of epithelium* into the iris sometimes occurs after perforating wounds or operations, giving rise to pearl cysts. When such wounds heal poorly the corneal epithelium may occasionally

spread over the iris and line the whole anterior chamber, causing glaucoma. Such cases are not true implantation cysts. Eyelashes are sometimes carried into the anterior chamber by perforating wounds and, lodging upon the iris, may be associated with cysts formed by the proliferation of the epithelium of their root-sheaths.

Tumours of the uveal tract

See Chapter 23.

SUMMARY

Inflammation or uveitis is a common disease of the uveal tract.

Uveitis is termed anterior if mainly the iris (iritis) and ciliary body (cyclitis) are involved, posterior if mainly the choroid (choroiditis), intermediate if only the pars plana (pars planitis) and panuveitis if inflammation involves all parts. The clinical course of uveitis can be acute, subacute, chronic or recurrent and the pathology may be granulomatous or non-granulomatous.

Anterior uveitis tends to be more painful and symptomatic with redness, watering and photophobia whereas with posterior uveitis pain and redness are less prominent symptoms and decrease in vision with floaters is commonly described.

Endophthalmitis is a particularly devastating condition with inflammation of one or more coats of the eye and adjacent intraocular spaces with a potentially destructive inflammation in the retina, choroid and adjacent vitreous cavity. If the inflammation extends beyond the sclera into the episcleral space it is termed panophthalmitis.

SUGGESTED READING

1. Nussenblatt RB, Whitcup SM, Palestine AG, 2nd ed. *Uveitis: Fundamentals and Clinical Practice.* St. Louis: Mosby; 1995, pp. 413.

Chapter 18

The Lens

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ANATOMY AND PHYSIOLOGY

The lens has all the physical attributes of a biconvex lens. Its circumference is known as the *equator*. Its diameter varies from 8.8 to 9.2 mm and the anteroposterior thickness changes with accommodation. The radius of curvature of the anterior surface of the lens is 10 mm and of the posterior surface is 6 mm. The former shortens with accommodation.

The function of the lens (like the cornea) is to transmit and refract light. The lens transmits 80% of light between 400 and 1400 nm and is responsible for 35% of the refracting power of the eye. The metabolism of the lens is anaerobic. Glycolysis is responsible for 85% glucose utilization and the pentose phosphate shunt accounts for 15%. Lactate produced by the anaerobic metabolism diffuses into the aqueous. The cortex is the most metabolically active region and the energy released from glucose metabolism is used for the production of glutathione, ion transportation and production of large molecules. Glutathione is required to maintain the proteins in reduced state and retain the lens pump integrity.

The lens is composed of 64% water, 35% protein, and 1% lipid, carbohydrate and trace elements. The protein concentration in the lens is actually the highest amongst body tissues. The main types of proteins are alpha (31%), beta (55%) and gamma (2%) crystallins, and insoluble albuminoids (12%).

The lens grows in size continuously throughout life, and in this respect it is unique among the organs of the body. At birth its weight is about 65 mg and by 80 years of age it has been found to weigh 258 mg.

The lens is suspended in the eye by *zonules* which are inserted on the anterior and equatorial lens capsule and attached to the ciliary body.

The lens is composed entirely of *epithelium* surrounded by a *capsule.* The lens capsule is a thick, collagenous basement membrane which is transparent, is thickest at the anterior pre equatorial region and thinnest at the posterior pole. The lens epithelium is a single layer of cells lining the capsule. The cells are of two types: those in the central zone that are not actively dividing, and cells in the pre-equatorial germinative zone that give rise to the lens fibres. The cells are interconnected by gap junctions and desmosomes and not by tight junctions or zona occludens, unlike typical epithelial cells. Ions and metabolites of low molecular weight can be exchanged. The epithelium contains Na^{+}-K+-ATPase and a calmodulin-dependent Ca^{++}-activated ATPase for the active transport of electrolytes. There is also an active transport mechanism for amino acids. The lens epithelium secretes the lens capsule and regulates the transport of metabolites, nutrients and electrolytes to the lens fibres.

The lens fibres are produced by the mitosis of epithelial cells in the pre-equatorial zone, which elongate and undergo differentiation with pyknocytosis and eventual loss of cell organelles and the nucleus. This is an important factor in the transparency of the lens. As the lens fibres elongate and new ones form, the older ones are pushed towards the depth of the lens so that the youngest lens fibres are the most superficially located. In contrast, the most superficial part of the lens capsule is the oldest. Ninety per cent of the mass of the lens fibres consists of proteins called *Crystallins* (alpha-crystallin, beta-crystallin and gamma-crystallin).

The substance of the lens has two distinct divisions—the cortex and the nucleus. The *nucleus* includes an embryonic nucleus consisting of primary lens fibres surrounded by the foetal nucleus. Clinically the yellow-brown, dense central zone viewed on slit-lamp examination is termed the nucleus but is in fact the nucleus with adjacent deep cortex. The nucleus consists of densely compacted lens fibres and has a higher refractive index than that of the cortex.

The *cortex* is seen as zones which are alternately dark and bright on oblique illumination with a slit-lamp, depending on the propensity to scatter light to a lesser or greater extent.

The transparency of the lens is maintained by the regular arrangement of the lens fibres which are devoid of organelles. The main function of the lens is to help in focusing light on the retina. Any factor that increases the absorption or scattering of light by the lens reduces its transparency.

Any opacity in the lens or its capsule, whether developmental or acquired, is called a *cataract.* As a general rule, developmental opacities are partial and stationary, acquired opacities progress until the entire lens is involved; but exceptions are well known in both types. Care, however, should be taken in using this term clinically as it often arouses anxiety which may be entirely unjustified. This applies particularly to the stationary types of opacity. It is to be remembered that even in senile cataract the opacities may remain localized for years without causing serious disability, or sometimes without being suspected. It is often wise, therefore, to tell such patients that they have 'lens opacities' and, if pressed, to suggest that the development of cataract may be long delayed and can be dealt with adequately should the need arise.

AETIOPATHOGENESIS OF CATARACT

Cataract is caused by the degeneration and opacification of the lens fibres already formed, the formation of aberrant lens fibres or deposition of other material in their place. The loss of transparency occurs because of abnormalities of the lens proteins and consequent disorganization of the lens fibres. The reasons for the degeneration of the lens fibres and consequent loss of transparency are not yet clear and probably vary in different cases. Any factor, physical or chemical, which disturbs the critical intra-and extracellular equilibrium of water and electrolytes or deranges the colloid system within the fibres tends to bring about opacification. Aberrant lens fibres are produced when the germinal epithelium of the lens loses its ability to form normal fibres, as may happen in posterior subcapsular cataract. Fibrous metaplasia of the fibres may occur in complicated cataract. Epithelial cell necrosis leads to focal opacification of the lens epithelium as 'glaucomflecken' in acute angle-closure glaucoma. Abnormal products of metabolism, drugs or metals can be deposited in storage diseases (Fabry), metabolic diseases (Wilson) and toxic reactions (siderosis).

Biochemically, three factors are evident in the process of cataract formation. In the early stages of cataract, particularly the rapidly developing forms, *hydration* is a prominent feature so that frequently actual droplets of fluid gather under the capsule forming lacunae between the fibres, and the entire tissue swells (*intumescence*) and becomes opaque. To some extent, this process may be reversible and opacities thus formed may clear up as in juvenile insulin-dependent diabetic patients whose lens becomes clearer after control of hyperglycaemia. Hydration may be due to osmotic changes within the lens or to changes in the semipermeability of the capsule. The process is dramatic in traumatic cataract when the capsule is ruptured and the lens fibres swell and bulge out into the

Table 18.1 Cataractogenesis

Risk factors for cataract	Pathomechanism of loss of transparency
• Increasing age	• Oxidative damage to membranes and proteins
• Sunlight (especially the UV-A, UV-B components)	• Hydration
• Severe diarrhoeal dehydration	• Denaturation of proteins
• Vitamins A, C, E deficiency	• Opacification of lens fibres with fibrous metaplasia
• Diabetes	• Opacification of lens epithelium
• Smoking	• Accumulation of pigmented molecules (3-hydroxykynurenine and chromophores which lead to yellowing)
• Corticosteroids	• Disturbance in osmotic balance
• Genetic	• Failure of ion pumps (increased intralenticular calcium and sodium with decrease in potassium)

anterior chamber. The second factor is *denaturation of lens proteins.* If the proteins are denatured with an increase in insoluble proteins, a dense opacity is produced, a process which is irreversible; opacities thus constituted do not clear up. Such an alteration occurs typically in the young lens or the cortex of the adult lens where metabolism is relatively active. It is rarely seen in the older and inactive fibres of the nucleus. Here the usual degenerative change is rather of a third type, one of *slow sclerosis.* Clinically, when the first process is predominant the condition is called a 'soft cataract'; the third is described as a 'hard cataract'.

Many factors lead to these changes (Tables 18.1 and 18.2). The most common is *age;* and it may be of significance that as age progresses the semipermeability of the capsule is impaired, the inactive insoluble proteins increase, and the antioxidative mechanisms become less effective. The normal lens contains sulphydryl-containing reduced glutathione and ascorbic acid (vitamin C), both of which decrease with age and in cataract. Experimentally, cataract can be produced in conditions of *deficiency,* either of amino acids (tryptophan) or vitamin B_2 (riboflavine), or by the administration of *toxic substances* (naphthalene, lactose, galactose, selenite, thallium, etc.). Dinitrophenol, used for slimming, and paradichlorobenzene, used as an insecticide, produce lens opacities in the posterior cortex, as do toxic products in the aqueous similar to that in cyclitis (*complicated cataract).* Cyanate from cigarette smoke, and from urea in renal failure and dehydration causes *carbamylation* and *protein denaturation* as do sugars by *glycation* in diabetics. *Hypocalcaemia* may lead to the same result perhaps by altering the ionic balance; this experimental finding is correlated with the cataract of parathyroid tetany. Cataractous changes may follow the use of the stronger anticholinesterase group of *miotics* and after the prolonged systemic use of *corticosteroids.* Physical factors may also induce the formation of a cataract; for example, *osmotic influences* (as may be largely responsible for juvenile diabetic cataract and dehydration-related cataract), *mechanical trauma* (traumatic cataract), or *radiant energy* in any form.

SYMPTOMS OF CATARACT

These are entirely visual, usually a *blurring of vision* (Table 18.3), though sometimes patients present late with an obvious *white opacity.* In children, an opacity may be noticed by parents or relatives. In the early stages, the vision is correctable with glasses but the power would change rapidly so one of the earliest symptoms could be a *frequent change of glasses.* Uniocular *polyopia,* another early symptom, is the doubling or trebling of objects seen with the eye. It is due to irregular refraction by different parts of the lens so that several images are formed of each object; it is more noticeable when the pupil is dilated and while viewing very distant objects. It is most commonly reported by patients as seeing multiple moons at night. Coloured halos may also be seen (*see* p. 91). There may also be a change in colour values owing to the absorption of the shorter wavelengths, so that reds are accentuated.

As the opacity extends and becomes denser, the acuity of central vision suffers—the deterioration depends on the density and position of the opacity. If the opacities are peripheral, as in senile cortical cataract, serious visual embarrassment may be long delayed and the vision is improved if the pupil is contracted in bright light. If the opacities are central, visual deterioration appears early, and the patient sees better when the pupil is dilated in dim illumination. Posterior cortical opacities often cause diminution of central vision apparently out of proportion to the amount of opacity observed. When nuclear sclerosis is prominent, the increasing refractivity leads to the development of a progressive myopia. It follows that with senile nuclear sclerosis, a previously presbyopic patient may be able to read again without the aid of spectacles; he refers to his 'improvement' in vision as 'second sight'.

As opacification proceeds, vision steadily diminishes until only perception of light remains. In many cases of advanced senile cataract, fingers can still be counted at a few feet, or at least hand movements discerned. In all

Table 18.2 Aetiopathogenesis and morphology of different types of cataract

Cause	Cataractogenic influence	Type of cataract	Other features
Age-related	Sunlight and UV radiation	Cortical and/or nuclear and/or subcapsular	
Systemic diseases			
• Adult diabetes mellitus	Hyperglycaemia	Same as age-related	
• Juvenile diabetes mellitus	Hyperglycaemia	'Snowflake'	
• Hypoglycaemia	Hypoglycaemia	Lamellar	
• Hypoparathyroidism	Hypocalcaemia	Flakes, iridescence in cortex, blue dots, subcapsular, total	Tetany
• Dystrophia myotonica		Posterior stellate, anterior or posterior cortical 'Christmas tree'	Muscle wasting, tonic relaxation of skeletal muscles, Pre-mature baldness, gonadal atrophy, cardiac conduction defects, mental retardation
• Galactosaemia	Galactitol in lens	Anterior and posterior subcapsular, later nuclear	Failure to thrive, mental retardation, hepatosplenomegaly
• Alport syndrome		Congenital, anterior and/or posterior lenticonus and microspherophakia	Sensorineural deafness, haemorrhagic nephropathy
• Lowe syndrome		Total	Congenital glaucoma, renal rickets, renal tubular acidosis
• Stickler syndrome		Cortical	
• Down syndrome		Anterior and posterior subcapsular 'snowflakes'	Mental retardation
Dermatological diseases			
• Atopic dermatitis		Shield cataract, posterior subcapsular	
• Ichthyosis		Cuneiform and nuclear	Dry skin
Physical factors			
• Traumatic		Flower-shaped rosette, anterior or posterior subcapsular, total	Other ocular signs of injury
• Electric shock		Anterior subcapsular	
• Radiation	Ionizing radiation	Posterior subcapsular	
	Non-ionizing radiation	True exfoliation of lens capsule	
Toxic agents			
• Corticosteroids		Discoid, posterior subcapsular	Open-angle glaucoma, Cushingoid features
• Anticholinesterases		Anterior subcapsular	
• Chlorpromazine		Yellow-brown anterior capsular granules or stellate or anterior polar opacity	
• Busulfan		Posterior subcapsular	
• Chloroquine		White, flaky, posterior subcapsular	
• Amiodarone		Anterior subcapsular	Cornea verticillata
• Cigarette smoker		Nuclear	Nicotine staining of fingers
• Copper		Sunflower	Kayser-Fleischer ring
• Iron		Brown discoloration	Other signs of siderosis
• Gold		Golden anterior capsular deposits	

Table 18.3 Symptoms of acquired cataract

Symptom	Pathogenesis	Type of cataract
Frequent change of glasses	Rapid change in refractive index of the lens	Cortical or nuclear
Reduced visual acuity usually gradual, painless, progressive	Reduction in transparency of the lens	All types
'Second sight' or myopic shift	Change in refractive index of the nucleus causes index myopia, improving near vision	Nuclear cataract
Loss of ability to see objects in bright sunlight, blinded by light of oncoming headlamps when driving at night	Loss of contrast sensitivity, which is greater at higher spatial frequencies; constriction of pupil cuts off peripheral vision from non-cataractous area	Posterior subcapsular
Monocular diplopia or polyopia	Cortical spoke opacities in conjunction with water clefts that form radial wedges containing a fluid of lower refractive index than the surrounding lens	Cortical cataract (spoke or cuneiform)
Glare	Increased scattering of light	Cortical and posterior subcapsular
Coloured halos around light	Irregularity in the refractive index of different parts of the lens	Cortical cataract
Colour shift (becomes more obvious after surgery)	Blue end of the spectrum is absorbed more by the cataractous lens	Nuclear
Visual field loss	Generalized reduction in sensitivity due to loss of transparency	All types

cases, however, light should be perceived readily and the direction of its incidence accurately indicated. In other words, cataract alone can never lead to inaccurate projection or no light perception.

In elderly patients with cataract, it is important to rule out other age-related diseases that impair vision gradually and progressively such as glaucoma, macular degeneration or optic atrophy.

AGE-RELATED (SENILE) CATARACT

This is rare in persons under 50 years of age unless associated with some metabolic disturbance such as diabetes, but is almost universal in varying degrees in persons over 70 years of age. It occurs equally in men and women and is usually bilateral, but often develops earlier in one eye than the other. There is a considerable genetic influence in its incidence. In hereditary cases it may appear at an earlier age in successive generations, the phenomenon being described as a history of 'anticipation'. The average age at onset of cataract is approximately 10 years earlier in tropical countries compared to that in temperate climates.

Two types of senile cataract may occur—*cortical cataract,* wherein the classical signs of hydration followed by coagulation of proteins appear primarily in the cortex, and *nuclear or sclerotic cataract* wherein the essential feature is a slow sclerosis in the nucleus.

In the *cortical type of senile cataract,* the most characteristic change is a demarcation of the cortical fibres owing to their separation by fluid. This phenomenon (*lamellar separation)* can only be seen with a slit-lamp and is invisible ophthalmoscopically. The general increase in the refractive index of the cortex in old people gives a grey appearance to the pupil in contradistinction to the blackness seen in the young; the greyness is initially due not to cataractous changes, but mainly to the increase in reflection and scattering of light.

In the next stage of *incipient cataract,* wedge-shaped spokes of opacity with clear areas between them appear in the periphery of the lens and lie in the cortex, some in front of and some behind the nucleus (*lens striae*). These are preceded by sectorial alterations in the refractive indices of the lens fibres, thus producing irregularities in refraction, some visual deterioration and polyopia. The bases of the wedge-shaped opacities (*cuneiform opacities,* Fig. 18.1 A and B) are peripheral and they are most common in the lower nasal quadrant. At first they can only be seen with the pupil dilated, but as they develop, their apices appear within the normal pupillary margin. With oblique illumination the pacities appear grey; seen with the ophthalmoscope, mirror retinoscope or slit-lamp in retroillumination, they are black against the red background of the fundus; and as they approach the axial area, vision becomes seriously disturbed.

As time goes on, opacification becomes more diffuse and irregular so that the deeper layers of the cortex become cloudy and eventually uniformly white and opaque. Meanwhile, the progressive hydration of the cortical layers may cause a swelling of the lens, thus

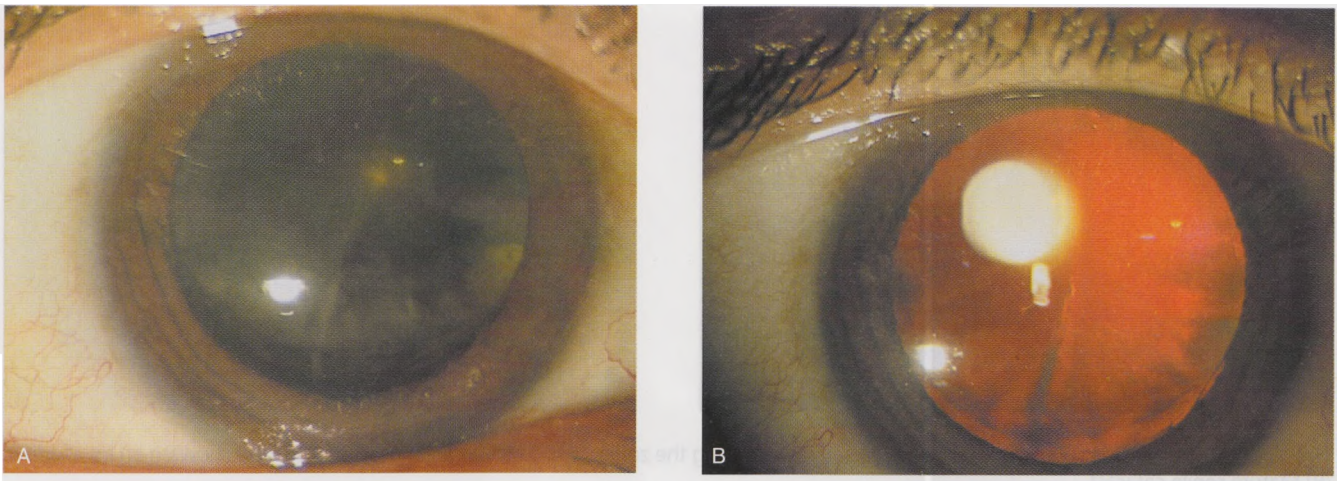


Fig. 18.1 Cuneiform cataract. (A) Diffuse illumination; (B) retroillumination.

making the anterior chamber shallow (*intumescent cataract).* Eventually the entire cortex becomes opaque, the swelling subsides and the cataract is said to be *mature.* In the meantime, the nucleus suffers little change except a progressive sclerosis.

As long as there is any clear lens substance between the pupillary margin of the iris and the opacity as in *immature* cataract, the iris throws a shadow upon the grey opacity when light is cast upon the eye from one side (Figs 18.2A and 18.3A). When the cortex is completely opaque the pupillary margin lies almost in contact with the opacity, separated only by the capsule; the iris then throws no shadow, and the cataract is said to be *mature* (Figs 18.2B and 18.3B).

If the process is allowed to go on uninterruptedly, the stage of *hffiermaturity* sets in when the cortex becomes disintegrated and is transformed into a pultaceous mass. The lens becomes more and more inspissated and shrunken, sometimes yellow in appearance. Such a cataract is termed a *shrunken cataract.* The anterior capsule becomes thickened due to proliferation of the anterior cubical cells, so that a dense white capsular cataract (sometimes with capsular calcification) is formed at the anterior pole in the pupillary area. Owing to shrinkage, the lens and iris become tremulous and the anterior chamber deep, and finally, degeneration of the suspensory ligament may lead to luxation of the lens.

Sometimes at the stage of maturity the cortex becomes fluid, and the nucleus may sink to the bottom of the lens. The liquefied cortex is milky, and the nucleus is seen as a brown mass limited above by a semicircular line, altering its position with changes in position of the head. Such a cataract is called a *morgagnian hypermature cataract* (Fig. 18.4).

The rate of *development* of senile cortical cataract varies greatly, sometimes taking many years; indeed, the cataract may never reach maturity in some individuals. Very

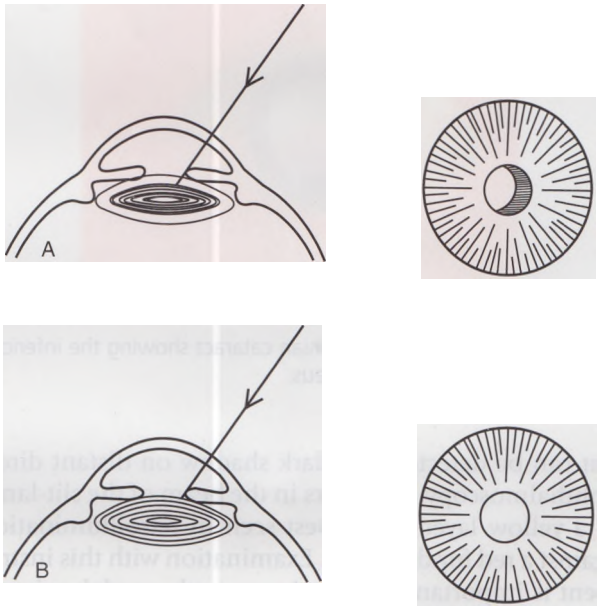
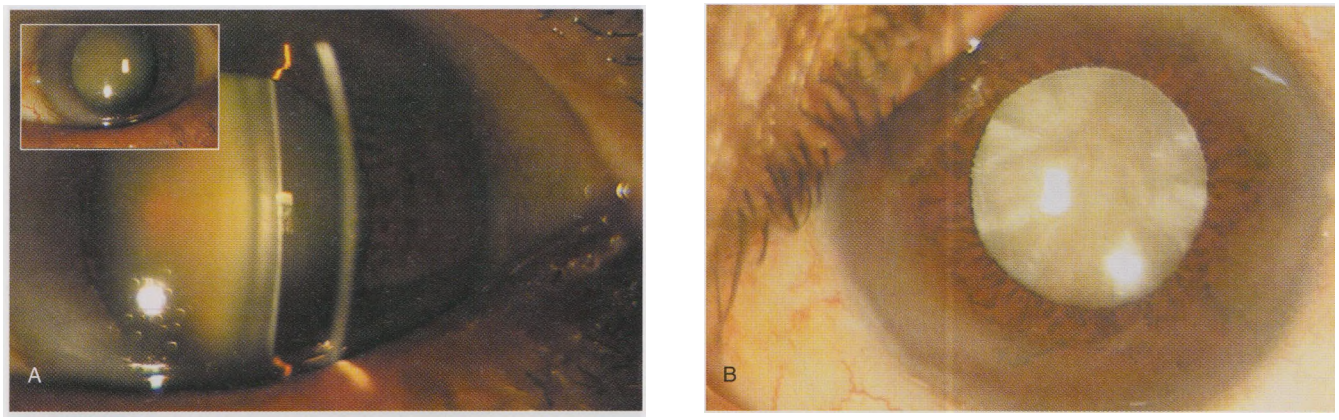


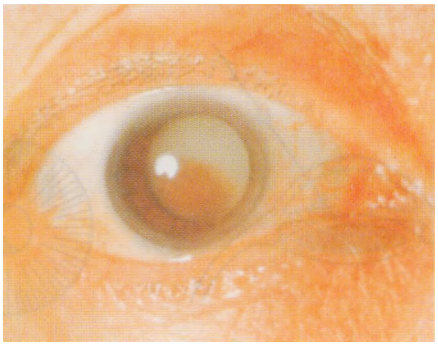
Fig. 18.2 (A and B) Use of iris shadow to diagnose the maturity of cataract. The eye is illuminated from the temporal side and shadow of iris cast on the lens surface is analysed (By courtesy of Hamblin). (A) is immature cataract with presence of an iris shadow. (B) is mature cataract, totally opaque lens with no iris shadow.

rapid maturation in younger patients usually indicates some complication such as cyclitis or diabetes. Cataracts with fine radial lines evolve more slowly than those with cloudy opacities. It is best to examine every case periodically, a careful drawing or clinical photograph of the opacities being recorded at each visit.

Another common type of cortical senile cataract is a *cupuliform cataract,* consisting of a dense aggregation of opacities, often forming a plaque, just beneath the capsule, usually in the posterior cortex. The cataract progresses towards the equator and not axially towards the nucleus. It is difficult to see with the ophthalmoscope



Fig, 18.3 (A) Slit-lamp view of an immature senile cataract showing the zones of disjunction and (inset) diffuse view showing an iris shadow. (B) Mature senile cataract.



Fig, 18.4 Hypermature morgagnian cataract showing the interiorly displaced brown lenticular nucleus.

but can be detected as a dark shadow on distant direct ophthalmoscopy. It appears in the beam of the slit-lamp as a yellow layer and is best seen in retroillumination against a red fundus reflex. Examination with this instrument is important since, being near the nodal point of the eye, the opacity may diminish the vision considerably in older people and the lens may appear relatively normal on diffuse examination.

In *senile nuclear sclerosis of the lens* or *nuclear* or *sclerotic cataract* the opposite process occurs; the normal tendency of the central nuclear fibres to become sclerosed is intensified while the cortical fibres remain transparent. This type of cataract tends to occur earlier than the cortical variety, often soon after 40 years of age. It typically blurs distant vision more than near vision. As time progresses the nucleus becomes diffusely cloudy, the cloudiness spreading gradually towards the cortex, and occasionally it becomes tinted dark brown, dusky red or even black, owing to the deposition in the lens of yellow pigmented proteins derived from the amino acid tryptophan, altered by the action of sunlight (*brown cataract: cataracta brunescens; black cataract: cataracta nigra).* In maturity the sclerosis may extend almost to the capsule so that the entire lens functions as a nucleus. Initially, little change may be seen with the ophthalmoscope, except that the details of the fundus are hazy. Occasionally, if there is much pigment, the pupillary reflex may be entirely blackened. There is, however, considerable visual disturbance—at first a progressive myopia owing to the increased refractive index of the nucleus, and then general impairment of vision; but progress is usually very slow and hypermaturity generally does not occur in nuclear cataract.

CATARACT ASSOCIATED WITH OCULAR DISEASE

Complicated cataract

This results from a disturbance of the nutrition of the lens due to inflammatory or degenerative disease of other parts of the eye, such as iridocyclitis, ciliary body tumours, choroiditis, degenerative myopia, anterior segment ischaemia, retinitis pigmentosa, gyrate atrophy or retinal detachment. After inflammations of the anterior segment, a nondescript opacification appears throughout the cortex which usually progresses and matures rapidly such as is seen in Fuchs heterochromic cyclitis (*see* p. 245). In inflammations or degenerations affecting the posterior segment a characteristic opacification usually commences in the posterior part of the cortex in the axial region *(posterior cortical cataract* or *posterior subcapsular cataract).*

Ophthalmoscopically, it appears as a vaguely defined, dark area, and with the slit-lamp the opacity is seen to have irregular borders extending diffusely towards the equator and often axially forwards towards the nucleus. Unlike developmental cataract, it is not sharply confined to a particular zone. In the beam of the slit-lamp the opacities have an appearance like breadcrumbs and a characteristic rainbow display of colours often replaces the normal achromatic sheen *(polychromatic lustre).* Such a cataract may remain stationary in the posterior cortex

for a long time or even indefinitely; in other cases, the opacification spreads peripherally until all the posterior cortex is affected, and progresses axially until the entire lens is involved. The total cataract formed in this manner is usually soft and uniform in appearance.

Even in the early stages, vision is usually impaired owing to the position of the opacity near the nodal point of the eye. The operative prognosis depends on the causal condition; but the presence of such a cataract, without obvious cause, should always call for a careful examination of the eye for keratic precipitates, pars planitis or other signs of disease.

CATARACT ASSOCIATED WITH SYSTEMIC DISEASE

Diabetic cataract

Senile cataract tends to develop at an earlier age and more rapidly than usual in diabetic subjects. The lenses of an adult diabetic are said to be in the same condition as a non-diabetic who is 15 years older. In diabetic adults, compared to non-diabetics, cataracts are more prevalent, are dependent on the duration of diabetes and progress more rapidly. The mechanisms are believed to be glycation, carbamylation of crystallins and increased oxidative damage.

True diabetic cataract is a rare condition occurring typically in young people in whom the diabetes is so acute as to disturb grossly the water balance of the body. A large number of fluid vacuoles appear under the anterior and posterior parts of the capsule, initially manifesting as myopia and then producing a diffuse opacity which at this stage is reversible.

The lens then rapidly becomes cataractous, with dense, white subcapsular opacities in the anterior and posterior cortex resembling a snowstorm—*'snowflake' cataract.* Fine, needle-shaped polychromatic cortical opacities may also form. With appropriate treatment to control hyperglycaemia, the rapid progression to mature cataract may be arrested at this stage.

Parathyroid tetany

Cataractous changes may occur due to hypo-calcaemia when the parathyroid glands become atrophic or have been inadvertently removed in the course of a thyroidectomy. Development of a cataract may be prevented by the administration of parathyroid hormone and calcium. In children, the cataract is lamellar; in adults it produces an anterior or posterior punctate subcapsular opacity. Clouds of small discrete opacities appear in the cortex separated from the capsule by a clear zone. These coalesce to form large, glistening, crystalline flakes and within 6 months the lens is usually opaque. The other ocular tissues are unaffected and the operative prognosis is good.

Myotonic dystrophy

Characteristic cataracts may develop with myotonic dystrophy and may be an early and prominent feature in 90% of patients. In a sharply limited zone of the cortex underneath the capsule both anteriorly and posteriorly, fine dust-like opacities appear interspersed with tiny iridescent spots. The polychromatic dots and flakes in the superficial cortex resemble a *'Christmas tree'* in appearance. The cataract may remain stationary or progress. As the opacities mature a characteristic stellate opacity appears at the posterior pole. The operative prognosis is good.

Galactosaemia

This is an autosomal recessive, inherited congenital disease characterized by an inborn inability of the infant to metabolize galactose. An absence of one of the three enzymes involved in the conversion of galactose into glucose leads to an increase in galactose levels in the blood and an accumulation of galactitol (sugar alcohol of galactose) within the lens, resulting in an osmotic swelling of the lens fibres. The clinical features manifest in infancy with failure to thrive, mental retardation, hepatosplenomegaly and cataract. Galactokinase deficiency is a milder disorder associated with galactosaemia and cataract, but without the other systemic manifestations.

Galactosaemia is frequently associated with the development of bilateral cataract in early life. The cataract is usually an anterior and posterior subcapsular lamellar opacity at first, which later becomes nuclear before it extends to eventually become total. Progression of cataract can be prevented and sometimes regression may occur if milk and milk products are eliminated from the diet in the early stages; otherwise, if the patient survives, surgical treatment must be adopted.

Down syndrome

Children with Down syndrome may have punctate subcapsular cataracts.

Atopic cataract

Cataract appears frequently in those suffering from severe and widespread skin diseases—-atopic eczema, poikiloderma vasculare atrophicans, scleroderma, keratosis follicularis, and others.

CATARACT DUE TO OTHER CAUSES

Most types of radiant energy produce cataractous changes, particularly heat, X-rays and gamma-rays of radium or neutrons. Ultraviolet light has been implicated as a factor in the aetiology of senile cataract, a suggestion due largely to the common occurrence of this condition in

tropical countries such as India and Northern Australia. The average age of onset of age-related cataract in these countries is 10 years younger than in Europe and North America.

Heat (infrared) cataract

This is a characteristic condition which may be induced experimentally in animals and occurs clinically in industry. The heat acts not directly on the lens but is absorbed by the pigment of the iris and ciliary body and thus influences the fibres of the lens indirectly; it has thus been found impossible to produce such cataracts experimentally in lightly pigmented or albino animals. The cataract is characteristic in appearance. In the early stages there is a small disc of opacity in the posterior cortex of the lens, thinner and more sharply defined than the posterior cortical opacity of complicated cataract, but it may extend throughout the cortex in the later stages. In addition, the zonular lamella of the capsule may be exfoliated, sometimes in large sheets which curl up in the pupillary area.

Such a cataract is seen industrially in two particular occupations. It is seen in *glassworkers* who have long been engaged in glass manufacture, particularly beer bottles and plate glass, but not in those who make flint-glass bottles or pressed glass articles, since the heat of such furnaces is less. It also occurs in certain *ironworkers*, especially tin-plate millmen and chainmakers.

Irradiation cataract

This may be caused by X-rays, gamma-rays or neutrons. The characteristic changes appear to be due to the direct action of the rays on the dividing cells and developing fibres of the lens itself. The initial changes are found near the equator shortly after radiation, and the first clinical evidences are apparent in the cortex near the posterior pole only after a period of 1 or 2 years when the equatorial cells have migrated posteriorly. They resemble those of heat cataract in appearance. Maturation of the cataract may occur fairly rapidly. Technicians who have been inadequately protected may be thus affected, or patients treated for malignant conditions near the eye. Such cataracts have also developed in workers in atomic energy plants and occurred among the survivors of the atomic bombs released over Japan in the Second World War.

Electric cataract

This may develop rapidly after the passage through the body of a powerful electric current as from a flash of lightning or the short-circuiting of a high-voltage current. The cataract usually starts as punctate, subcapsular opacities and matures rapidly.

Traumatic cataract

This may be either due to concussion or a perforating wound *(see* Chapter 24).

DEVELOPMENTAL CATARACT

Developmental cataract may be present *at birth (congenital)* or it may develop later. It assumes the most variegated forms and is common in its minor manifestations. Indeed, the lenses of most people show minute points of opacity of th is type when examined with the beam of the slit-lamp under full mydriasis. The lens is formed in layers, the central nucleus being the earliest formation, around which concentric zones are subsequently laid down, the process continuing until late adolescence *(see* Fig. 1.9). Developmental cataract has, therefore, a tendency to affect the particular zone which was being formed when this process was disturbed; the fibres laid down previously and subsequently are often normally formed and remain clear. As time goes on, such an opacity is thus usually deeply buried in the substance of the lens by the subsequent formation of normal fibres. Developmental cataract thus tends to follow the architectural pattern of the lens and from its location an estimate can be made of the stage of development at which the anomaly occurred.

The deleterious influences which may cause such developmental anomalies are yet largely unknown. Maternal (and infantile) malnutrition is possibly one, as in zonular cataract; maternal infections by viruses another, as in rubella; deficient oxygenation owing to placental haemorrhages probably a third. Hypocalcaemia and storage disorders are other cataractogenic conditions. Such cataracts tend to be stationary, although progressive opacification of a senile type is also well known. From the functional point of view, most such cataracts are of little or no significance unless they are considerable in size and central in position.

Among the many morphological types, the following are the most common.

Punctate cataract

This is the most common manifestation and, in minute degrees, is almost universal in occurrence. When the small opaque spots are multiple and scattered all over the lens, appearing as tiny blue dots by oblique illumination with the slit-lamp, they are known as *cataracta coerulea,* or *blue-dot cataract* (Fig. 18.5A); when crowded in the Y-sutures, the terms *sutural cataract* and *anterior axial embryonic cataract* have been used. Another variant is a dominantly inherited non-progressive type of cataract with a central spheroidal or biconvex opacity consisting of powdery fine white dots within the embryonic or foetal nucleus *(cataracta centralis pulverulenta,* Fig. 18.5B).

Usually most of these are non-progressive and not of major visual significance.

Zonular cataract

This accounts for approximately 50% of all visually significant congenital cataracts. Here, development is interfered with at a later stage and a zone around the *embryonic nucleus* (usually in the area of the *foetal nucleus*) becomes opacified, its extent depending on the duration of the inhibiting factor. The opacity is usually sharply demarcated (Fig. 18.6) and the area of the lens within and around the opaque zone is clear, although linear opacities like spokes of a wheel (called *riders*) may run outwards towards the equator. Occasionally two such rings of opacity are seen. Such cataracts are usually bilateral and if, as is frequently the case, they are formed just before or shortly after birth, they may be of sufficient diameter to fill the pupillary aperture when the pupil is undilated, thus affecting vision.

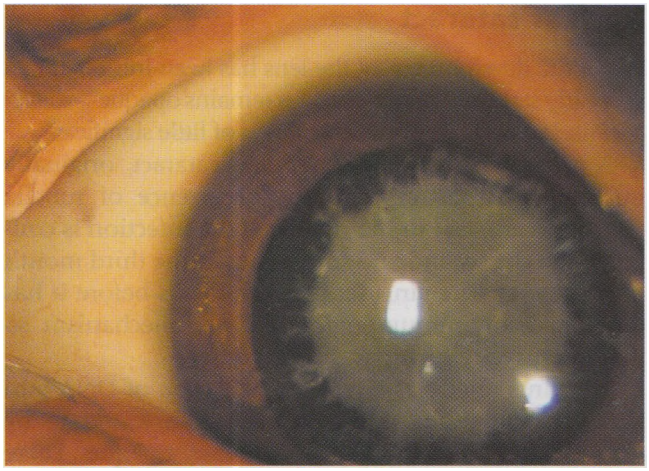


Fig. 18.6 Zonular cataract. Linear, spoke-like riders run towards the equator.

Such zonular cataracts may have a genetic origin with a strong hereditary tendency of the dominant type. On the other hand, they may be environmental in origin, usually due to a period of malnutrition at some stage of late intrauterine or early infantile life. Lack of vitamin D is apparently a potent factor and evidence of rickets may be found in affected children. This deficiency inhibits the development of other epithelial structures, especially the enamel of the permanent teeth which is being formed at the time; the permanent incisors and canines particularly have an eroded appearance with transverse lines across them.

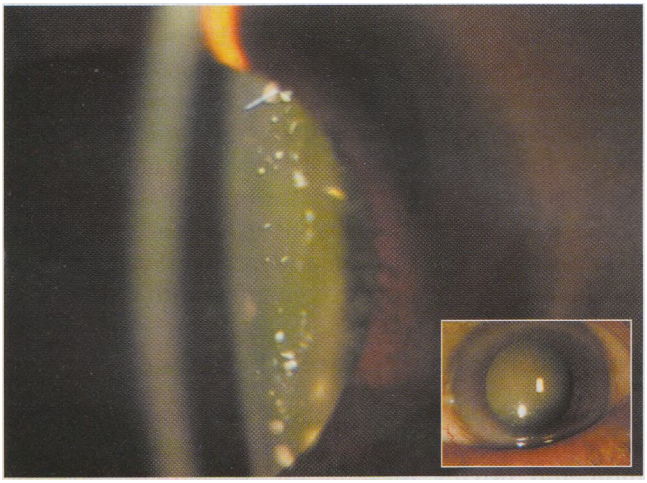


Fig. 18.5 (A) Punctate blue-dot cataract *(cataracta coerulea).*

Fusiform cataract

This is also called *spindle-shaped, axial,* or *coralliform,* and is an anteroposterior spindle-shaped opacity, sometimes with offshoots giving an appearance resembling a coral. It is genetically determined and shows a tendency to occur in families. *Discoid cataract* is also a familial form, showing a somewhat ill-defined disc of opacity just behind the nucleus in the posterior cortex.

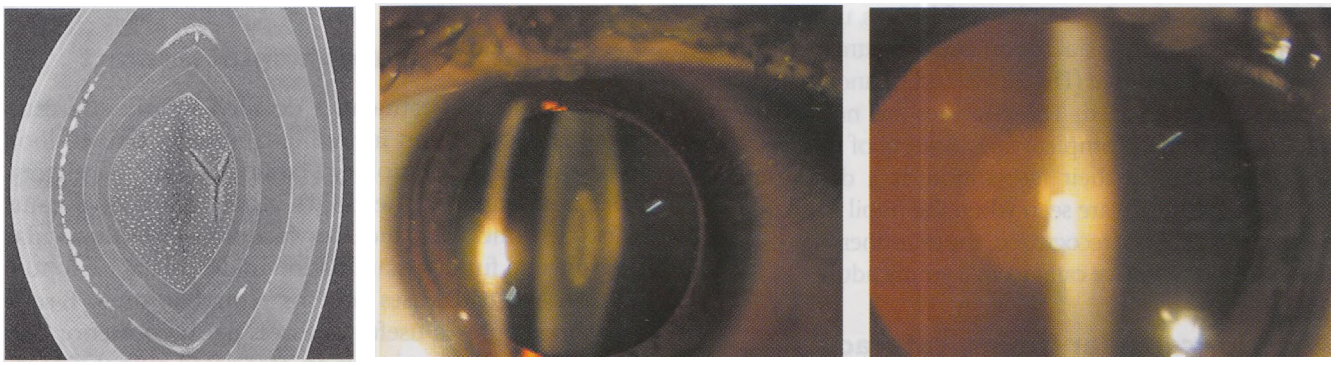


Fig. 18.5 (B) Central pulverulent cataract: diagrammatic representation with opacities in the adult nucleus (extreme left). Slit-lamp picture of the same eye in a 26-year-old patient with a visual acuity of 6/9 (centre and right).

Nuclear cataract

When the development of the lens has been inhibited at a very early stage, the central nucleus remains opaque—*embryonal nuclear cataract.* Ordinarily this is of little significance.

A progressive type of congenital cataract, originally nuclear, is associated with the occurrence of rubella (German measles) in the mother if the infection is contracted in the second and sometimes in the third month of pregnancy. The virus reaches the foetus before it has developed an immunological defence mechanism so that extensive cellular parasitism occurs.

The virus interferes with the translation of DNA into RNA. Pathologically, the lens nucleus is found to be necrotic and the whole lens becomes opaque. There may be an accompanying retinitis, which appears as a fine pigmentary deposit (salt-and-pepper retinopathy) at the posterior pole. Other congenital anomalies occur in association with the cataract, particularly congenital heart disease (patent ductus arteriosus), microphthalmos, micrencephaly, mental retardation, deafness and dental anomalies. Unless all lens matter is removed, aspiration of the cataract may be followed by a chronic inflammatory endophthalmitis associated with the presence of residual lens matter. The frequency of this combination with maternal rubella raises the serious question of medical termination of pregnancy if there is evidence of infection at this stage. Administration of the MMR (measles-mumps-rubella) vaccine as part of the primary immunization schedule, and/or rubella vaccine to prepubertal girls or women who are to start a family and are found to be rubella antibody negative, are measures to reduce the morbidity of the teratogenic effects of congenital rubella infection. The possibility of other viruses traversing the placental barrier should be kept in mind.

Coronary cataract

This represents a similar type of developmental cataract as the zonular, occurring around puberty. It is therefore situated in the deep layers of the cortex and the most superficial layers of the adolescent nucleus. It appears as a *corona of club-shaped opacities* near the periphery of the lens, usually hidden by the iris, while the axial region and the exUeme periphery of the lens remain free (Fig. 18.7A and B) and hence vision is usually not affected. The opacities are not progressive and do not lead to complete opacification of the lens. Their importance lies in their recognition as a developmental anomaly, for if they are seen when the pupil is dilated and their character is not recognized, the examiner may be led to diagnose a progressive cataract in a young adult.

Anterior capsular (polar) cataract

This may be developmental owing to delayed formation of the anterior chamber and, in this case, the opacity is

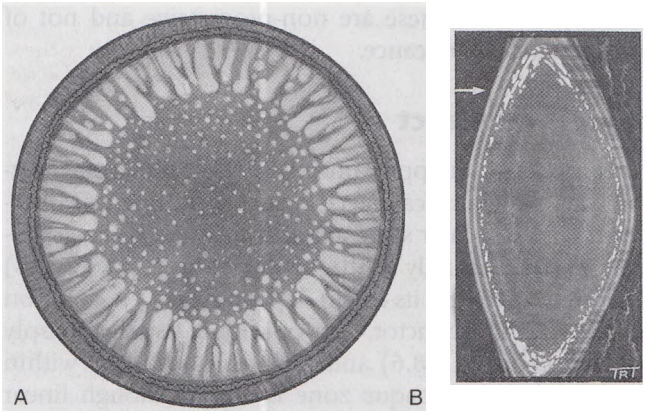


Fig. 18.7 (A) Coronary cataract by oblique illumination; (B) in optical section with the beam of the slit-lamp.

congenital. More commonly the condition is acquired, and follows contact of the capsule with the cornea, usually after the perforation of an ulcer in ophthalmia neonatorum. Where contact has occurred, usually in the central pupillary area, a white plaque forms in the lens capsule, which sometimes projects forwards into the anterior chamber like a pyramid (*anterior pyramidal cataract).* Occasionally, the underlying layers of cortex are opaque forming an *anterior cortical cataract.* When this occurs it may well be that the subcapsular epithelium grows in between the capsular and cortical opacities so that the clear lens fibres subsequently growing from there lay down a transparent zone between the two opacities. The buried opacity is called an *'imprint'* and the two together constitute a *reduplicated cataract.* Such opacities are not progressive and rarely interfere with vision.

Posterior capsular (polar) cataract

This is due to persistence of the posterior part of the vascular sheath of the lens. In minimal degrees it is common and usually insignificant. Sometimes, however, particularly in cases with a persistent hyaloid artery, the lens is deeply invaded by fibrous tissue (*see also* p. 259) and a total cataract is formed.

Treatment of developmental cataract

Before planning treatment, a detailed history and careful clinical evaluation including laboratory tests to look for the underlying aetiology (Table 18.4) are mandatory. Basic assessment of the child's vision and ocular status must be done. This includes recording the intraocular pressure and fundus examination under dilatation to rule out associated diseases such as retinoblastoma. B-scan ultrasonography is useful in assessing the posterior segment of the eye to rule out an associated retinal detachment or retinoblastoma in a child with total cataract in whom the fundus is not visible. A-scan ultrasonography

Table 18.4 Laboratory investigations for the diagnosis of bilateral, non-hereditary paediatric cataract

Blood tests
- Serum biochemistry for levels of blood glucose, calcium and phosphorus
- Red blood cell transferase and galactokinase levels
- Serology for estimating the titres of antibody for infections such as toxoplasmosis, rubella, cytomegalovirus and herpes simplex virus (TORCH) and hepatitis B virus

Urine tests
- Urine assay for the presence of reducing substances after milk feeding (for galactosaemia)
- Screening for amino acids in the urine (if Lowe syndrome is suspected)

to record and compare the axial lengths of the two eyes should be done. Refraction by retinoscopy under atropine should be done in partial cataracts. An assessment of the density of cataract is made based on the child's vision and the visibility of the fundus on ophthalmoscopy.

The timing of surgery, surgical technique, type of optical rehabilitation for aphakia (glasses, contact lens or intraocular lens) and the post-operative management of amblyopia are all-important issues.

Treatment is not indicated in a developmental cataract unless vision is considerably impaired. If the cataract is central and reasonably good vision can be obtained through the clear cortex around it, the child should be kept under mydriasis if required with careful follow-up to monitor the acuity of distant and near vision and look for progression of the cataract, at least until puberty. If the opacity is large or dense, an operation for removal of the cataractous lens must be undertaken. A decision on this issue depends upon whether vision with corrected refraction and retained accommodation is to be preferred to probably improved vision after operation without accommodation. Contact lenses can often be worn by relatively young children or can be made available in later life. Intraocular lenses implanted during primary surgery or secondarily at a later date are another option.

It is not advisable to operate on lamellar cataracts until the child is 1 or preferably 2 years old, but when the lens is completely opaque, or the pupil will not dilate, and when squint or nystagmus is developing, it is wise to operate at an earlier age. Moreover, the results of surgery in unilateral cataract in children are universally poor, unless the operation is carried out as early as possible within the first 6 weeks of birth and is followed immediately by the fitting of a contact lens. *The critical period for developing the fixation reflex in both unilateral and bilateral visual deprivation disorders is between 2 and 4 months of age. Any cataract dense enough to impair vision must be dealt with before this age and the earliest possible time is preferred,* provided the child is otherwise medically fit for general anaesthesia. The use of a contact lens requires the expert co-operation of interested parents and even with their cooperation binocular vision may be difficult to establish and amblyopia difficult to avoid.

Paediatric cataracts are soft and can be aspirated through incisions that are 1-1.5 mm in size at the limbus (Table 18.5). They can also be subjected to lensectomy through the pars plana using a vitreous cutting and aspirating instrument. The decision to insert an intraocular lens depends on the age of the child, laterality of the cataract, the surgeon's assessment of the family's ability to cope with handling a contact lens and personal preferences of the surgeon. Generally, intraocular lenses are favoured in children whose ocular growth is almost complete (over 2 years of age) and in those with unilateral cataract. The intraocular lens material recommended is polymethylmethacrylate (PMMA) which has been in use for more than 40 years and has stood the test of time. Newer foldable materials, particularly hydrophobic, foldable, acrylic polymer lenses are fast gaining popularity. The intraocular lens should be of a single-piece type, i.e. optic and haptics in one piece with an overall diameter not exceeding 12 mm and should be fitted in the capsular bag in the posterior chamber. The implantation of anterior chamber intraocular lenses in children was discontinued in the mid-1980s due to maj or complications including secondary glaucoma and comeal decompensation. The intraocular lens power is calculated according to the axial length and keratometry. Emmetropic power is prescribed for children over 8 years, 90% of that required for emmetropia in those 2-8 years old and 80% of emmetropic power in those less than 2 years of age to allow for any further growth of the eyeball. Post-operative management includes careful follow-up for monitoring visual recovery, treatment of amblyopia and evaluation for complications such as astigmatism, fibrinous uveitis, secondary glaucoma, lens optic capture or displacement, posterior capsular opacification (PCO), cystoid macular oedema and retinal detachment.

OTHER CONGENITAL AND DEVELOPMENTAL ABNORMALITIES OF THE LENS

Besides the various forms of *congenital cataract,* abnormalities in the shape and position of the lens occur, often associated with other malformations of the eye (Fig. 18.8).

Abnormal shape or size

In *coloboma of the lens,* there is a notch-shaped defect usually in the inferior margin; less frequently it occurs in some other part of the margin. It is due to defective development of part of the suspensory ligament.

Cataract associated with anterior persistent hyperplastic *primary vitreous (PHPV). A* total cataract is associated with a developmental anomaly related to persistence of the

Table 18.5 Surgical techniques for removal of paediatric cataract

Technique	Method	Advantages	Disadvantages	Usual indications
Lens aspiration*	Limbal route, either single incision or two-port bimanual technique, 5 mm anterior capsulorhexis^	Versatile, can manoeuvre with poorly dilated pupil, can implant intraocular lens in the bag	Theoretical risk of astigmatism and endothelial loss. Not clinically seen to be a problem	Preferred method when intraocular lens implanted
Lens aspiration with anterior vitrectomy	Limbal route, 5 mm anterior capsulorhexis, 4 mm planned posterior capsulorhexis with anterior+ vitrectomy	Reduces chances of posterior capsular opacification	Risk of cystoid macular oedema	Preferred method in infants less than 2 years of age
Lensectomy	Limbal route or pars plana route. The lens is completely eaten away with a vitrectomy instrument. Some surgeons leave a rim of capsule peripherally for secondary intraocular lens implantation	No posterior capsular opacification	Incarceration of the vitreous in the scleral incision. Surgery hindered if pupil constricted. Risk of retinal detachment	Mainly advocated for neonates and infants less than 2 years of age but is not preferred at any age by some surgeons

*Lens aspiration can be performed manually with an irrigation—aspiration cannula or by an automated electronically controlled irrigation–aspiration system.
Kapsulorhexis, see p. 563.

primary vitreous and hyaloid arterial system. The posterior capsule of the lens may be invaded by a fibro-vascular membrane, contracture of which leads to an elongation of the ciliary processes which become visible through the pupil. The eye is usually microphthalmic. The condition must be differentiated from retinoblastoma and retrolental fibroplasia. The presence of microphthalmos with visibly elongated ciliary processes usually confirms the diagnosis of anterior PHPV (*see* p. 335).

Spherophakia, microphakia and *microspherophakia* are all variants of the shape of the lens where it is spherical instead of lenticular and is smaller in size. It is frequently associated with the Weil-Marchesani syndrome in which patients are of stocky build and have small, stubby fingers.

Lenticonus is an abnormal curvature of the lens so that the surface is somewhat conical instead of spherical. It is more commonly posterior than anterior (Fig. 18.8). Posterior lenticonus is seen in Alport syndrome.

Ectopia lentis

This is a congenital dislocation or subluxation of the lens, usually upwards and bilateral. Lens displacement from its normal position is described as *subluxation of the lens* if there is a partial displacement and *dislocation* of the lens if there is a complete displacement of the lens from its normal position. The condition is often hereditary. The lens is small, but the edge is generally invisible until the pupil is dilated. The usual signs of subluxation are then seen. It is sometimes associated with arachnodactyly, i.e. in *Marfan syndrome* (usually *superotemporal* displacement) or *homocystinuria* (usually *inferotemporal* displacement).

Aetiopathogenesis

The basic *defect* is breakage or weakening of the zonules (Table 18.6). The degree of displacement depends on whether this affects only a sector or local area or the entire circumference of the lens.

Table 18.6 Causes of ectopia lentis

Familial
Autosomal dominant form
Autosomal recessive form (associated with iris coloboma, aniridia, microspherophakia, ectopia pupillae)

Other systemic diseases: Marfan, Ehlers–Danlos, Weil–Marchesani, homocystinuria, sulphite oxidase deficiency, hyperlysinaemia

Secondary to eye diseases: uveitis, hypermature cataract, pseudoexfoliation syndrome, ciliary body tumour

Secondary to trauma: (may or may not be associated with underlying defective zonules due to syphilis)

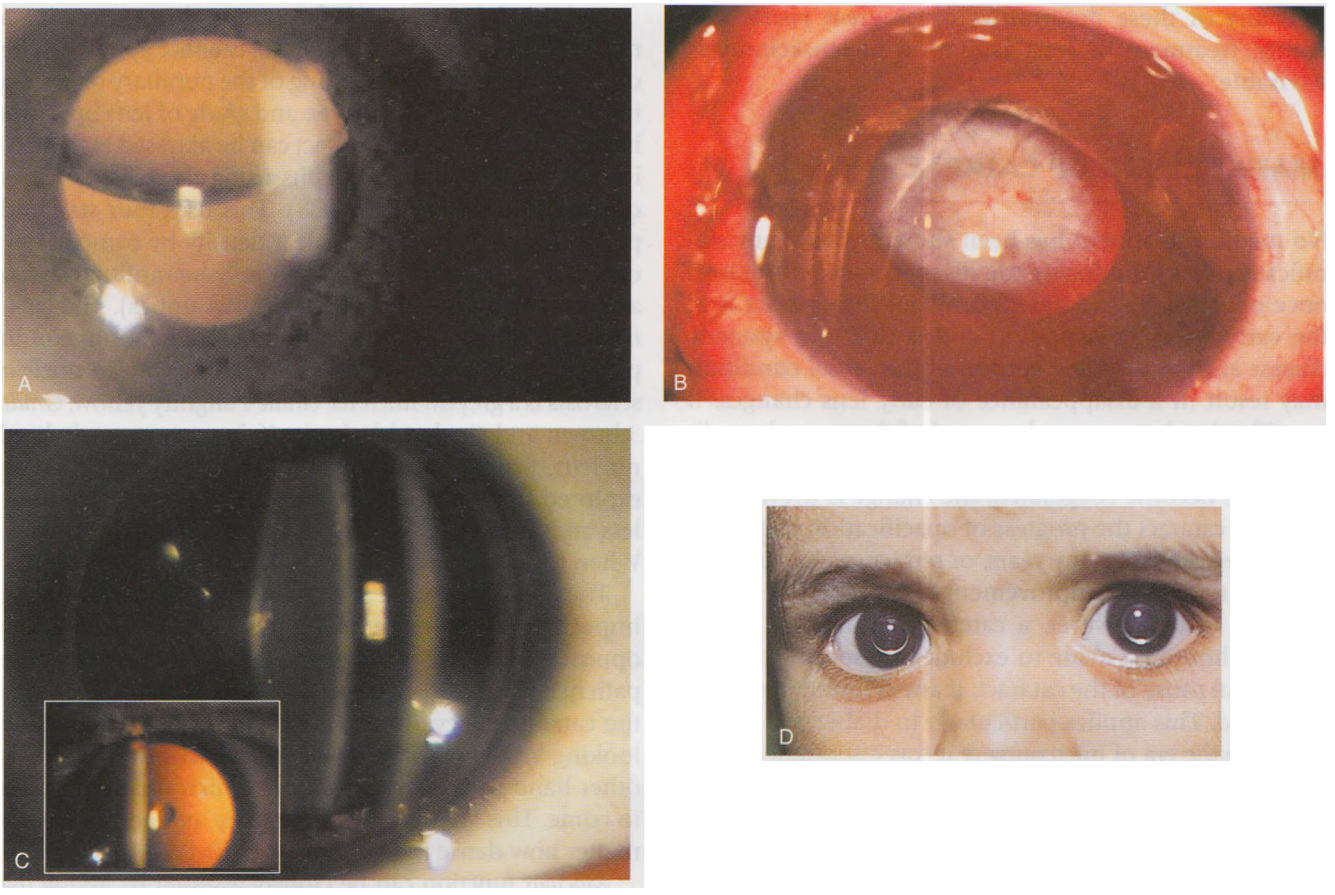


Fig. 18.8 (A) Subluxation of the lens with corectopia; (B) anterior persistent hyperplastic primary vitreous; (C) posterior lenticonus; (D) anterior dislocation of both lenses.

Marfan syndrome is an autosomal *dominant* connective tissue disorder affecting the skeletal and cardiovascular systems and the eye. Bilateral subluxation of the lens is common and retinal detachment is an important complication after surgery.

Homocystinuria: This is *transmitted* as an autosomal recessive disease. A deficiency in the enzyme cystathionine synthetase gives rise to excessive amounts of homocystine in the urine and widespread abnormalities characterized by dislocation of the lens and mental retardation. Homocystine in the urine is detected by the cyanide nitroprusside test.

In this disease, ectopia lentis becomes more marked with age and gives rise to glaucoma. Such patients are poor operative risks because of the tendency to venous thromboses. Other signs include laxity of joints and a marfanoid habitus.

Clinical features

Apart from poor vision, patients may complain of uniocular diplopia and glare. Myopia, astigmatism and reduced amplitude of accommodation are common. Loss of vision may be noticed suddenly. Signs include an obvious lens displacement; however, sometimes this may not be visible through an undilated pupil. Tremulousness of the iris (*iridodonesis*) and lens (*phacodonesis*) accentuated by eye movement, and a deep anterior chamber are other signs. The pupil should be dilated to look for the extent of displacement and assess whether the zonules are intact. The vitreous may be seen to herniate forward into the anterior chamber and glaucoma due to pupillary blockage is common. Posterior displacement of the lens into the vitreous may cause lens-induced uveitis.

Treatment

If *anteriorly* dislocated, with inverse glaucoma, the patient must be treated as an emergency. Lens removal is indicated after controlling the intraocular pressure.

If the lens is *subluxated,* the extent is assessed and refraction through the aphakic portion is performed to give the best possible correction.

If the lens is *posteriorly dislocated,* with uveitis, removal is indicated; if there is no uveitis no treatment is required.

If the vision is poor due to excessive *lenticular astigmatism* or presence of the lens edge in the visual axis, removal of the lens is required.

If any of these deformities cause great visual disability, treatment by lens aspiration or lensectomy is advisable.

MANAGEMENT OF CATARACT

No medical treatment has been shown to have any significant effect in inducing the disappearance of cataract once opacities have developed. When the cataract is at the early stages of hydration and is due to a systemic disease such as diabetes, control of the causal condition may result in a disappearance of early lens changes. If opacification has occurred, control of the general condition may stay its progress, but once the proteins of the lens have become coagulated, the change is irreversible. In senile cataract the progress of opacification may cease spontaneously for many years, or refractive changes may result in temporary improvement of vision.

In all cases, however, a careful examination of the patient should be made to exclude any specific or constitutional cause of the cataract; if any is found, it should be treated. This applies particularly to diabetes.

Before the era of microsurgery it was important to wait for total opaqueness of the lens before operating and in *incipient cataract* the condition of the patient would be much ameliorated during the tedious process of maturation by refraction, avoiding bright light and so on. The refraction, which often changes with considerable rapidity, should be corrected at frequent intervals. Some advice can be given to the patient in the initial stages of cataract with regard to the adjustment of illumination. If the pupillary area is free, brilliant illumination will be found best. If, however, the opacities are largely central a dull light placed beside and slightly behind the patient's head will allow the patient to see around the opacity. In this case, dark glasses are usually of great value and comfort when worn out-of-doors, an effect obtained with greater certainty by instilling a very weak mydriatic (phenylephrine 5%) or mydriatic-cycloplegic (cyclopentolate 0.5%) every morning, provided the angle of the anterior chamber is not narrow. Finally, in every case of incipient cataract the pupil should be dilated to allow a thorough examination of the central and peripheral fundus at the stage when it can still be seen. However, *immature cataracts are routinely successfully operated on today and the decision to operate is determined by the degree of the patient's handicap and visual need.*

When the cataract has become visually significant enough to warrant definitive intervention, the only effective treatment is its operative removal. Before this is contemplated, however, a *general examination* of the patient should be done to determine the presence of serious systemic disease. A disease such as diabetes does not preclude operation but it should be adequately controlled before and after surgery.

A *thorough examination of the eye* is also a necessity, a routine particularly vital when the cataract appears to be of the complicated type. Testing of the pupillary reflexes is important. Recording the type and grade of lens opacities is useful. The degree of cataract can be assessed by matching with standard photographs using the lens opacities classification system II (LOCS). This uses four standard photographs for grading nuclear density by comparison, or special instruments such as the Scheimpflug camera and the early cataract detector (KOWA optics). The *grading of nuclear hardness* is useful to the cataract surgeon in planning surgery by phacoemulsification. *Grade 1* nuclear sclerosis is a greyish nucleus, *Grade 2* slightly yellow, *Grade 3* brown and *Grade 4* black, signifying an extremely hard nucleus. Retinal and optic nerve function must then be explored since, if it is defective, operation may be valueless and the patient warned of possible disappointment. When the fundus cannot be seen, five tests are of value.

The detection of the *projection of light* is of the utmost importance. It is tested as follows in a dark room. The opposite eye is covered completely by the palm of the patient's hand. A bright focused light is then shone into the cataractous eye from various directions, the patient looking straight ahead. He is asked to point with his other hand in the direction from which the light seems to come. This should be done readily and accurately, no matter how dense the cataract may be.

Macular function can be crudely assessed by asking the patient to look at two 'point' sources of light 2 inches apart at a distance of 2 feet in a darkened room. If he can appreciate the presence of two lights, the central area of the retina is probably good. He should also be asked to look at a distant light through a Maddox rod; if the red line is continuous and unbroken, macular function is probably good.

An *entoptic view of the retina* will often allow the patient to supply valuable information. If the eyes are closed and the globe is steadily and firmly massaged through the lower lid with the bare lighted bulb of an electric ophthalmoscope or torch, he will see clearly the entire vascular tree of the retina on an orange ground. An intelligent patient will describe any blanks or scotomata; particular attention should be given to the central area.

Ultrasonic investigation by the B-scan technique gives valuable information concerning the posterior segment such as the vitreous and retina in cases with total cataract and no view of the retina. Gross abnormalities such as vitreous haemorrhage, retinal detachment, intraocular tumours and posterior staphyloma can be detected.

A *foveal electroretinogram* may give useful information of the functioning of this region but this test is not required in routine clinical practice.

When surgery is considered worthwhile, disease in the anterior segment should be excluded. The pupil should react promptly and normally to light and it should dilate readily with mydriatics, while the most careful search

must be made for precipitates on the back of the cornea. When the cataract is complicated by intraocular disease, treatment must be directed in the first place to rendering it quiescent. Some cases are not suitable for operation, mostly on account of cyclitis or defective projection of light, but even in these, if there is a possibility of success, operation may be undertaken after warning the patient of a guarded or possibly poor prognosis, for the loss of such an eye weighs little against a reasonable probability of improved vision. In such cases, also, in which an inflammatory condition may be expected to flare up, topical and oral administration of steroids is often of great value in forestalling or controlling a relapse.

The possibility of infective complications should be excluded as far as possible. Gross focal sepsis, such as abscessed teeth, should be eliminated. The conjunctival sac should be examined, and any infection cleared up by suitable antibiotic treatment. Finally, the lacrimal sac should receive attention. If regurgitation is found on pressure (*see* Chapter 29) or a mucocele is present, a nasal drainage operation should be performed first.

The *presence of increased intraocular pressure* constitutes an anxiety in operating for cataract. The tension may be raised owing to the swelling of the lens in the incipient stage, or due to phacolytic glaucoma, in which case an extraction is indicated. On the other hand, primary glaucoma may be pre-existent. If the glaucoma is medically controlled, the lens may be extracted and the treatment continued; if it is not, probably the best procedure is to perform a trabeculectomy followed later by cataract extraction, or a combined procedure.

In some cases, eyes with cataract have already had surgery for simple glaucoma. Theoretically, it is obviously objectionable to make a cataract incision through a drainage area, but although such cases often do well it is probably better to make the incision in the upper part of the cornea in front of the drainage area. A safe alternative is to make the incision for the cataract extraction in an area separate from the filtering bleb, as on the temporal side.

CATARACT SURGERY

Cataract surgery or removal of the crystalline lens is performed if the lens is causing visual loss by virtue of opacification (cataract), displacement from its normal position (subluxation or dislocation), defect in shape (coloboma, lenticonus, spherophakia) or lens-induced complications such as phacolytic uveitis or glaucoma, phacoanaphylactic endophthalmitis, phacomorphic glaucoma or lenticular tumour. There are different methods of cataract surgery.

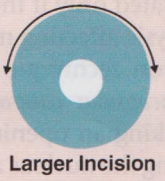
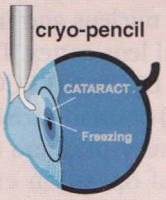
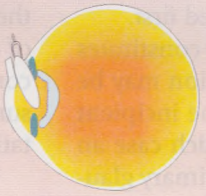
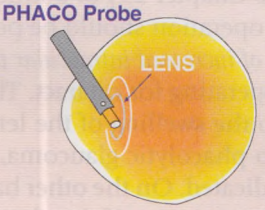
A method (now becoming obsolete) by which the entire lens including the capsule is removed by rupturing the zonules is termed *intracapsular cataract extraction* or *ICCE*) (Fig. 18.9A). This can be done mechanically by pulling on the lens with a special forceps to hold the lens capsule, cryoextraction using a cryoprobe to freeze and hold the lens or by inducing the lens to slide out or tumble out using a lens hook and spatula. The technique is no longer used because of the large incision needed, inability to implant a posterior chamber intraocular lens, and a high rate of complications particularly astigmatism, vitreous loss, retinal detachment and cystoid macular oedema (Fig. 18.9B). This technique is therefore indicated only if the lens is dislocated or there is zonular dialysis affecting more than 180°.

The extraction technique which has replaced ICCE is that of *extracapsular cataract extraction* or *ECCE.* This is done by making an opening in the capsule (capsulotomy), removing the nucleus and washing out the cortical substance (Figs 18.9Aand 18.10). There are different techniques of performing extracapsular cataract extraction. They vary in terms of incision size, shape of capsulotomy, instruments used for capsulotomy, technique of removing the hard lens nucleus and instruments used for removal of the residual lens cortex. The different methods are: (i) conventional ECCE; (ii) ECCE by small-incision cataract surgery (SICS) or small-incision manual nucleus fragmentation; (iii) lensectomy and (iv) phacoemulsification.

The type of operation employed depends upon the case. In young patients up to the age of 30 years, lens aspiration or lensectomy (Table 18.5) is usually effective. In older patients, the nucleus of the lens is hard and must be extracted. This is done by either manually delivering the lens or fragmenting the lens within the eye or emulsifying and aspirating the pulverized nucleus.

The pupils must be dilated pre-operatively for all types of ECCE to enable the surgeon to view the periphery of the lens and thoroughly remove the lens cortex including the portion normally hidden by the iris. The pupils are usually dilated using a combination of medications which includes topical cycloplegics which paralyse the sphincter pupillae (cydopentolate, tropicamide, or homatropine drops in adults and the same or atropine ointment in children with pigmented irides), mydriatics which stimulate the dilator pupillae (phenylephrine) and non-steroidal anti-inflammatory agents (diclofenac or ketorolac). The latter inhibit prostaglandin release from the iris on mechanical stimulation during surgery and prevent intra-operative miosis, so that a dilated pupil for adequate view is maintained during surgery.

Surgery is performed under some form of anaesthesia. General anaesthesia is used for children, psychiatric patients and those suffering from dementia or Alzheimer disease. All others are operated under local anaesthesia (regional block or topical). A regional block (peribulbar, parabulbar or retrobulbar injections of 2% lignocaine with or without a facial nerve block) provides akinesia as well as anaesthesia and is the method used for routine ECCE.

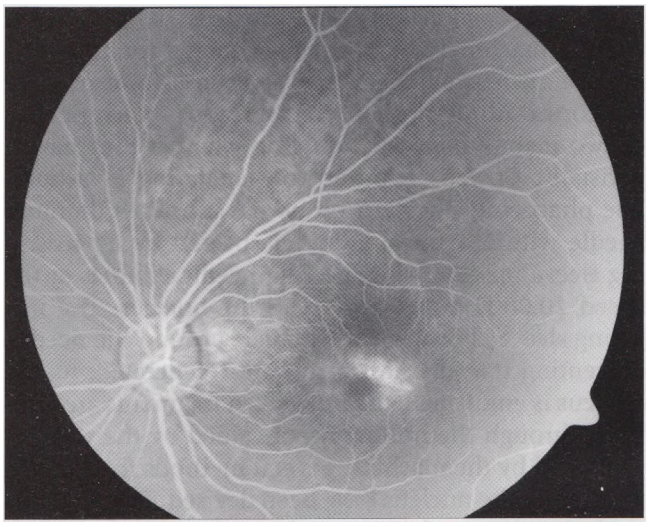
	Intracapsular cataract extraction (ICCE)	Extracapsular cataract extraction* (ECCE)	Phacoemulsification
General principles	Whole lens removed with intact capsule	Lens nucleus and cortex removed leaving the capsular bag behind	Same as ECCE
Dilatation of pupil	Not required	Required	Required
Magnification	Binocular loupe or Microscope	Microscope	Microscope
Incision	Large, 180°, 10–12 mm	Medium, 120°, 7–8 mm	Small, 30°, 3.2–3.5 mm
			
Lens removal	Intact lens delivered		
			
Capsulotomy		'Can-opener' or rhexis	Rhexis
Nucleus delivery		manual sliding	Phacoemulsification
Cortex removal		Irrigation aspiration, Manual or automated	Irrigation aspiration, automated
Intraocular lens	Anterior chamber or none	Posterior chamber 'in the bag'	Posterior chamber 'in the bag'
Sutures	Required, continuous or interrupted (5–7)	Required, continuous or interrupted (3–5)	Not required

'Conventional ECCE. Small-incision 'non-phaco' cataract surgery (SICS) is similar except that a sclerocorneal tunnel incision of 5–6 mm is made and the nucleus fragmented in the eye or delivered with the help of hydrostatic pressure by 'hydroexpression' or 'viscoexpression'.

Fig. 18.9 (A) The principles of various types of cataract surgery.

Topical anaesthesia with paracaine, ophthaine or 2% lignocaine jelly supplemented with intracameral injection of preservative-free lignocaine, if required, provides only anaesthesia and is suitable only for phacoemulsification in willing patients. Conventional ECCE requires a large incision of 7-8 mm at the limbus to deliver the nucleus of the lens. As the incision is large, the wound has to be sutured with three to five fine nylon sutures (10-0 monofilament nylon) and wound healing requires 4-6 weeks after which the sutures can be removed. Associated problems include astigmatism and delayed optical and physical rehabilitation. Small incision cataract surgery or SICS overcomes these problem by permitting surgical extraction of the lens through a smaller wound which is self-sealing because of its valvular nature and can be left without a suture or at the most will require a single suture.

Phacoemulsification is today the most popular method worldwide and has now virtually replaced all other techniques in most countries. The nucleus is emulsified by a phacoemulsifier and the lens matter removed by suction while a physiological aqueous substitute such as balanced salt solution (BSS) replaces the evacuated fluid under electronic control. This technique requires a small incision and the surgery is sutureless (Fig. 18.11). Even through the cost of equipment is high, the overwhelming overall benefits of this technique have made phacoemulsification universally acceptable as the preferred technique for cataract extraction across the world. In



Fig, 18.9 (B) Late phase of fluorescein angiography in a patient who complained of diminution of vision 3 months after uncomplicated ICCE. There is petalloid hyperfluorescence in the macular region typical of cystoid macular oedema.

developing countries, a low-cost alternative in the form of manual SICS is still operationally used.

Cataract surgery is performed with an operating microscope. The eye is first cleaned externally with 5 or 10% povidone-iodine lotion applied to the skin of the eyelids and allowed to dry. A spirit swab can additionally be used to clean the area again. One drop of 5% povidone-iodine solution is instilled into the conjunctival sac to eliminate local saprophytic microbiological flora. A sterile, self-adhesive plastic drape is applied to the skin on and around the eyelids and the eyelashes are excluded from the operative field by folding the edges of the drape around them and inserting a self-retaining speculum to hold the lids open.

There are numerous variations in the choice of surgical technique and only the general principles are briefly described here. The site of incision can be superior or temporal. The incision could be at the limbus after cutting the conjunctiva and cauterizing bleeding vessels, or 'clear corneal' just anterior to the limbus. The incisions can be uni-, bi- or triplanar and can be made with disposable blades or reusable sharp diamond blades of various sizes and shapes. For phacoemulsification, a main valvular incision is made using a keratome and one or two side ports or stab incisions are made for bimanual control or manipulations using a lanceolate knife such as an MVR or 15° blade. The anterior chamber is filled with an ocular viscosurgical device (OVD)—previously termed viscoelastic. These are transparent viscous materials and are useful in replacing the aqueous and maintaining the depth of the anterior chamber to facilitate surgical manoeuvres without damaging the delicate corneal endothelium. They are of two main categories: (i) dispersive such as hydroxypropyl methylcellulose (HPMC) 2% and chondroitin sulphate; and (ii) viscoadhesives such as sodium hyaluronate 1, 1.4 and 5%.

After injecting viscoelastic material in the anterior chamber, an opening is made in the anterior capsule of the lens (*capsulotomy*). An initial nick is made with a bent 26 gauge disposable needle and the capsulotomy completed by multiple perforations in a circular pattern (can opener), superior linear or curved opening (endocapsular envelope technique), or the flap is torn off in a continuous curvilinear fashion (continuous curvilinear capsulorhexis) using either the bent 26 gauge disposable needle, an irrigating cystotome or a capsulorhexis forceps to tear the capsule. Trypan blue dye can be used to stain the lens capsule for better visibility. A bubble of air is injected in the anterior chamber, a few drops of Trypan blue dye is injected underneath the air bubble on the anterior lens capsule and spread evenly on the surface which stains in a few seconds. The air and residual dye are irrigated and washed out of the eye using BSS and then replaced with viscoelastic to fill the anterior chamber before proceeding with the capsulorhexis.

After completing the capsulotomy, a fine, 2 7 gauge blunt-tipped cannula is used to inject BSS under the lens capsule to separate the cortex from the capsule. This is termed *hydrodissection.* BSS is also injected at the junction of the central dense core of the nucleus to separate the hard nucleus from the relatively softer epinucleus, termed *hydrodelineation* if

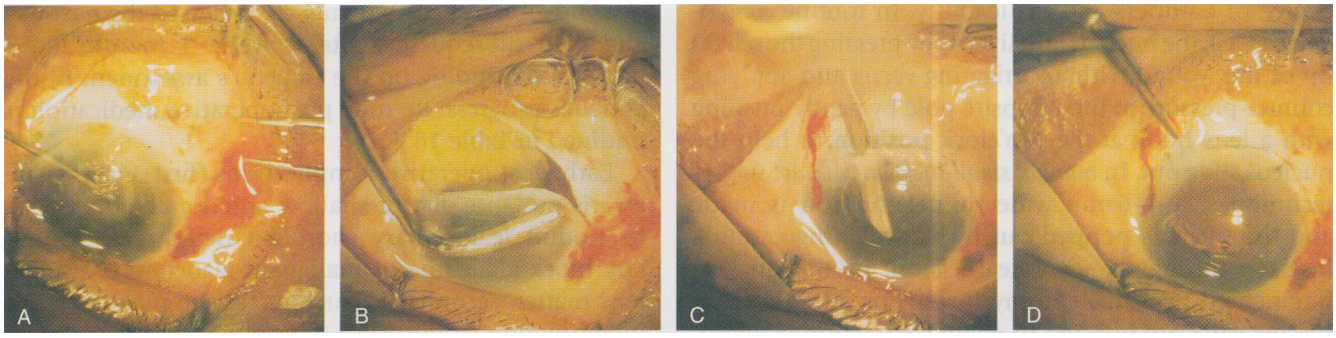


Fig. 18.10 Extracapsular cataract extraction: (A) Anterior capsulotomy; (B) delivering the nucleus; (C) removal of the residual cortex by irrigation–aspiration; (D) implantation of a posterior-chamber intraocular lens.

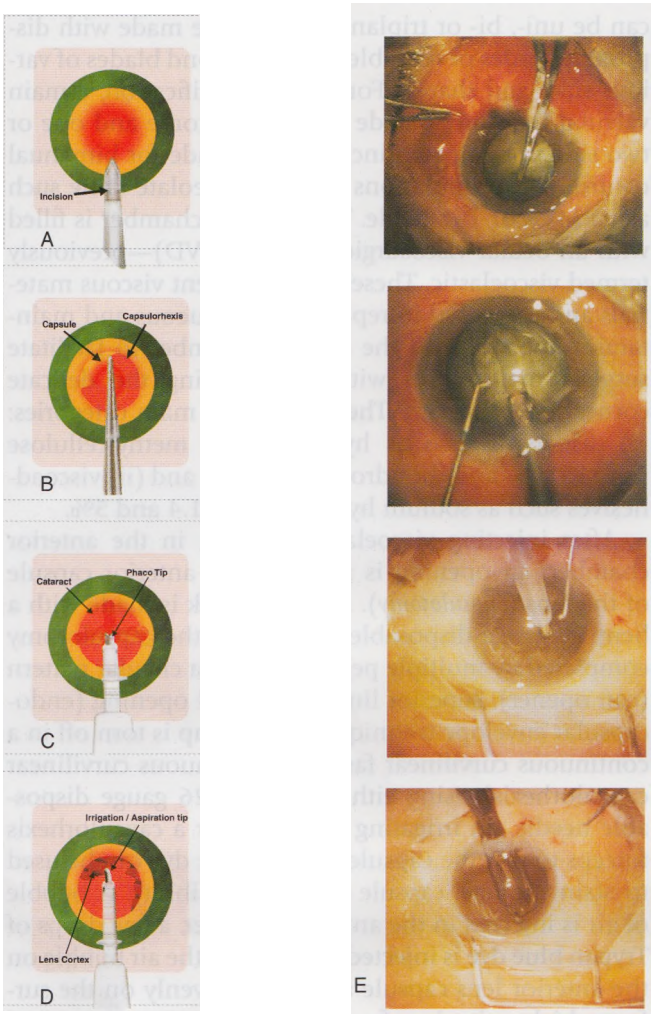


Fig. 18.11 Phacoemulsification: (A) Incision with a keratome; (B) anterior capsulotomy by capsulorhexis assisted by the use of Trypan blue dye; (C) phacoemulsification of the nucleus; (D) aspiration of the residual cortex by automated irrigation–aspiration; (E) implantation of a foldable intraocular lens.

performing a small incision, manual non-phacoemulsification cataract surgery or phacoemulsification.

The nucleus is then delivered in conventional ECCE by enlarging the incision to about 8 or 9 mm (10-2 o'clock), depending on the pre-operative assessment of nuclear size, degree of hardness and malleability. In routine *conventional* ECCE the nucleus is delivered by pressing the scleral lip of the wound with an irrigating vectis and applying counter-pressure at the opposite pole by gently pushing with a lens hook at the 6 o'clock position to help the nucleus slide out. In *manual small-incision cataract surgery* techniques, a 4-6 mm wide tunnel incision is made and the nucleus popped out by an irrigating cannula inserted through a separate incision, or the nucleus fragmented by a nucleotomy forceps or other devices. Viscoelastics are injected to enable extraction by viscoexpression.

In *phacoemulsification* the nucleus is emulsified using a machine which provides energy for emulsifying the nucleus and generates a vacuum for aspirating the cortex. Modern phacoemulsification machines are of two main types, depending on whether they have a peristaltic or Venturi pump for generating a vacuum. The phacoemulsification probe has a hollow titanium needle within a metallic barrel covered by an irrigating sleeve made of silicone. The needle vibrates at the speed 20,000 Hz and pulverizes the nucleus. The irrigating sleeve allows BSS to circulate around the needle, preventing transmission of the heat generated. As the nucleus is emulsified, the pulverized fragments are aspirated through the hollow needle aided by the vacuum generated by the machine. Several methods for efficient removal of the nucleus have been devised. The methods are being constantly improved to minimize the risk of complications, particularly tearing of the capsule and dropping of the nucleus into the vitreous, and corneal endothelial damage.

Residual cortical matter is aspirated manually using a two-way irrigation-aspiration cannula or an automated irrigation-aspiration probe. A posterior chamber intraocular lens is then implanted in the bag. In case of complications it may be necessary to implant the lens in the ciliary sulcus anterior to the remnant of the anterior capsule or in the anterior chamber.

Residual viscoelastic substances are aspirated at the end of surgery. The wound is then sutured with 10-0 monofilament nylon interrupted or continuous sutures in ECCE. In phacoemulsification with a foldable lens, the small valvular incision is self-sealing and does not need to be sutured.

Complications due to the local anaesthesia include retrobulbar haemorrhage, inadvertent perforation of the globe, oculocardiac reflex and accidental intracranial spread of the anaesthetic. Common complications during surgery include injury to the cornea such as detachment of Descemet's membrane, damage to the endothelium, vitreous upthrust, zonular dialysis (tearing of the zonules), posterior capsular tear with or without vitreous loss, falling back of the nucleus into the vitreous cavity, and expulsive choroidal haemorrhage.

Following surgery, patients are reviewed the next day and then subsequently after 1 week, 1 month and 3 months, depending on the surgeon's assessment of the patient's progress. Routine post-operative medication is outlined in Table 18.7.

Early post-operative complications (first 3 weeks) are an iris prolapse, flat or shallow anterior chamber (due to wound leak, ciliary choroidal detachment, pupillary block glaucoma or malignant glaucoma), residual lens matter, secondary glaucoma, severe post-operative inflammation (iridocyclitis, phacotoxic uveitis and phacoanaphylactic uveitis) and endophthalmitis.

Table 18.7 Summary of post-operative medication and care

	Extracapsular	Phacoemulsification
	Cataract extraction	
Topical steroid-antibiotic eye drops*	6-8 weeks	3-4 weeks
Topical mydriatic-cycloplegic	1-2 weeks	1-2 weeks
Topical medication to reduce the intraocular pressure	1-2 weeks	1-2 weeks
Refraction and prescription of glasses	6-8 weeks*	1-2 weeks
General precautions, restriction of physical activity	6-8 weeks	1-2 weeks

'Some surgeons use non-steroidal anti-inflammatory agents.
tFollowing ICCE and ECCE, sutures are removed at this stage.

Late adverse effects of cataract surgery are cystoid macular oedema, posterior capsule opacification ('after cataract' or secondary cataract), anterior capsule contraction or phimosis, retinal detachment, corneal endothelial decompensation (aphakic or pseudophakic bullous keratopathy) and intraocular lens malposition in the form of 'windshield wiper' syndrome where the intraocular lens haptic rubs on the endothelium, 'sunset' syndrome (inferior subluxation), 'sunrise' syndrome (superior subluxation), lens optic capture by the iris, or complete dislocation of the intraocular lens.

OPTICAL REHABILITATION OR CORRECTION OF APHAKIA

Removal of the cataractous lens renders the patient aphakic, which is a refractive state of extreme hypermetropia, with the exception of patients with high axial myopia whose refractive error may remain slightly myopic or become mildly hypermetropic after undergoing lens exttaction. For the patient to be able to see clearly some form of optical rehabilitation must be provided. This may be in the form of spectacles, contact lenses or an intraocular lens. Aphakic spectacles and contact lenses have inherent disadvantages (Table 18.8) and implantation of an intraocular lens after removal of the lens is the norm today and is in fact considered to be very much a part of cataract surgery. All patients, including those with intraocular lens implants, must be prescribed additional optical correction in the form of reading glasses due to a loss of accommodation after removal of the natural crystalline lens.

Intraocular lenses

The best optical rehabilitation following removal of a cataractous lens is implantation of an intraocular lens (Table 18.8). The first intraocular lens was implanted in a human eye by Sir Harold Ridley at St Thomas Hospital in London on 29 November 1949. This historic milestone in medical science marked the beginning of a new era in rehabilitation of patients with cataract. Generations of research and clinical practice have led to progressive technological advances which have led to the evolution of the intraocular lenses that are currently being used. Modern day intraocular lenses are made of different materials (Table 18.9) and are of different designs (Fig. 18.12). The central part overlying the optic axis is called the *optic* and the peripheral arms used for placement and stabilization are the *haptics.* They vary in material, polymethylmethacrylate, hydroxyethylmethacrylate, hydrophobic, hydrophilic or silicone; rigidity, rigid or flexible; optic size (5.0-7.0 mm), optic-haptic junction and material (single piece, three piece), different types of haptic angulation relative to the plane of the optic (usually posterior chamber intraocular lens have a 10° anterior angulation to keep the optic away from the pupil, and anterior chamber lenses have posteriorly angulated haptics to vault the intraocular lens away from the pupil), shape (round or oval; spheric or aspheric; planoconvex or biconvex), edge (square or rounded) and presence or absence of holes in the optic to assist in positioning of the intraocular lens. Intraocular lenses are specifically designed according to the intended location (posterior chamber, anterior chamber and scleral fixated) keeping in view the local anatomy; they must be selected and inserted accordingly. The lens is best placed in the posterior chamber in the capsular bag. In the event of some complication during surgery such as a posterior capsule tear or zonular dialysis, this is not possible. Alternative positions for a posterior chamber intraocular lens include lens placement in the ciliary sulcus supported by the remnant of the anterior capsule. If this is not feasible a lens is inserted in the anterior chamber supported by the angle of the anterior chamber.

The power of the intraocular lens to be implanted is calculated by various formulae. The most widely used formula is the modified Sanders-Retzlaff-Kraff (SRK) formula, which is based on a statistical correlation

Table 18.8 Comparison of different optical devices for refractive correction of aphakia

	Comfort and convenience	Optical aberrations	Aniseikonia* and related symptoms	Indications
Spectacles	• Heavy • Patient 'blind' without glasses • Cosmetically poor	• Visual distortion, pin-cushion effect because of relative central magnification • Restricted field with 'jack-in-the-box' phenomenon[1]" and roving ring scotoma*	Magnification of 20-30% so produces diplopia	Fellow eye aphakic and good vision with previous aphakic correction; high axial myopia with intraocular lens power <8 D; patient refuses intraocular lens implantation
Contact lenses	• Stringent daily schedule for cleaning and maintenance • Insertion and removal cumbersome • 'Blind' without lenses	Nil	Magnification about 8%, tolerable	Young children <2 years
Intraocular lenses	Comfortable in every way	Nil	Magnification 1-2%, negligible	Universal

'Aniseikonia: A difference in size of images perceived by the two eyes. Occurs because of magnification due to the optical correction.
◆'Jack-in-the-box': images suddenly pop into view.
◆Roving ring scotoma: images suddenly disappear from view.

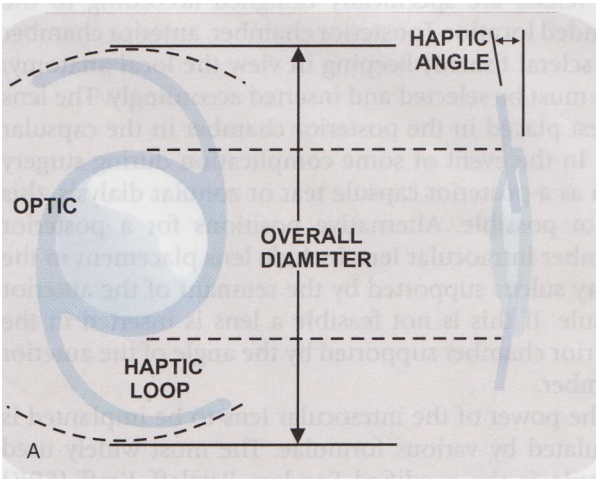
Table 18.9 Materials for manufacturing intraocular lenses

Optic materials	Haptic materials
Non-foldable	• Polypropylene
• Polymethyl methacrylate (PMMA)	• PMMA
Foldable	• Acrylic
• Silicone	
• Hydrophobic acrylic	
• Hydrophilic acrylic	

between calculated and observed refractive error after intraocular implantation. The parameters used in the formula are estimated by A-scan ultrasonographic biometry and keratometry. If A is a pre-determined constant for each intraocular lens and E is the emmetropic power designated for the eye in question,

$$E = A - 2.5\,L - 0.9\,K$$

where L is the axial length in mm and K is the average of the keratometry readings.



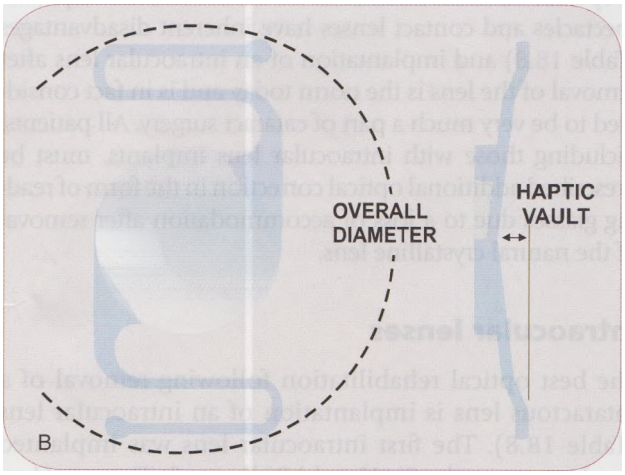


Fig. 18.12 Intraocular lens designs. (A) Posterior chamber; (B) anterior chamber.

Adjustments in the formula are required and several have been suggested such as Holladay (which is recommended for long eyeballs), SRK II and Hoffer, by determining a new intraocular lens constant, Al. The SRK II formula is detailed in Table 18.10. Another regression based formula recommended for abnormally long or short eyeballs is the SRK-T formula which is incorporated in the computer software of the IOL Master biometry machine which measures the axial length and keratometry by an optical system using a non-contact technique.

Intraocular lens power needs to be calculated carefully to meet the visual requirements of the individual patient. Correction to provide for postoperative emmetropia would result in the patient having difficulty with near vision. It is therefore common for the patient to be given an intraocular lens correction such that he can see reasonably well for near and distance, but requires a spectacle addition for best corrected vision at both distances. Further calculations are required to derive the power (J), necessary to produce the required postoperative refraction *(R)*.

I = E-cr *R*

E is derived from the modified SRK formula, and 'cr' is another empirical constant defined as

'cr '=1 if£ < 14

'cr'=1.25 if E > 14

Eyes that have undergone penetrating keratoplasty, refractive surgery or vitreoretinal surgery with the use of silicone oil require more elaborate calculations.

The intraocular lens optic may be monofocal, toric, multifocal or accommodative, but monofocal lenses with a separate pair of glasses for close work are still the most widely used. Modern day premium IOL designs have been developed to provide greater spectacle independence to take care of astigmatism, higher order aberrations and presbyopia by virtue of their design, i.e. toric aspheric, multifocal, bifocal or accommodative, respectively, but monofocal lenses with a separate pair of glasses for close work are still the most widely used.

Table 18.10 The modified Sanders-Retzlaff-Kraff formula (SRK II)

A (new IOL constant)	Axial length of the eye
A + 3	20 mm
A + 2	20 to <21 mm
A+1	21 to <22 mm
A	22 to 24.5 mm
A—0.5	>24.5 mm

COMPLICATIONS OF CATARACT SURGERY

Before surgery or pre-operative complications

- Excessive anxiety with anxiety-induced exacerbated hypertension or angina attack.
- Attack of angle closure glaucoma precipitated by dilatation of pupil for ECCE in a patient with shallow anterior chamber or swollen lens.
- Complications of anaesthesia include the following:
  - Retrobulbar or parabulbar haemorrhage.
  - Accidental perforation of the globe with intraocular injection of the anaesthetic.
  - Accidental injection into the optic nerve sheath with intracranial spread.
  - Anaphylactic shock.
  - Vasovagal reflex with collapse.

During surgery or perioperative or intra-operative complications

Poor pre-operative preparation

- Excessive bleeding from conjunctiva if conjunctival flap is made and the patient is on anticoagulants.
- Rise in blood pressure or attack of angina if patient forgot to take usual dose of medications.
- Hypoglycaemic attack if patient is fasting and has taken his antidiabetic medications.
- Patient starts moving and coughing during surgery if not properly counselled preoperatively.

Poor surgical technique

- Damage to superior rectus muscle while passing bridle suture.
- Poorly constructed wound with irregular edges.
- Damage to delicate intraocular tissues especially corneal endothelium, iris, lens zonules and posterior capsule.

Other complications

- Subluxation of lens.
- Posterior dislocation of lens.
- Rupture of posterior capsule or posterior capsular rent with vitreous loss.
- Nucleus dropping back into vitreous cavity through a posterior capsular rent.
- Expulsive choroidal haemorrhage.
- Failure to implant the intraocular lens in the bag.
- Damage to the intraocular lens with scratches on the optic or breaking of the haptic.

After surgery or post-operative complications

Early postoperative complications (within first few days to 4 weeks)

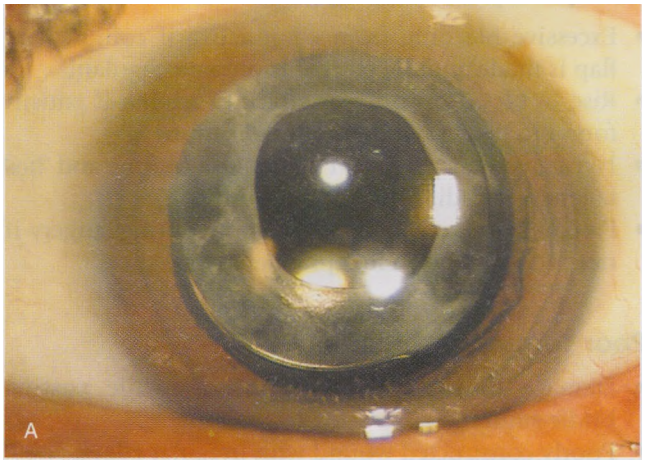
- Endophthalmitis
- Uveitis
- Retained lens matter
- Corneal oedema
- Wound leak
- Wound dehiscence
- Hyphaema
- Astigmatism
- Retinal detachment
- Posterior vitreous detachment with retinal tear or vitreous haemorrhage
- Exacerbation of diabetic retinopathy
- Refractive surprise, i.e. high refractive error due to wrong power intraocular lens
- Toxic anterior segment syndrome
- Toxic lens syndrome

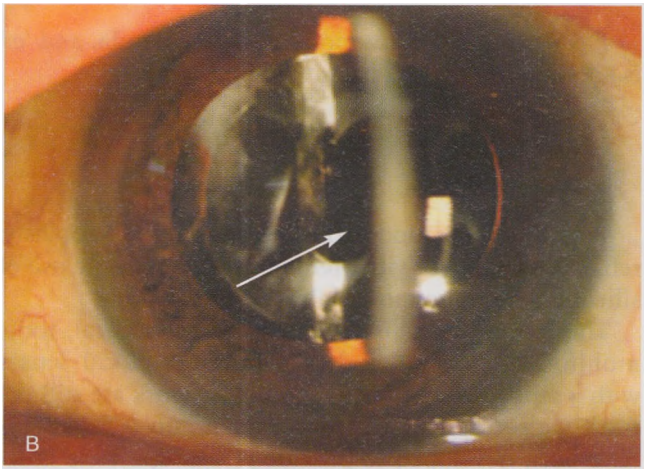
Late post-operative complications (after 1 month to years)

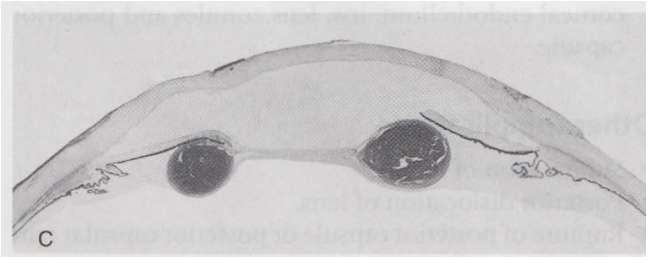
- Endophthalmitis
- Retinal detachment
- Cystoid macular oedema
- Exacerbation of diabetic retinopathy
- Displacement of intraocular lens
- Persisting astigmatism
- Secondary glaucoma
- Posterior capsule opacification
- Anterior capsule phimosis.
- Late weakening of zonules with total dislocation of lens posteriorly in capsular bag.

POSTERIOR CAPSULAR OPACIFICATION ('AFTER' OR 'SECONDARY' CATARACT)

PCO, also called 'after' or 'secondary' cataract, is the opacity which follows extracapsular extraction of the lens. In this operation the posterior and part







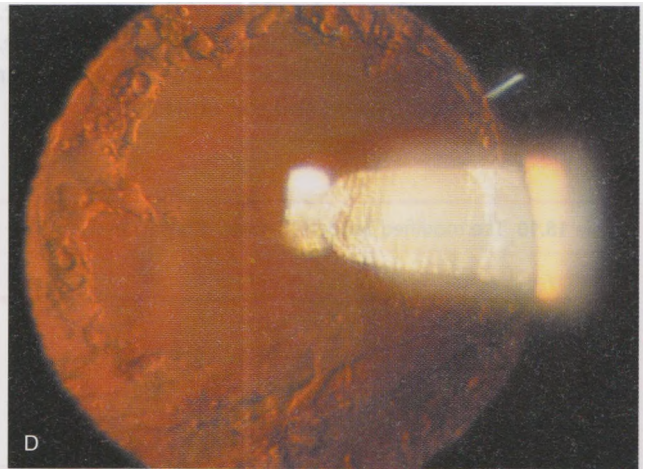


Fig. 18.13 Types of 'after' cataract. (A) Anterior capsular opacification; (B) posterior capsular opacification treated with YAG laser capsulotomy; (C) Sommerring ring (By courtesy of Ashton); (D) Elschnig pearls.

of the anterior capsule are left *in situ.* In many cases these remnants are fine, forming a thin membrane (Fig. 18.13) which is difficult to see, particularly following operation with modern suction and infusion devices. In other cases, especially when the cataract was not mature, some soft, clear cortex sticks to the capsule. This becomes partially absorbed by the action of the aqueous but often becomes shut off by adhesion of the remains of the anterior to the posterior capsule. In such cases the cubical cells which line the anterior capsule also persist; they continue to fulfil their function of forming new lens fibres, although those formed under these abnormal conditions are abortive and opaque. Sometimes these fibres, enclosed between the two layers of capsule, form a dense ring behind the iris *(the ring of Sommerring,* Fig. 18.13); it may cause subsequent trouble by becoming dislocated into the anterior chamber. At other times, the subcapsular cells proliferate and instead of forming lens fibres, develop into large balloon-like cells which some-times fill the pupillary aperture *(Elschnig pearls).* If these remnants lie in the pupillary area a dense membrane is formed so that vision is impaired. If the previous operation has been followed by iritis, exudates also adhere to the lens remnants and organize, thus contributing a fibrous membrane in addition.

The rate of posterior capsule opacification following ECCE and phacoemulsification varies with the age of the patient, the surgeon, surgical technique, the type of intraocular lens used and the duration after surgery. Higher rates (20-50% by 1-2 years) are reported in younger patients, with PMMA lenses and hydrophilic acrylic lenses. Lower rates (10-20% by 2-4 years) are seen with older patients, and those with hydrophobic acrylic lenses and new-generation silicon lenses with square posterior edges.

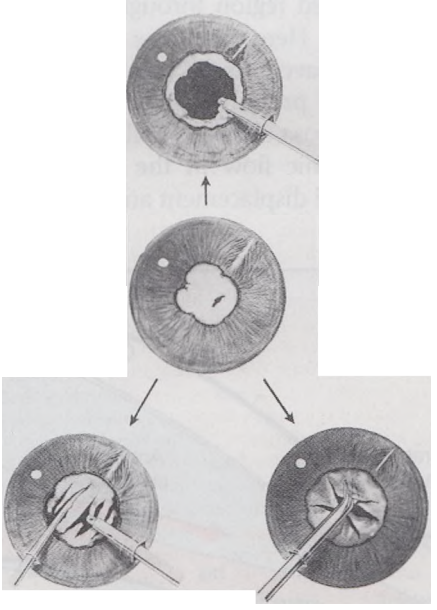


Fig. 18.14 Removal of a pupillary membrane: (A) with a vitreous cutter; (B) preliminary discission with a Ziegler knife; (C) preliminary discission with vitreous scissors. (By courtesy of Kanski)

Treatment

After' cataracts, if thin, can be cleared centrally by a YAG laser capsulotomy (Fig. 18.13). In children they are very thick and may require discission or they can be removed by a vitreous cutter alone (Fig. 18.14A). Tough and non-pliable membranes have first to be cut into smaller pieces before they can be aspirated into the cutting port. This can be done with a Ziegler knife (Fig. 18.14B), or by using vitreous scissors (Fig. 18.14C).

SUMMARY

The lens is the second most important contributor to the refractive power of the eye, the cornea being the first. The most important disease affecting the lens is cataract and its definitive treatment is surgery. Advances in operative equipment and microsurgical instruments have made cataract surgery very safe and effective in restoring vision. Smaller incision sizes achievable with the techniques of phacoemulsification and manual small incision surgery with insertion of foldable intraocular lenses or small optic phaco profile lenses has made the post-operative recovery quicker with faster optical and physical rehabilitation of the patient.

The pseudophakic patient still has to wear glasses post-operatively, and the power will depend on the power of IOL inserted and the visual requirements of the patient. Though the surgery is now safe and successful in the large majority of cases, it is not without its inherent problems and potential complications so proper preoperative counselling must be done and informed consent must be obtained before surgery.

SUGGESTED READING

1. David F. Chang, MD (ed). *Cataract and Refractive Surgery Today. Virtual Textbook of Cataract Surgery.* Retrieved August 10, 2010, from *www. crstoday. com/cvt/.*
2. Edward WM. *Pediatric Cataract Surgery: Techniques, Complications, and Management.* Philadelphia: Lippincott Williams & Wilkins.

19

The Glaucomas

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INTRODUCTION

Glaucoma is a chronic, progressive optic neuropathy caused by a group of ocular conditions which lead to damage of the optic nerve with loss of visual function. The most common risk factor known is a raised intraocular pressure. A sustained increase in intraocular pressure may be due to increased formation of the aqueous humour, difficulty in its exit, or a raised pressure in the episcleral veins. Of these, the first and last rarely occur, and it follows that raised intraocular pressure is essentially due to an increased resistance to the circulation of the aqueous at the pupil and/or to its drainage through the angle of the anterior chamber (Fig. 19.1). If the outflow pathway via the trabecular meshwork is blocked, some drainage does occur through theuveoscleral outflow, but these alternative channels are not efficient and they are incapable of dealing with sudden changes of intraocular pressure.

Pathogenesis

The pathogenesis of glaucomatous damage is attributed to a combination of factors affecting axonal health, with each factor being interlinked in its effects to all the others (Flowchart 19.1). The two main influences are:

- mechanical changes due to the rise of intraocular pressure and
- vascular perfusion of the optic nerve head.

Mechanical changes: The coats of the eye can with-stand fairly high intraocular pressures except at the lamina cribrosa, the fenestrated region through which optic nerve fibres enter the eye. Here, the nerve fibres are supported by glial tissue and have to bend over the edge of the disc. A raised intraocular pressure causes mechanical pressure on the lamina cribrosa altering capillary blood flow and decreasing axoplasmic flow in the initial stages. Later, significant backward displacement and compaction of the

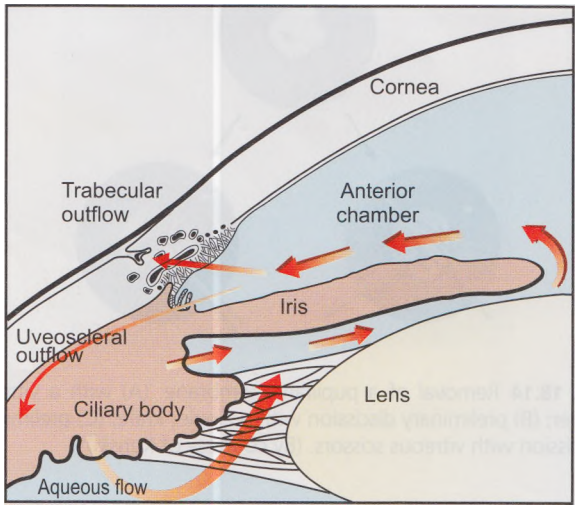
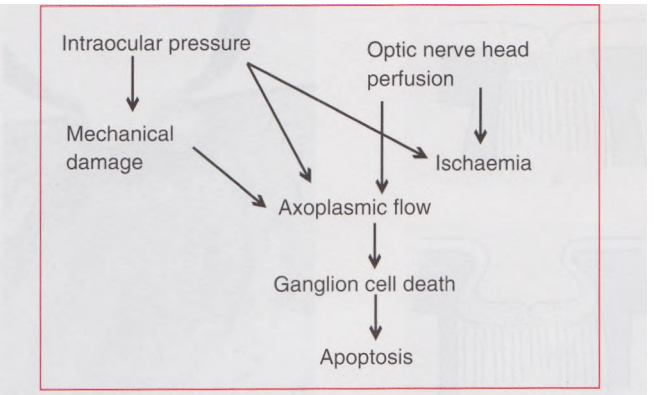


Fig. 19.1 Aqueous pathway and structures in the angle of the anterior chamber.



Flowchart 19.1 Pathophysiology of glaucomatous optic nerve damage.

laminar plates narrows the openings through which the axons pass, directly damaging the nerve fibre bundles.

Vascular perfusion: The perfusion of the optic nerve head may be affected because of a lack of an adequate autoregulatory mechanism. A substantial rise in intraocular pressure can also decrease the capillary blood flow due to mechanical compression of vessels at the lamina cribrosa or a decreased flow in the annulus of Zinn, which supplies nutrition to the laminar and post-laminar optic nerve head. A fall in perfusion pressure at the optic disc may additionally be caused by systemic factors such as hypotension, vasospasm and acute blood loss.

Other factors: It is believed that patients with primary open-angle glaucoma (POAG) have a susceptibility to damage, in some part, because of the presence of larger openings in the lamina cribrosa that allow for greater mechanical displacement of the nerve fibres coursing through.

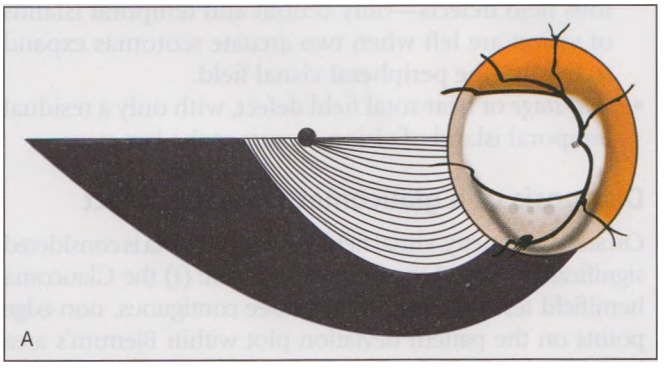
Dysfunctional axoplasmic transport, due to these mechanical or vascular changes, leads to fewer trophic factors reaching the ganglion cells. This causes damage and eventually death of the ganglion cells, which triggers apoptosis of adjacent cells. As the loss of nerve fibres extends beyond the normal physiological overlap of functional zones, visual field defects become apparent. This loss of nerve fibres is seen to occur initially and predominantly at the superior and inferior poles. The normal distribution of nerve fibres in the retina is such that polar loss of nerve fibres translates into a loss of function in an arch above and below the macular area, ending in a horizontal line nasally, with neither crossing it *(see* Fig. 19.2).

Diagnosis

The diagnosis of glaucoma is made after looking for a combination of clinical signs—characteristic changes in the optic nerve head, abnormalities in the visual field and a rise in intraocular pressure. The type of glaucoma is determined by the clinical features and the status of the anterior chamber angle as determined by gonioscopy. A diagnosis of primary open-angle glaucoma can be made if at least two of these three abnormalities are detected. In acute and subacute primary angle-closure glaucoma (PACG) and the secondary glaucomas, the presence of a raised intraocular pressure is enough to make a diagnosis of glaucoma.

Optic nerve head changes associated with glaucoma are thought to be seen prior to the development of visual field loss. The ratio of cup diameter to disc diameter is normally 0.3:1. The following changes are commonly seen in the optic nerve head in glaucoma (Fig. 19.3):

- asymmetry of the cup: disc ratio (>0.2) between the two eyes;
- a localized notch or thinning of the neuroretinal rim;
- an enlarged cup: disc ratio (>0.5), especially if in the vertical axis;
- pallor of the neuroretinal rim;
- superficial disc haemorrhages;



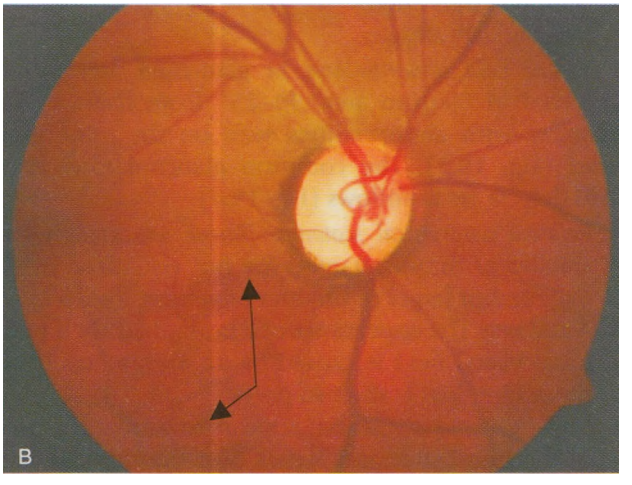


Fig. 19.2 (A) Diagrammatic representation of inferior polar narrowing of the neuroretinal rim leading to the loss of arcuate nerve fibres that arch over the macula, and end at the horizontal raphe. (B) Corresponding wedge-shaped nerve fibre layer defect seen as a dark wedge leading off from an inferotemporal notch of the neuroretinal rim.

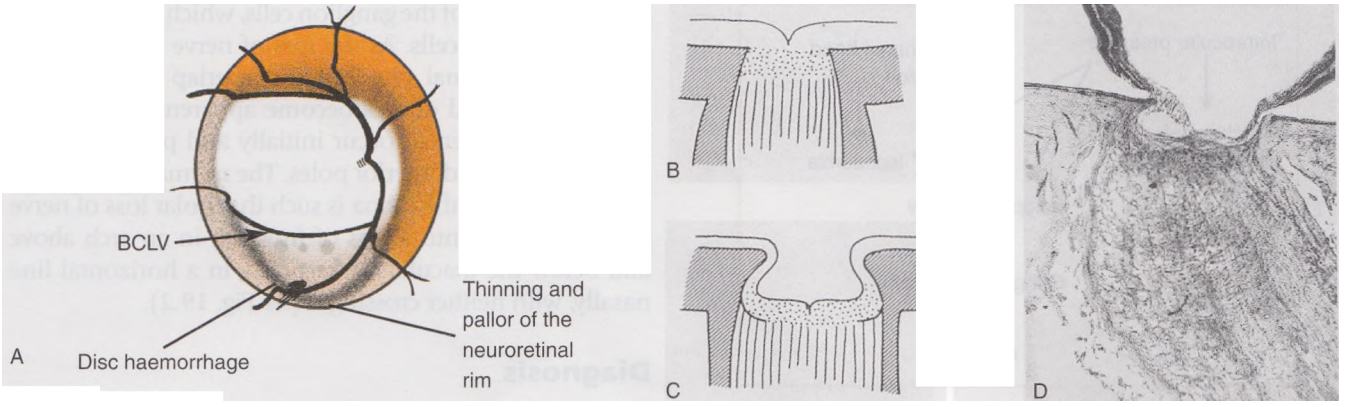


Fig. 19,3 Optic nerve head changes in glaucoma. (A) Diagram showing inferior neuroretinal thinning and pallor, baring of the circumlinear vessels, BCLV, and a splinter haemorrhage; (B) cross-sectional view of a normal optic nerve head; (C) glaucomatous optic atrophy; (D) histological section of glaucomatous optic atrophy.

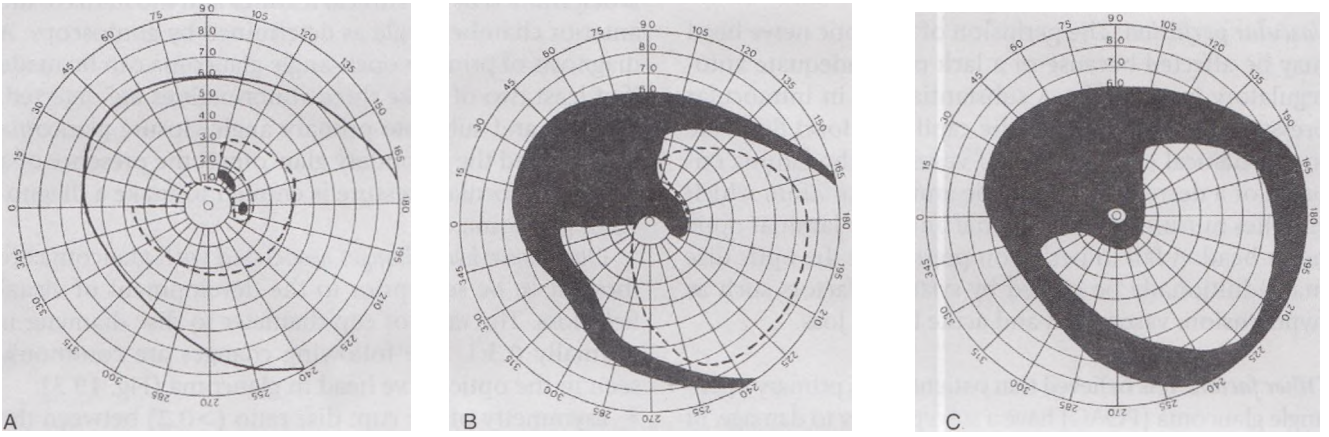


Fig. 19.4 Glaucomatous visual field changes as depicted by kinetic perimetry. (A) Early sickle-shaped Seidel scotoma (5/330, 1/2000); (B) sector defect, Roenne's nasal step and arcuate scotoma (5, 2/330); (C) double arcuate scotoma and quadrantic defect (5/330).

- vascular signs suggestive of an acquired cupping, such as baring of the circumlinear vessels and 'overpass' of central vessels and
- parapapillary atrophy.

Visual field abnormalities in glaucoma are initially observed in Bjerrum area, 10-25° from fixation, and correlate with abnormalities seen on the optic nerve head (Fig. 19.3). The common glaucomatous visual field defects are as follows (Fig. 19.4);

- *Relative paracentral scotomas:* These are areas where smaller or dimmer targets are not visualized by the patient, but larger or brighter targets are appreciated.
- *Nasal step:* The appearance of a horizontal shelf in the nasal visual field is caused by an asymmetry in the nerve fibre loss at the two poles.
- *Seidel scotoma* is one that appears to start at the poles of the blind spot and arches over the macular area, without reaching the horizontal meridian nasally.
- *Arcuate scotomas* also appear to start at the superior or inferior poles of the blind spot and arch over the macular area, widening as they curve down or up to end as a horizontal line nasally, which never crosses the horizontal divide of the visual field.
- *Double arcuate* or *ring scotoma:* Advanced glaucomatous field defects—only central and temporal islands of vision are left when two arcuate scotomas expand to involve the peripheral visual field.
- *End-stage* or near-total field defect, with only a residual temporal island of vision, occurs at the last stage.

Diagnosis of a glaucomatous field defect

On static perimetry, visual field loss in glaucoma is considered significant if one of the following is seen: (i) the Glaucoma hemifield test is abnormal; (ii) three contiguous, non-edge points on the pattern deviation plot within Bjerrum's area have a probability of <5% of being seen in a normal population, one of which should have a probability of <1% or (iii) the corrected pattern standard deviation (CPSD) should have a probability of <5%, confirmed on two consecutive tests. Print-outs of static perimetry are shown in Fig. 19.5.

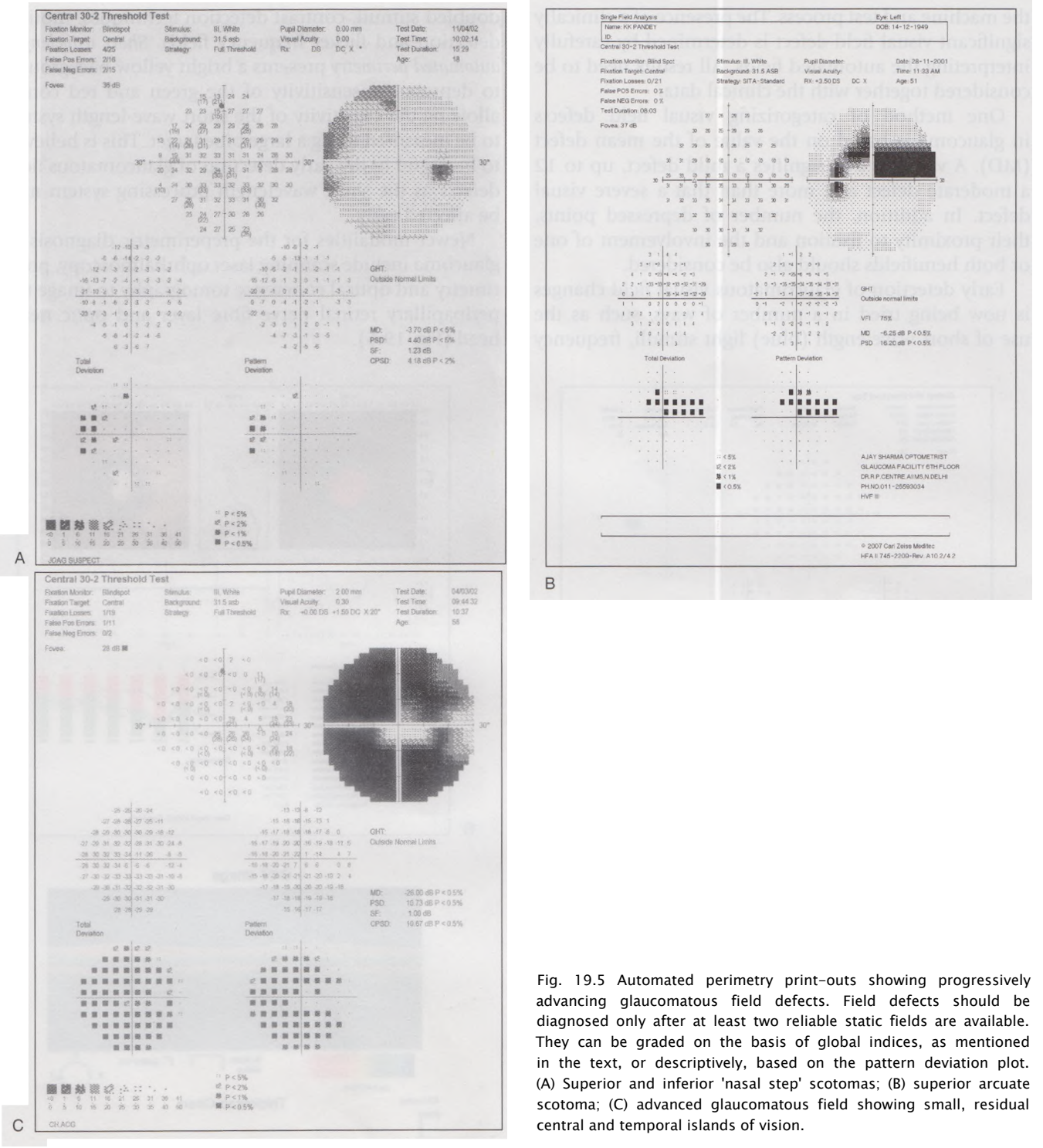


Fig. 19.5 Automated perimetry print-outs showing progressively advancing glaucomatous field defects. Field defects should be diagnosed only after at least two reliable static fields are available. They can be graded on the basis of global indices, as mentioned in the text, or descriptively, based on the pattern deviation plot. (A) Superior and inferior 'nasal step' scotomas; (B) superior arcuate scotoma; (C) advanced glaucomatous field showing small, residual central and temporal islands of vision.

The *glaucoma hemifield test* (GHT) compares the sensitivity of five clusters of points above and below the horizontal midline which resemble nerve fibre bundle patterns. This type of loss is common in glaucoma and is usually asymmetrical about the horizontal meridian. The analysis is identified as abnormal if one or more of the five regions demonstrate asymmetry across the horizontal midline which are beyond the 1% probability level for normal population values. It is regarded as borderline if the asymmetry is within the 1% probability level for all five regions, but beyond the 3% probability level for one or more regions. At least two such fields plotted on different occasions are required before a diagnosis of glaucoma can be made, as there is often a significant improvement in the field when plotted a second time because patients become more familiar with

the machine and test process. The presence of a clinically significant visual field defect is determined by carefully interpreting the automated fields. All results need to be considered together with the clinical data.

One method of categorizing visual field defects in glaucoma is based on the value of the mean defect (MD). A value of 0-6 signifies a mild defect, up to 12 a moderate defect and more than that a severe visual defect. In addition, the number of depressed points, their proximity to fixation and the involvement of one or both hemifields should also be considered.

Early detection of glaucomatous visual field changes is now being tried in a number of ways, such as the use of short wavelength (blue) light stimuli, frequency doubled stimuli, contrast detection techniques, motion detection and flicker frequency fields. *Short wavelength automated perimetry* presents a bright yellow background to depress the sensitivity of the green and red cones, allowing the sensitivity of the short wave-length system to be measured using a large blue target. This is believed to be useful in the early detection of glaucomatous field defects as the short wavelength processing system may be affected early.

Newer modalities for the preperimetric diagnosis of glaucoma include scanning laser ophthalmoscopy, polarimetry and optical coherence tomography to image the peripapillary retinal nerve fibre layer and optic nerve head (Fig. 19.6).

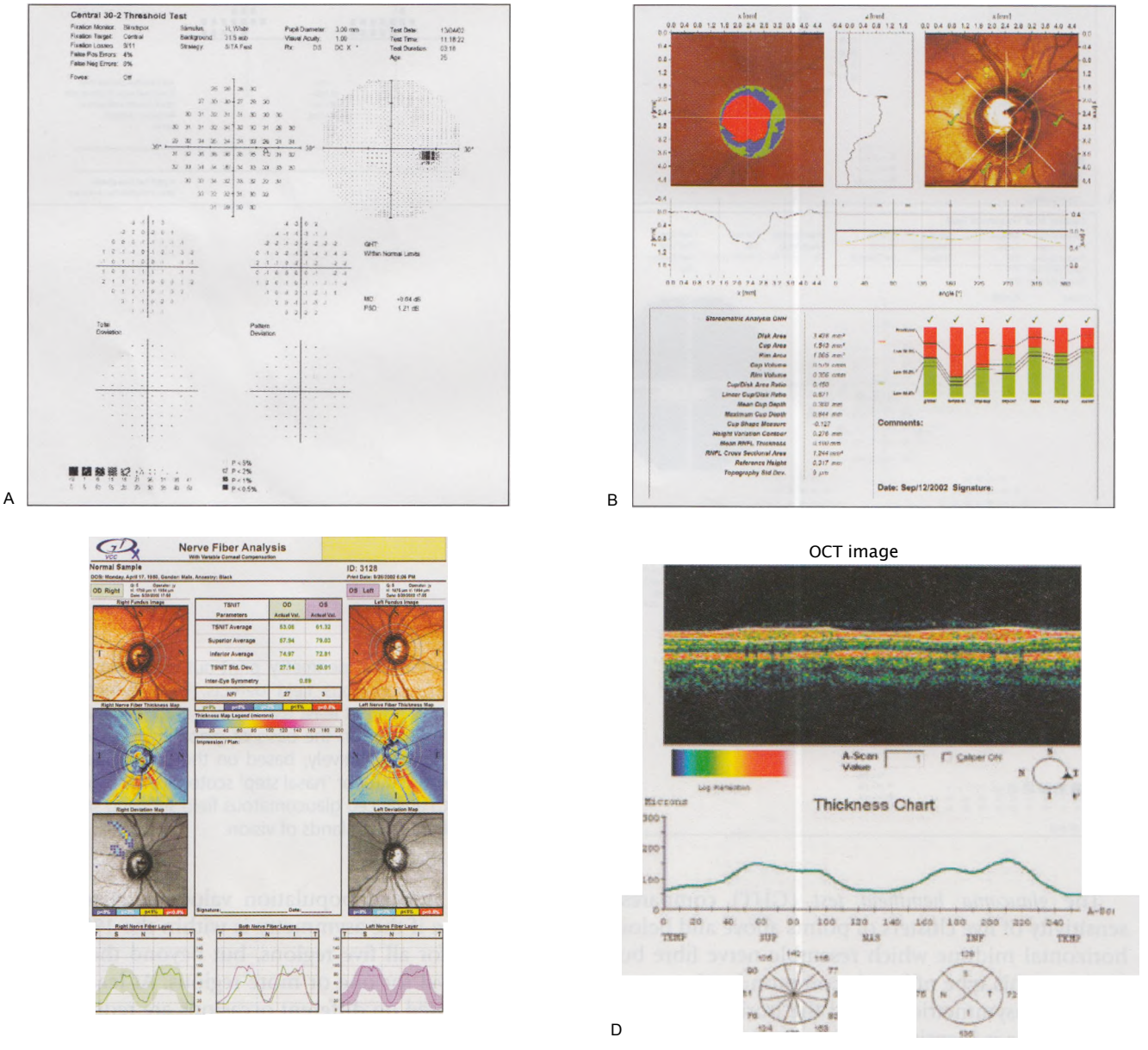


Fig. 19.6 The preperimetric diagnosis of glaucoma in eyes with no detectable visual field deficit (A) but damage to the nerve fibres can now be demonstrated using scanning laser ophthalmoscopy (B), scanning laser polarimetry (C) and optical coherence tomography (D).

Intraocular pressure changes in the glaucomas

Raised intraocular pressure is the most important risk factor for glaucoma. It must be stressed that in the initial stages the intraocular pressure is not necessarily permanently raised, and variability is an important feature. A single reading of the intraocular pressure, if normal, is therefore of no value, since this may coincide with a temporary fall to a basal pressure which may be within the normal range. A *diurnal variation in the intraocular pressure of over* 6-8 *mmHg should always raise a suspicion of glaucoma even though the reading may fall within the limits generally accepted as normal (20 mmHg).* This periodic variation in intraocular pressure can cause damage to the eye and produce field defects and cupping of the disc.

Types of glaucoma

It is convenient to divide the glaucomas into

- primary adult glaucoma which consists of two separate conditions—open-angle and angle-closure glaucoma;
- secondary glaucomas due to a specific anomaly or disease of the eye and
- congenital or developmental glaucomas.

A summary of the types of glaucomas and their distinguishing features are given in Table 19.1 *(see* p. 8 and 9).

PRIMARY ADULT GLAUCOMAS

Primary open-angle glaucoma

POAG characteristically has an adult onset and is a bilateral, almost symmetrical disease. Ocular examination would be expected to show an open anterior chamber angle, glaucomatous optic nerve head changes, visual field damage and an intraocular pressure of more than 21 mmHg recorded on at least a few occasions.

POAG is the commonest form of glaucoma in Caucasians and Africans and constitutes about half the primary glaucomas seen in Asians and Eskimos. It occurs in the elderly, rarely being seen earlier than 40 years of age, and tends to run in families. The inheritance is thought to be multifactorial and polygenic, although genetic analysis in some families with juvenile POAG has identified a link to the long arm of chromosome 1 *(see* Chapter 33). Patients who develop the frank disease probably inherit a number of abnormal genes. These genes appear to influence the height of the intraocular pressure, the facility of outflow and the cup: disc ratio. Diabetes mellitus and myopia also occur more frequently in persons with glaucoma than in the general population.

An intraocular pressure of less than 21 mmHg is recorded repeatedly in about 15% of patients with all the other features of POAG. This condition is labelled as *normal tension glaucoma.* Some individuals, physiologically, have an intraocular pressure of more than 21 mmHg, without any optic nerve head or field abnormalities and are called *ocular hypertensives.* Patients with optic nerve head changes suggestive of glaucoma, but without a raised intraocular pressure or visual field changes, are termed POAG *suspects.*

Pathogenesis

The rise in intraocular pressure in POAG is related to an increased resistance to the outflow of aqueous at the trabecular meshwork, especially at the juxtacanalicular region. In part, this is due to age-related changes in this tissue.

Clinical features

POAG is generally asymptomatic and patients may have non-specific complaints such as headache and frequent changes in presbyopic correction. Some may notice a scotoma, especially if present in the inferior field, and some experience difficulty in dark adaptation.

At least two of the first three signs detailed below must be present to make a diagnosis of POAG, in the presence of a normal, open angle confirmed by gonioscopy (Fig. 19.7A and B).

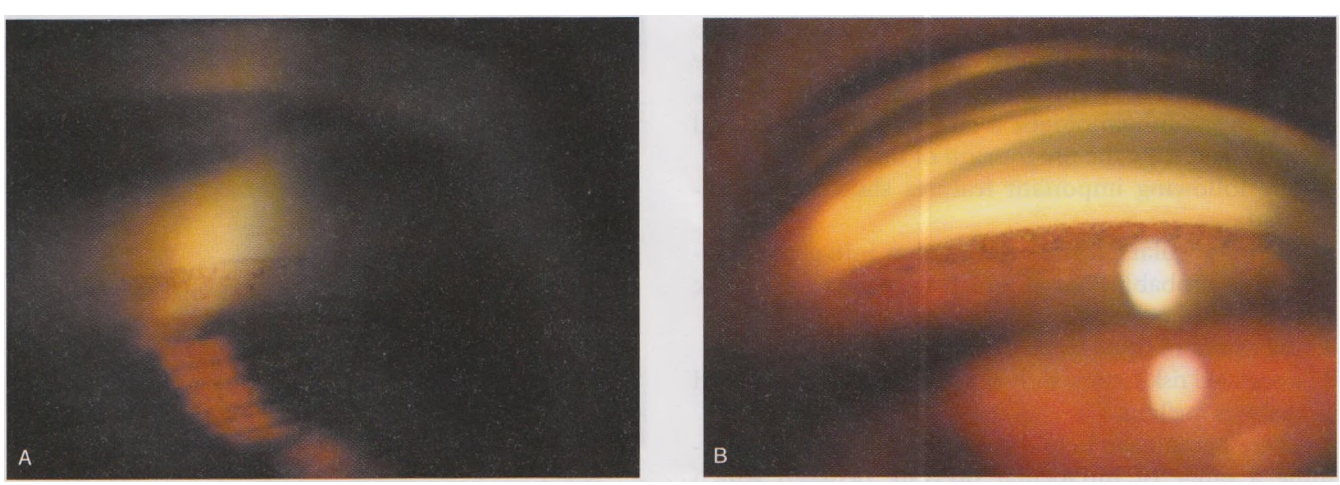


Fig. 19.7 (A and B) Gonioscopic view of an open angle of the anterior chamber in primary open-angle glaucoma.

1. An intraocular pressure of more than 21 mmHg on more than one occasion, and a circadian variation in intraocular pressure of more than 8 mmHg. There could also be an asymmetry of the intraocular pressure of more than 5 mm Hg between the two eyes.
2. The presence of optic nerve head changes suggestive of glaucomatous damage. These include a cup:disc ratio of more than 0.5, an asymmetry between the two optic nerve heads of more than 0.2, narrowing, notching or pallor of the neuroretinal rim, disc haemorrhages and abnormalities of the blood vessels suggestive of an acquired enlargement of the optic cup. Records of the appearance of the optic disc appearance over many years are imperative for the review and treatment of patients. This can be in the form of a drawing, photographs, stereophotographs or objective topography by scanning laser ophthalmoscopy.
3. Visual field changes consistent with glaucomatous defects.
4. Defects in the nerve fibre layer, which can be seen extending from the optic nerve head in an arc from the superior and inferior poles of the disc. These are best appreciated after dilatation of the pupil, and examination with a red-free light (Fig. 19.3B).

Management

Damage to the optic nerve is irreversible and it is therefore imperative to detect glaucoma early so that visual morbidity can be avoided. Patients at risk for glaucoma—those with an affected first-degree relative, diabetics and myopes—should be examined regularly after the age of 40 years. Ideally, everyone over the age of 40 years should be examined to rule out glaucoma. As it is a chronic, insidious disease, the patient requires close follow-up throughout life. A good baseline evaluation and a record of all parameters—intraocular pressure, perimetry, optic nerve head evaluation and gonioscopy—over the years should be available for proper management. Repeated gonioscopic examinations would identify eyes in which the use of miotics or age-related thickening of the lens causes a narrowing of the angle. Glaucomatous damage generally tends to occur over years, not days or weeks, giving the ophthalmologist a chance to intervene and 'modify' and slow the progression of this disorder.

The following important features should be documented:

- the intraocular pressure recorded at initial presentation is probably that at which damage to the optic nerve head occurred;
- the extent of optic nerve damage and
- associated risk factors, such as cardiovascular disease and diabetes mellitus.

These parameters help the ophthalmologist to determine a range of intraocular pressure between which glaucomatous damage is not likely to progress; this would be the *'target pressure'* for therapy in that individual. Long-term studies have shown that if the intraocular pressure is maintained at less than 16-18 mmHg, it leads to stabilization of POAG in most patients.

Treatment

Treatment options presently available can only lower the intraocular pressure. Medicines, laser or surgery can be used to achieve the set 'target pressure'. Medical and surgical therapies to lower the intraocular pressure are similar in all glaucomas and are described at the end of this chapter. Medications such as betaxolol are thought to increase the perfusion of the optic nerve head. Certain drugs such as memantine are currently being evaluated for their possible efficacy in protecting the retinal ganglion cells.

Laser therapy for POAG consists of laser trabeculoplasty. In this procedure, laser spots are applied gonioscopically to coagulate the trabecular meshwork. This causes the collapsed trabecular beams to become taut, increasing the space available for aqueous to drain out. It has also been observed that endothelial cells which migrate to cover the areas that have been subjected to laser therapy change the biochemical properties of the extracellular matrix in the trabecular meshwork. Argon, diode or frequency-doubled Nd:YAG lasers have been used to apply 50-100 spots over 180-360° of the angle (Fig. 19.8). The laser spots, each of 50 micron size, are placed at the junction of the anterior and posterior trabecular mesh-work to produce blanching of the tissues. This is followed by a transient rise of intraocular pressure which requires prophylactic treatment with topical apraclonidine or other antiglaucoma medications. The intraocular pressure falls by an average of 5-7 mmHg, but the effect is said to diminish over time. Laser trabeculoplasty is therefore indicated if medications do not adequately control the intraocular pressure or if patients are not compliant or do not want surgery.



Fig. 19.8 Argon laser trabeculoplasty. Blanched spots can be seen in the anterior trabecular meshwork.

Table 19.1 Clinical summary of the primary glaucomas

	Symptoms	Anterior segment	Gonioscopy	Intraocular pressure	Optic nerve head	Therapy
Open-angle						
Primary open-angle glaucoma	Occasional headaches, frequent change of presbyopic glasses, rarely scotomas	Normal	Open angle	Mild-to-moderate elevation	Pallor, narrowing and irregularity of the neuroretinal rim, splinder haemorrhages	• Medical: *First-line* beta-blockers, brimonidine, prostaglandin analogues *Adjunctive:* dipivefrine, dorzolamide, pilocarpine • Laser trabeculoplasty and trabeculectomy if required trabeculectomy if required
Normal tension glaucoma	Non-specific	Normal	Open angle	<21 mmHg	Pallor and irregularity of the neuroretinal rim, splinter haemorrhages	• Brimonidine, prostaglandin analogues • Trabeculectomy with antifibroblastic agents
Ocular hypertension	Nil	Normal	Open angle	Moderately elevated	Normal	• Nil • Monitoring
Closed or narrow angle						
Primary angie-closure glaucoma						
Subacute	Episodic blurring, unilateral browache, coloured halos	Shallow anterior chamber	Angle recess <20°, pigment clumps, occasional peripheral anterior synechiae	Normal range	Normal	• Nd:YAG iridotomy both eyes • Lifelong monitoring of intraocular pressure and visual fields
Acute	Severe Unilateral headache, diminution of vision, nausea	Shallow anterior chamber, corneal oedema, vertically oval mid-dilated pupil Ciliary congestion Sphincter and iris atrophy	Closed angles	Very high	Disc oedema, occasional haemorrhage	• IV acetazolamide or mannitol, oral acetazolamide, syrup glycerol, maximal topical medical therapy • Nd:YAG iridotomy both eyes • Lifelong monitoring of intraocular pressure and visual fields
Chronic	Unilateral headache, diminution of vision, nausea or asymptomatic	Shallow anterior chamber, iris atrophy—sphincter, sector or generalized	Angle recess <20°, peripheral anterior synechiae	Moderately high	Glaucomatous optic nerve changes	• Medications as required for control of intraocular pressure • Nd:YAG iridotomy both eyes • Surgery if target pressure not achieved

Table 19.1 *(continued)*

	Symptoms	Anterior segment	Gonioscopy	Intraocular pressure	Optic nerve head	Therapy
Congenital glaucoma						
	Photophobia, tearing, corneal opacification	Megalocornea, tears in Descemet's membrane. iris anomalies	Anterior insertion of the iris	Moderate-to-high	Large, pale, cupping	• Goniotomy, trabeculotomy • Trabeculectomy augmented with 5-FU/mitomycin-C
Secondary open-angle glaucoma						
Corticosteroid-induced	Coloured halos and blurring of vision	Normal	Open angle	Very high	Glaucomatous cupping if chronic	• Stop steroids • Medical therapy • Surgery if target pressure not achieved
Angle-recession glaucoma	Diminution of vision	Mydriasis, tears of the iris sphincter, iridodialysis	Angle recession >180°	Moderate-to-high	Glaucomatous cupping if chronic	• Medical therapy • Surgery
Secondary angle-closure glaucoma						
Pupillary block (uveitis, pseudophakia)	Episodes of pain, redness and blurring of vision	Irregularly shallow anterior chamber	Peripheral anterior synechiae	Moderate-to-high	Glaucomatous cupping if chronic	• Control inflammation and intraocular pressure • Large laser iridotomy • Trabeculectomy augmented by 5-FU/mitomycin-C
Angle closure because of fibrosis (neovascular glaucoma)	Severe pain and diminution of vision	Peripherally shallow anterior chamber neovascularization of the iris	Closed angle with neovascularization	Very high	Glaucomatous cupping; ischaemic changes in the retina	• Maximal medical therapy • Panretinal photocoagulation or cryotherapy • Trabeculectomy with mitomycin-C/ drainage implant

Primary angle-closure glaucoma

PACG includes a spectrum of conditions in which the peripheral iris moves forwards to block the openings of the trabecular meshwork at the angle, causing a rise of intraocular pressure (Figs 19.9-19.11).

PACG is common among Asians and Eskimos but uncommon among Africans and Caucasians. It accounts for about 6% of all glaucomas among Caucasians, in whom it presents in the sixth to seventh decade. It occurs at least a decade or more earlier in Asians and accounts for 50% of primary adult glaucomas in this ethnic group. Females are more commonly affected by acute PACG, but in the asymptomatic or 'creeping' chronic variety, males and female are equally affected. First-degree relatives are at increased risk of developing the disease.

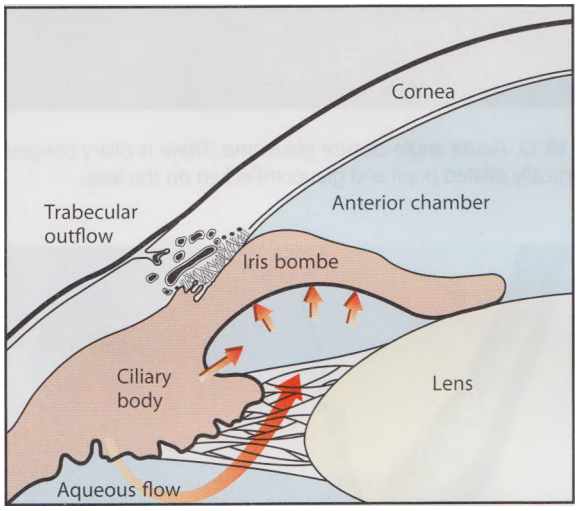


Fig. 19.9 Relative pupillary block. Mid-dilated pupil with iridolenticular contact allowing the lax iris to bow forwards and block the trabecular meshwork.

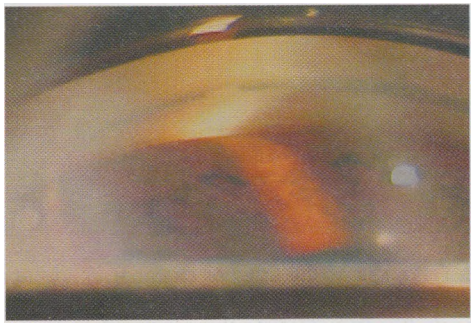


Fig. 19.10 Primary angle-closure glaucoma. A slit-beam examination shows a narrow angle recess of about 20°.

Predisposing factors

Anatomical factors predisposing to PACG are a short eye, smaller corneal diameter, a shallow anterior chamber, and a relative anterior positioning of the lens-iris diaphragm. These lead to a very narrow space at the angle of the anterior chamber. As the lens develops separately from the rest of the eye, a developmentally small eye may have a normal-sized lens. The lens also continues to grow in size throughout life, thus crowding the anterior chamber and allowing a larger area of contact between the iris and the lens. A relative pupillary block then occurs, which impedes forward movement of the aqueous through the pupil, and the iris balloons forwards onto the trabecular meshwork (Fig. 19.9). Angle-closure glaucoma occurs when physiological states such as close work in twilight or an emotional crisis cause a mid-dilated pupil to come in contact with an accommodated lens that is thicker and more anteriorly positioned. This precipitates a 'bowing' forward of the lax peripheral iris and a closure of extensive areas of the trabecular meshwork, causing a sudden rise in the intraocular pressure. Other suggested mechanisms for closure are a plateau iris configuration and peripheral crowding of the iris.

Clinical features

The disease is generally bilateral, though involvement of the two eyes is often asymmetrical. A number of clinical subtypes have been described, which may or may not show a stepwise progression in a given eye.

Manipulative gonioscopy in narrow angles necessitates moving the gonioscope towards the angle viewed or by asking the patient to look towards the mirror. Indentation gonioscopy displaces aqueous peripherally to push back the iris and allow visualization of the structure *(see* Chapter 11).





Fig, 19.11 Indentation or manipulative gonioscopy in primary angle-closure glaucoma may reveal peripheral anterior synechiae. (A) Iridocorneal adhesions of the peripheral iris to Schwalbe line or (B) goniosynechiae—-iridotrabecular adhesions of the peripheral iris to the trabecular meshwork.

Primary angle-closure glaucoma suspect: These eyes are identified by a shallow anterior chamber associated with an 'occludable' angle, i.e. one in which the pigmented trabecular meshwork is not visible without indentation or manipulation in at least three of four quadrants (Fig. 19.9). The angle recess in such eyes is generally less than 20°. No other gonioscopic abnormalities are present. A dark room prone provocative test may be used to precipitate closure of the angle in some of these eyes. Baseline intraocular pressure and gonioscopic findings are recorded and the patient is asked to stay in a dark room, in the prone position for 1 hour, without sleeping. Thereafter, the intraocular pressure and gonioscopy are noted with minimal illumination. A rise in intraocular pressure of 8 mmHg or more in the presence of a closed angle identifies eyes predisposed to PACG. Mydriatic/cycloplegic tests appear to be less physiological.

Subacute or intermittent primary angle-closure glaucoma: *Subacute PACG* occurs in eyes with a shallow anterior chamber and an occludable angle in which physiological factors such as reading in dim illumination, or watching a film in a darkened cinema hall have precipitated a pupillary block. This causes a sharp rise in intraocular pressure for a short period of time—a minute to a couple of hours—followed by a spontaneous resolution of the pupillary block, possibly due to physiological miosis which may occur in sleep or otherwise. The patient complains of a unilateral headache or browache, blurring of vision on the same side and unbroken coloured halos around lights during the episode *(see* p. 91). Between these recurrent attacks, the eyes are free of symptoms and only show signs of a narrow angle recess, clumping of pigment in the angle or occasional peripheral anterior synechiae (Fig. 19.11).

Acute primary angle-closure glaucoma: *Acute* or *congestive angle-closure glaucoma* is caused by a sudden occlusion of the entire angle with a resultant acute rise of intraocular pressure to extremely high levels. Patients complain of a severe unilateral headache and diminution of vision in a 'red' eye. Nausea may be frequently associated. On examination, ciliary and conjunctival congestion, corneal oedema, a shallow anterior chamber, and iris bombe with a vertically oval, mid-dilated pupil are present (Fig. 19.12). After resolution of the corneal oedema, a gonioscopically closed angle can be seen, i.e. extensive iridocorneal synechiae, and the optic disc may be found to be either hyperaemic or normal.

Chronic primary angle-closure glaucoma: A diagnosis of *chronic PACG* is reached if the intraocular pressure is chronically raised in eyes having synechial closure (Fig. 19.13) over at least 180°. Changes in the optic nerve head and visual field may or may not be present.

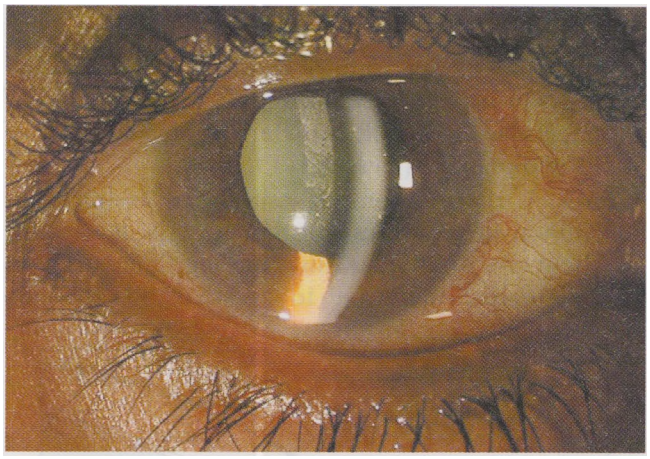
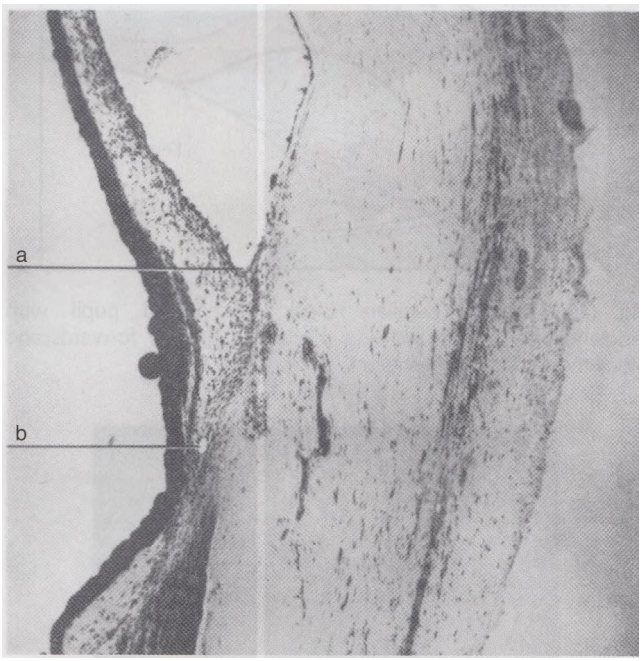


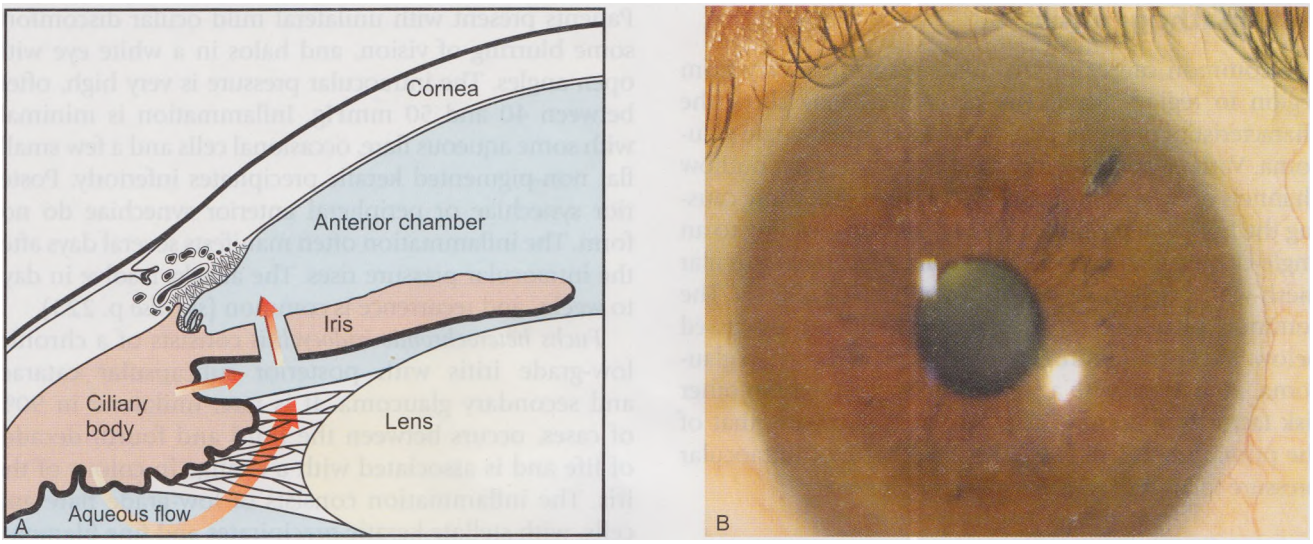
Fig. 19.12 Acute angle-closure glaucoma. There is ciliary congestion, a vertically dilated pupil and glaucomflecken on the lens.



Fig, 19.13 The angle of the anterior chamber in advanced angle-closure glaucoma, a, The level of the false angle; b, the level of the true angle (the line points to the canal of Schlemm) and ab, a peripheral anterior synechia. (By courtesy of Ashton)

Chronic PACG can be due to a variety of causes;

- repeated subacute attacks of PACG leading to extensive synechial closure and a chronically elevated intraocular pressure;
- acute PACG which persists for more than a few hours can lead to irreversible synechial closure of the angle and permanent damage to the trabecular meshwork;
- asymptomatic or 'creeping' angle closure, in which synechial closure occurs within the depth of the angle, i.e. iridoUabecular synechiae, and progressively involves the entire angle.



Fig, 19.14 Laser iridotomy allows the flow of aqueous from the posterior chamber to the angle, bypassing the pupil.

Treatment

If the intraocular pressure is elevated, this is controlled by topical and systemic medications. Eyes with acute PACG generally have an intraocular pressure of over 50 mmHg. This needs to be controlled immediately with intravenous acetazolamide 500 mg, and/or intravenous mannitol, after ensuring that the patient has no cardiovascular disease. These measures reduce the intraocular pressure, relieve ischaemic changes in the iris and lead to a decrease of the corneal oedema. Gonioscopy can be repeated if possible. Then, topical pilocarpine 2% should be instituted to constrict the pupil and pull the iris away from the angle. Other topical antiglaucoma medications can be used as required.

If the pupil continues to be blocked, pressure can be applied on the central part of the cornea with a moist cotton swab to displace aqueous in the centre of the anterior chamber towards the angle recess. This helps to mechanically push the iris away from the cornea. After the control of intraocular pressure, a laser iridotomy is mandatory in all eyes with any form of PACG and also prophylactically in the unaffected (fellow) eye.

Peripheral laser iridotomy: In this procedure, a hole is made in the periphery of the iris allowing the aqueous to drain directly from the posterior chamber into the region of the trabecular meshwork. This prevents the iris from being pushed forwards onto the trabecular openings by eliminating the higher aqueous pressure behind the iris, and allows the iris to fall back (Fig. 19.14). This procedure is commonly performed using an Nd:YAG laser and a hole—at least 150-200 microns in size—is made in the iris. Depending upon the thickness of the iris, the power used varies from 3 to 6 mj. A drop of topical pilocarpine instilled 30 minutes before laser therapy keeps the peripheral iris taut. A crypt in the iris is identified and the laser with an anterior offset is then used to create an opening in the iris. Postoperatively, steroids and antiglaucoma medications are required for 5-7 days to prevent a rise in intraocular pressure and control any inflammation. On the first postoperative visit, the iridotomy is examined for patency and size, and gonioscopy is re-evaluated.

The eyes are evaluated 2-4 weeks after an iridotomy to rule out a *chronically raised intraocular pressure.* If this is present, antiglaucoma medications and surgery (described at the end of this chapter) are used to achieve a 'target pressure' that is individually determined, as in eyes with POAG.

Combined mechanism glaucoma

Combined mechanism glaucoma is a term used to denote eyes in which there is an occludable angle with a few peripheral anterior synechiae, the extent of which, alone, does not explain the raised intraocular pressure or glaucomatous damage. There is thus a possibility that the patient may have underlying trabecular changes of POAG and the angle closure is incidental or additive.

SECONDARY GLAUCOMAS

Secondary glaucomas form a large proportion of the glaucomas seen in any practice, especially in developing countries. This is because of a high incidence of ocular infections, inflammations, complicated cataract surgery and trauma. The attending ophthalmologist treats the primary cause but often an undiagnosed secondary glaucoma leads to substantial loss of vision before it is identified and specific therapy instituted.

Aetiopathogenesis

The common causes of secondary glaucomas vary from region to region. Secondary glaucomas may show the characteristics of either angle-closure or open-angle glaucoma. Various pathological conditions affect the outflow channels of the eye, and may be classified into those causing the iris to be pushed or pulled forwards leading to an angle-closure glaucoma, or those that affect the trabecular mesh-work itself, for example, by means of fibrosis. The common causes of secondary glaucomas are discussed below. They occur more often in eyes predisposed to glaucoma, as in those with a family history or in whom other risk factors are present. The treatment is usually that of the primary cause, followed by the control of intraocular pressure to an individualized 'target pressure'.

Inflammatory glaucomas

Uveitic glaucoma is thought to result from swelling and dysfunction of the endothelial cells or infiltration and obstruction of the trabecular meshwork by inflammatory material such as white blood cell aggregates, macrophages, lymphocytes and fibrin. This leads to a diminished outflow of aqueous with a subsequent rise in intraocular pressure. Inflammatory material may be seen as precipitates on the meshwork.

Postinflammatory glaucoma: Once the inflammation subsides, extensive posterior synechiae may cause an occlusio or seclusio pupillae, iris bombe and angle closure by peripheral anterior synechiae (Fig. 19.15). Even without extensive posterior or peripheral anterior synechiae, repeated episodes of iridocyclitis can cause fibrosis and obstruction of the meshwork.

Glaucomatocyclitic crisis is an acute, recurrent, very mild uveitis with secondary glaucoma. The glaucoma is characteristically out of proportion to the inflammation.



Fig. 19.15 Healed anterior uveitis with 360° of posterior synechiae, and extensive iris bombe. A large laser iridotomy has been done to relieve the pupillary block.

Patients present with unilateral mild ocular discomfort, some blurring of vision, and halos in a white eye with open angles. The intraocular pressure is very high, often between 40 and 50 mmHg. Inflammation is minimal, with some aqueous flare, occasional cells and a few small, flat non-pigmented keratic precipitates inferiorly. Posterior synechiae or peripheral anterior synechiae do not form. The inflammation often manifests several days after the intraocular pressure rises. The attacks resolve in days to weeks, and recurrence is common (*see also* p. 223).

Fuchs heterochromic iridocyclitis consists of a chronic, low-grade iritis with posterior subcapsular cataract and secondary glaucoma. It is rare, unilateral in 90% of cases, occurs between the third and fourth decades of life and is associated with a change in colour of the iris. The inflammation consists of low-grade flare and cells, with stellate keratic precipitates and fine filaments scattered over the entire endothelium. Anterior vitreous opacities may be present and occasionally small white nodules on the anterior surface of the iris. Secondary glaucoma has been reported in 15% of patients at presentation. Vision decreases as the cataract progresses. Control of the uveitis with topical corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) is a priority. The intraocular pressure is initially reduced below 20 mmHg by medical means. Glaucoma therapy is re-evaluated once the inflammation subsides completely, as in POAG.

Secondary glaucoma after perforation of the cornea

Perforation of a corneal ulcer or a penetrating corneal injury leads to a loss of aqueous and forward movement of the lens diaphragm, as the pressure in the vitreous cavity exceeds that of the anterior chamber. The iris or lens capsule becomes incarcerated in these corneal dehiscences, and the accompanying inflammation induces the formation of adhesions at the wound as well as peripherally between the iris and cornea, as the anterior chamber becomes shallow or lost. Once the inflammation subsides and peripheral anterior synechiae form, a chronically raised intraocular pressure is frequently seen.

Neovascular glaucoma

This follows extensive retinal ischaemia and is commonly seen in association with central retinal vein obstruction and proliferative diabetic retinopathy. It is due to the presence of neovascularization over the iris *[rubeosis iridis*) and consequent fibrosis, leading to zip-like adhesions of the iris to the cornea at the angle (Fig. 19.16). Neovascular glaucoma remains a difficult problem, which needs anti-VEGF agents and retinal photocoagulation or cryotherapy to eliminate the stimulus for neovascularization. The raised intraocular pressure can then be alleviated by

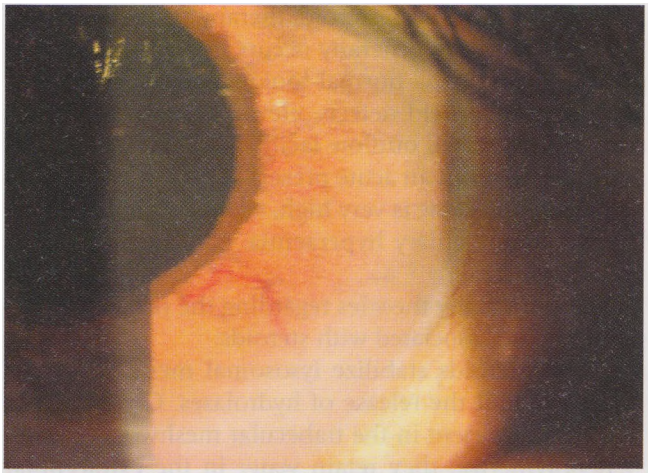


Fig. 19.16 Neovascular glaucoma showing neovascularization of the iris and ectropion of the pupil.

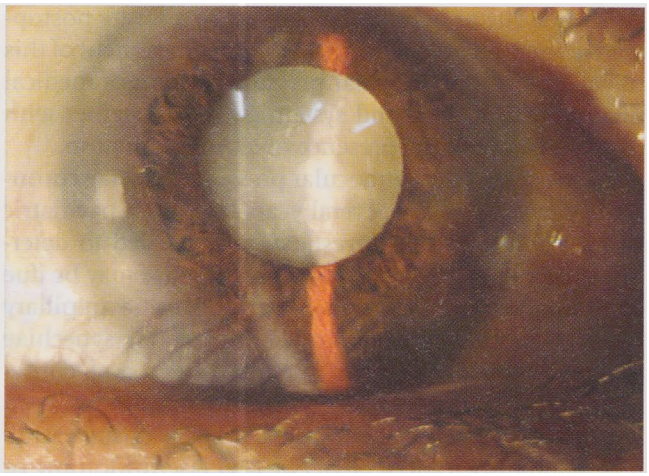


Fig. 19.17 Phacomorphic glaucoma.

a trabeculectomy in conjunction with antifibroblastic agents or an anterior chamber drainage implant.

Lens-induced glaucoma

- *Secondary angle closure* due to changes in the lens may arise in two circumstances:
  - The lens becomes intumescent, either by the rapid development of cataractous changes or after a traumatic rupture of its capsule. The swollen lens obliterates the drainage angle by forcing the root of the iris against the cornea. This is called a*phacomorphic glaucoma* (Fig. 19.17). Unless the condition is rapidly relieved by surgery, extensive peripheral synechiae causing a permanent rise of intraocular pressure will result, even if the lens is subsequently removed or gets absorbed.
  - An anterior subluxation or dislocation of the lens acts similarly. In partial subluxation, a large segment of the angle of the anterior chamber may be compressed or blocked. In complete dislocation into the anterior chamber, the entire angle may be blocked, especially if the iris becomes firmly contracted over the posterior surface of the lens. This is called *phacotopic glaucoma.*
- *A secondary open-angle glaucoma* may develop if the lens has been damaged or if lens proteins from a hypermature senile cataract escape into the aqueous. This is called *phacol)tic glaucoma* (Fig. 19.18) and is obstructive in origin. Cortical lens matter excites a reaction by large phagocytes, which engulf the lens particles. These cells are swept into the ttabecular spaces by the normal current of aqueous, where they block the exit of aqueous from the eye. The patient presents with a sudden rise of intraocular pressure. Careful examination reveals an active and free pupil with cells in the anterior chamber and keratic deposits on the back of the cornea.

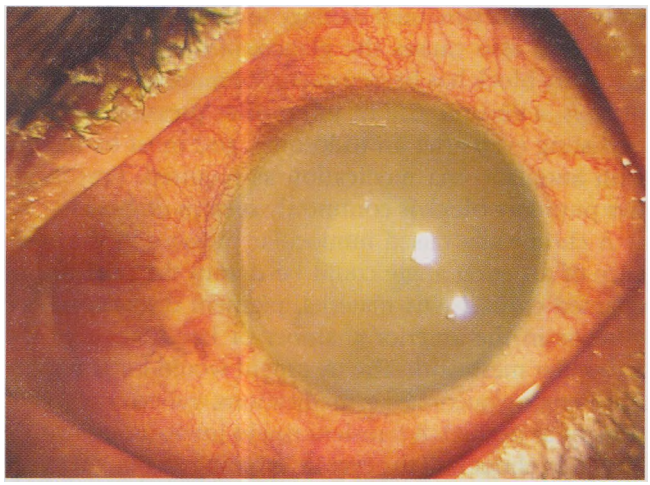


Fig. 19.18 Phacolytic glaucoma.

Treatment of lens-induced glaucoma is by extraction of the lens after lowering of the intraocular pressure by medical therapy. All lens matter must be evacuated. Insertion of a posterior chamber intraocular lens is not contraindicated.

Aphakic or pseudophakic glaucoma

Pseudophakic and aphakic glaucomas are among the commonest forms of secondary glaucoma, due to the large number of cataract surgeries performed all over the world. This term is employed to describe a secondary rise of intraocular pressure after cataract surgery that can be attributed to the surgery or its complications. This complication is seen most commonly after surgery for paediatric cataract, and following the use of anterior chamber intraocular lenses in adult eyes. A rise of intraocular pressure may occur transiently after surgery, and resolve spontaneously in a few days to weeks, as caused by the use of viscoelastics, distortion of the angle

structures due to tight limbal sutures or a severe postoperative reaction or haemorrhage. The management of this transient rise in intraocular pressure consists of medical therapy with topical and systemic drugs, together with corticosteroids in the presence of an inflammation.

In some eyes the intraocular pressure may stay chronically elevated, or rise several years later as in paediatric cases, when thorough investigation is needed to determine the cause. The intraocular pressure rise may be due to a secondary angle-closure mechanism—a pupillary block produced by uveitis causing posterior synechiae to the intraocular lens or vitreous phase, and consequent bowing forwards of the iris. Mydriatics are used to break early posterior synechiae; if this is unsuccessful, it is mandatory to do a large Nd:YAG laser iridotomy or even multiple iridotomies to open loculated pockets of aqueous, after controlling the initial rise of intraocular pressure with medications. Breaking the pupillary block early prevents structural damage to the trabecular meshwork and also causes the glaucoma to subside. If the pupillary block has been present for more than a couple of days, a chronic rise of intraocular pressure is likely, persisting even after an iridotomy, and must be treated with antiglaucoma medication as required. Postoperative pupillary block is commonly seen in diabetics.

A chronically raised intraocular pressure in the presence of an open angle could be due to the presence of retained cortical lens material, pigment dispersion, free vitreous in the anterior chamber or late fibrosis of the trabecular meshwork. The treatment would be as for any open-angle glaucoma, i.e. medications, trabeculoplasty or surgery, as needed. A transient rise in intraocular pressure is seen in about half the eyes undergoing an Nd:YAG laser capsulotomy, induced by the obstruction of trabecular outflow by capsular debris and inflammatory cells.

Systemic carbonic anhydrase inhibitors and hyperosmotic agents are used in all such cases as an interim measure. Epinephrine and prostaglandin derivatives should be avoided as they can lead to cystoid macular oedema. Traditional guarded filtering surgeries have a high failure rate, therefore the use of antifibroblastic agents in such eyes is common. Drainage implants have also been used with reasonable success.

Corticosteroid-induced glaucoma

Topical, systemic or periocular corticosteroid administration can cause a decrease in aqueous outflow and an increase in the intraocular pressure. This tends to occur in the eyes of genetically predisposed individuals. Of the normal population, 5-6% develop a markedly increased intraocular pressure of more than 31 mmHg after 4-6 weeks of topical corticosteroid therapy. In contrast, almost all patients with POAG or low-tension glaucoma develop some elevation of the intraocular pressure after topical steroid therapy. Corticosteroid-induced glaucoma generally occurs in a white, painless eye with an open, normal-looking angle, optic disc cupping, visual field defects, elevated intraocular pressure and decreased outflow facility. Patients are usually asymptomatic but an acute presentation can occur if the intraocular pressure is very high, when corneal oedema, blurred vision, ciliary hyperaemia, coloured halos and pain may occur.

There are many theories regarding the rise in intraocular pressure associated with steroids:

- Corticosteroids stabilize lysosomal membranes and thus inhibit the release of hydrolases. Glycosaminoglycans (present in the trabecular meshwork) cannot depolymerize; they retain water in the extracellular space which leads to narrowing of the trabecular openings.
- Endothelial cells lining the trabecular meshwork act as phagocytes of debris in the aqueous humour and with corticosteroids suppressing their activity, there is a further blockage of the trabecular meshwork and consequently decreased outflow.
- In POAG, an abnormal accumulation of dihydrocortisols, especially five hydrocortisol, in the trabecular cells may potentiate exogenous glucocorticoid activity leading to an increased susceptibility to elevation of pressure from corticosteroids.
- Corticosteroids can also inhibit synthesis of both prostaglandins E and F, whose normal function is to lower the intraocular pressure by increasing the outflow facility.

The use of steroids should be stopped immediately and the intraocular pressure controlled medically. In a third of such eyes the intraocular pressure gradually returns to normal, the rest need treatment as for POAG.

Secondary glaucoma due to an intraocular tumour

An intraocular tumour may cause secondary glaucoma, not by its increase in volume but by infiltration of the angle by neoplastic tissue or aqueous seeding.

Elevated episcleral venous pressure

Secondary glaucoma is readily caused by elevated episcleral venous pressure, which impedes the drainage of aqueous. This occurs in conditions such as orbital inflammations, large orbital tumours, carotid-cavernous communications, exophthalmos, Sturge-Weber syndrome and orbital varices.

Pigmentary glaucoma

Pigmentary glaucoma is a secondary open-angle glaucoma due to pigment release in young male myopes

who present with intermittent halos, an open angle and a Krukenberg spindle of pigment visible on the corneal endothelium on slit-lamp microscopy. Increased pigmentation in the trabecular meshwork seen as Sampaolesi line on gonioscopy is also characteristic. Pigmentary glaucoma develops in about a third of patients with pigment dispersion syndrome. The long-term prognosis is good, and field loss occurs in only a few eyes.

Malignant glaucoma

Malignant glaucoma is also known as ciliovitreal block or aqueous misdirection syndrome. The normal flow of aqueous is blocked at the level of the ciliary body, lens or anterior vitreous face, causing misdirection posteriorly of aqueous humour into the vitreous. The vitreous volume increases, pushing the iris-lens diaphragm forward in phakic and pseudophakic eyes, or the anterior hyaloid in aphakic eyes. Small, hyperopic eyes with angle-closure glaucoma are more prone to develop malignant glaucoma following an iridectomy, filtering surgery or laser iridotomy. It can also occur after cataract surgery, capsulotomy or even spontaneously.

Patients complain of severe pain with blurring of vision. On examination, the anterior chamber is found to be extremely shallow or flat in the presence of a patent iridectomy, and the intraocular pressure is very high. The clinician must rule out a choroidal detachment, pupillary block or suprachoroidal haemorrhage to reach a diagnosis of malignant glaucoma.

Cycloplegic agents, especially topical atropine, decrease the tone of the sphincter muscle of the ciliary body, tautening the zonules. This causes a thinning and posterior displacement of the lens, deepening the anterior chamber. Phenylephrine also tightens the zonules by contraction of the longitudinal muscle of the ciliary body. Osmotic agents are used to dehydrate the vitreous and lower the intraocular pressure. Aqueous production is decreased by using topical beta-blockers, alpha-adrenergic agonists and carbonic anhydrase inhibitors. Medical therapy is effective in some cases, but needs to be continued for months or years. YAG laser hyaloidotomy can be undertaken in pseudophakic or aphakic eyes. If such conservative measures do not work, a pars plana vitrectomy, with or without lensectomy, reduces the volume of the vitreous and re-establishes the flow of aqueous from the posterior to the anterior chamber. Medical therapy needs to be continued for a long time. Prognosis for the control of intraocular pressure is currently better, but the condition tends to recur, and the other eye is at great risk of developing a similar problem.

Pseudoexfoliation syndrome

Pseudoexfoliation syndrome is a condition in which exfoliative material is deposited on the iris, ciliary region and capsule of the lens. Clinically these appear as flakes on the anterior capsule of the lens and the edge of the iris, and are particularly evident in the mid-peripheral region where the anterior capsule is rubbed upon by the iris; the axial region is usually free. These flakes tend to collect in the angle of the anterior chamber and may obstruct the drainage of the aqueous humour. This material is evidence of a widespread degenerative change in the anterior uvea, particularly the ciliary region. Patients with pseudoexfoliation of the lens capsule have a high chance of developing glaucoma (Fig. 19.19).

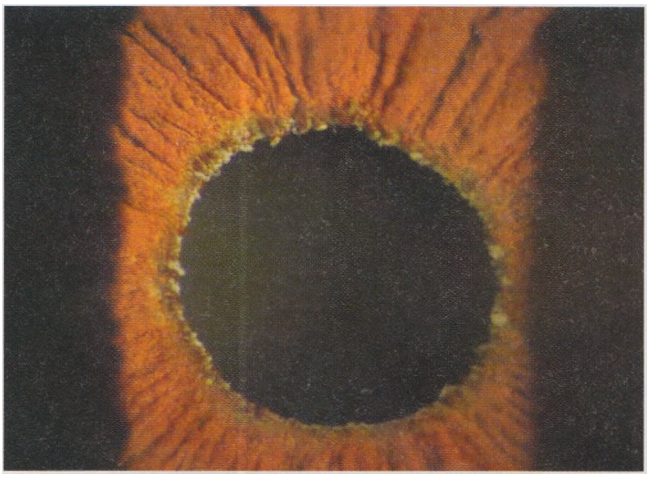


Fig. 19.19 Pseudoexfoliation syndrome. White, flaky material is deposited all over the anterior chamber, seen here at the pupil.

PAEDIATRIC GLAUCOMAS

Glaucoma in the young has been vastly underestimated in the past. We are now aware that glaucomatous damage ordinarily takes a long time to develop. Symptomatic damage in a patient detected at the age of 45 years might be the result of elevated intraocular pressure for 20 years. Glaucoma, however, does increase in frequency with age. As mentioned earlier, pigmentary glaucoma develops in the twenties and thirties. Juvenile open-angle glaucoma, often hereditary, is probably second in frequency to pigmentary glaucoma. Glaucoma in childhood is much less common and is often associated with specific syndromes.

Congenital glaucoma

Congenital or *infantile glaucoma* occurs in about 1 in 10,000 births. It is defined as glaucoma appearing between birth and the ages of 3-4 years. Up to this age, the eye wall is distensible, so that the eye can noticeably and progressively enlarge when the intraocular pressure is elevated (Fig. 19.20). It may occur without

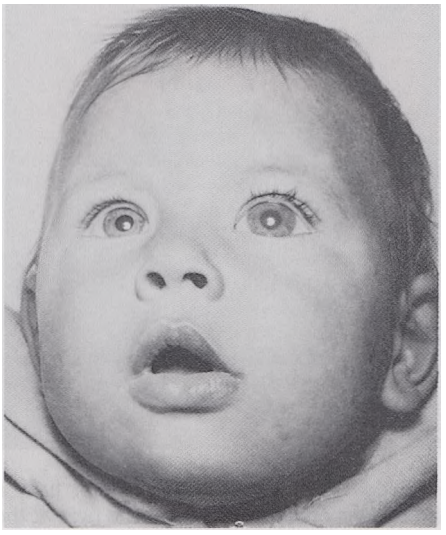


Fig. 19.20 Buphthalmos in an 8-month-old child. The left eye is larger than the right.

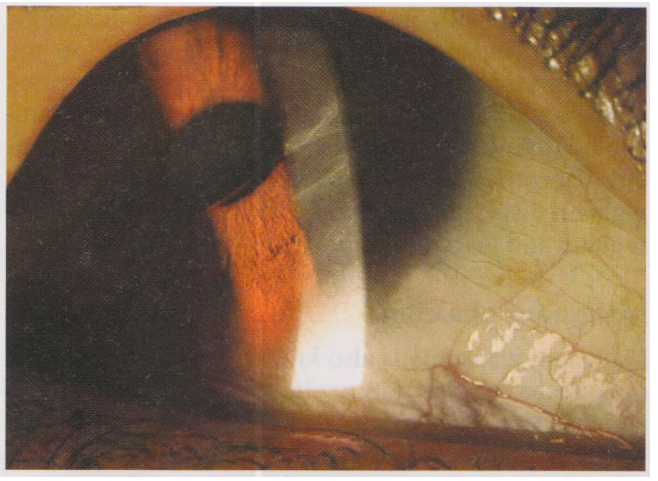


Fig. 19.21 Haab striae, tears in Descemet's membrane seen as double 'tram-track' lines concentric to the limbus.

other ocular findings (primary congenital glaucoma) or in association with other syndromes, or may occur after injury, congenital cataract extraction, or inflammation (secondary congenital glaucoma).

Pathogenesis

Primary congenital glaucoma is due to failure or abnormal development of the trabecular meshwork. The iris may not completely separate from the cornea *(see* p. 5) so that the angle remains closed by persistent embryonic tissue. Depending on the degree of obstruction, the result is a permanent rise in the tension of the eye, but since the circulation of the aqueous is maintained, although at a lower rate, by the anterior ciliary veins and the uveoscleral outflow, the rise in tension is usually neither marked nor acute. Both eyes are generally affected, and congenital glaucoma occurs more often in boys than in girls.

Neonatal congenital glaucoma occurs with more extensive congenital malformations and has a poor prognosis.

Owing to the distensibility of the sclera in children, the eye behaves differently from the adult organ under this increase of pressure. Not only does the lamina cribrosa give way, producing deep cupping, but also the entire cornea and sclera stretch so that the globe gradually enlarges; this stretching and expansibility may mask the increased pressure on clinical examination.

Most cases of primary congenital glaucoma occur sporadically. In approximately 10% in whom a hereditary pattern is evident, it is believed to be autosomal recessive. Much progress has been made in our understanding of the genetics of glaucoma, and at least three different chromosomes which can contain abnormal genes causing congenital glaucoma have been identified. Common associations with congenital glaucoma are neurofibromatosis *(see* Chapter 32) and the cutaneous angioma of the face associated with cavernous haemangiomas of the choroid and the brain (Sturge-Weber syndrome, *see* Chapter 32).

Clinical features

Symptoms: Congenital glaucoma is usually detected by parents when the affected eye is noted to enlarge or the cornea becomes hazy. As the cornea stretches, breaks occur in the corneal endothelium, which pumps water out of the cornea to maintain its transparency. When these breaks occur, aqueous humour enters the cornea, causing it to swell, and assumes a hazy, frosted-glass appearance. The baby is sensitive to light and tearing may be present. As the cornea stretches, the ruptures allow more aqueous into the corneal stroma and epithelium, causing a sudden increase in oedema and haze. An infant may become irritable to the point of burying its head in a pillow to avoid light.

Signs: In early cases, the first sign may be an oedema of the cornea with watering of the eyes and marked photophobia, occasionally with the development of corneal opacities. At a later stage, due to rupture of Descemet's membrane, more discrete corneal opacities appear as lines with a double contour (Haab striae, Fig. 19.21). As the disease progresses the entire globe stretches. The thinned sclera of the ciliary region appears bluish in colour, owing to the uveal pigment showing through. The junction of the cornea and sclera also stretches, so that the cornea is forced forwards and assumes a globular

shape resembling keratoglobus *(see* Chapter 15); care should be taken to differentiate between the two conditions. The anterior chamber is therefore extremely deep. The lens does not participate in the general enlargement but is flattened and displaced backwards, owing to the expansion of the ciliary region and stretching of the suspensory ligament. This removes some support to the iris, which may become tremulous (iridodonesis). As a result of the expansion, the eyes are usually myopic, although much less so than might be anticipated from their length due to the flattening and backward displacement of the lens. Equilibrium may be established in some cases with reversal of the cupping and no further loss of vision but, in other cases, rapid deterioration occurs.

Treatment

Medications are not very effective. The most effective surgery is *goniotomy* or *trabeculotomy* in which the anomalous architecture of the angle is cut through to allow the entry of aqueous into the canal of Schlemm. In goniotomy (Fig. 19.22A), a specially constructed knife introduced at the limbus is swept round the angle of the anterior chamber in the opposite segment of the eye under direct gonioscopic observation. In trabeculotomy, a small flap of conjunctiva and a partial thickness flap of sclera are made at the upper limbus, exposing the canal of Schlemm by a vertical incision, dissecting through the sclera. A small trabeculotome (Fig. 19.22B) is passed into the canal of Schlemm and rotated in the anterior chamber so as to break the inner wal 1 over one quarter of the canal. This is then repeated on the other side so that eventually the upper half of the canal wall is opened. Localization of the canal itself, however, is sometimes difficult.

If all forms of trabeculotomy fail then a trabeculectomy with pharmacological modulation may be considered.

Surgical treatment is often successful, although more than one operation may be necessary. The prognosis is worse if the glaucoma is present since birth and best from 2 months to 1 year of age.

Juvenile primary open-angle glaucoma

Glaucoma occurring between the ages of 4 and 10 years is called late congenital glaucoma or developmental glaucoma. In these eyes trabecular anomalies are not as severe. POAG developing between the ages of 10 and 35 years is termed as juvenile POAG. About 35% of people with this disease are high myopes.

Aetiopathogenesis

Juvenile POAG has a strong autosomal dominant inheritance. Some of these families have a genetic anomaly on the long arm of chromosome 21. Numerous mutations in this gene have been found in several large families with hereditary glaucoma. This gene produces a protein called TIGR or myocilin, which makes the trabecular meshwork less permeable to aqueous humour draining

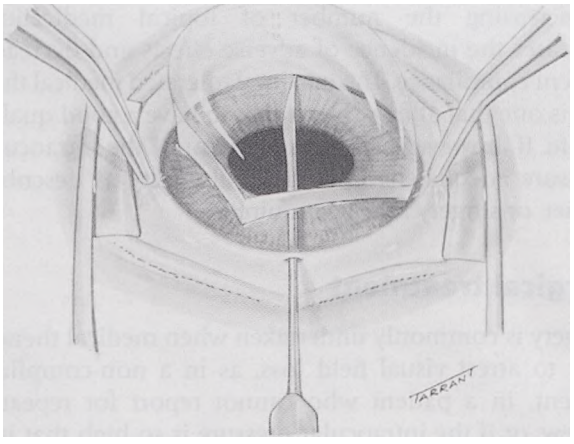
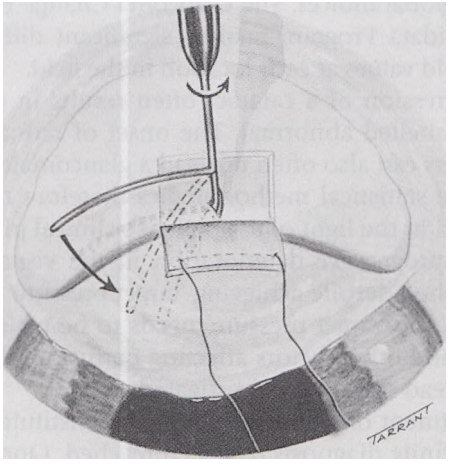


Fig. 19.22 (A) Goniotomy. A Barkan goniotomy knife is passed obliquely through the limbus on the temporal side at 3 or 9 o'clock position. Under gonioscopic control the knife is passed across the anterior chamber to the nasal part of the angle. An incision is made in the angle approximately mid-way between the root of the iris and Schwalbe ring through approximately 75°. The knife is then withdrawn. [Reproduced from: Eyes. In: Miller SJH (ed). *Rob and Smith's Operative Surgery*, 3rd edn. London: Butterworths, 1976.]



Fig, 19.22 (B) Harms trabeculotomy. The lower prong of a Harms trabeculotomy probe is passed along Schlemm's canal to the right, the upper prong being used as a guide. (Reproduced from: Eyes. In: Miller SJH (ed). *Rob and Smith's Operative Surgery*, 3rd edn. London: Butterworths, 1976.)

out of the eye. When susceptible individuals are treated with steroids the concentration of myocilin may increase resulting in a rise in intraocular pressure.

MANAGEMENT OF THE GLAUCOMAS

Glaucoma is a chronic disease that requires lifelong therapy and review. The importance of treatment and regular follow-up must be explained and emphasized.

Management requires continued supervision by an ophthalmologist and consists of simple recordings of readings of applanation tonometry and status of the optic nerve head. Careful and repeated charting of the visual fields is also required.

To determine the progression of visual field defects in glaucoma, one must establish a baseline by doing at least three chartings of the visual field in a newly diagnosed patient of glaucoma. Disease progression is best assessed if the follow-up programmes and all parameters are the same as those used for the baseline. If a change in the visual field is detected at any time during follow-up, it must be confirmed by another test and correlated with any associated clinical finding. Typically, six or more examinations at 3-6-month intervals are required to confirm progressive deterioration.

The first step in evaluating the progression of a visual field defect is to study a series of chronologically arranged visual field recordings of a particular patient. Overview print-outs are helpful for this purpose, as they place the grey-scale threshold value table and probability plots of total and pattern deviation of each examination in a row, with the rows arranged in chronological order, making it easier to scan a series of recordings. Statistical packages are available in the form of box plots which analyse changes in the global indices. The Glaucoma Change Program or the Peridata Program analyse significant differences in threshold values at each location in the field.

Progression of a cataract often results in these tests being labelled abnormal. The onset of retinal vascular disorders can also often mislead a glaucomatologist. All of these statistical methodologies therefore need to be assessed in the light of the patient's clinical picture.

If a progressive deterioration in the visual fields is established despite achieving 'target pressure' in a given patient, the 'target pressure' needs to be revised downwards and other factors affecting perfusion of the optic nerve head should be investigated.

Treatment of glaucoma should be instituted as soon as a definite diagnosis has been reached. Once the ganglion cells have been damaged and the vision carried by those nerve fibres lost, they cannot be replaced. Loss of vision in glaucoma is irreversible. To minimize or prevent further visual loss, the intraocular pressure must be constantly controlled, and closely monitored.

The glaucomas can be treated with medicines, laser or by surgery. The initial treatment of glaucoma is generally medical or by laser procedures. A 'target pressure' has to be defined for each patient with a chronic glaucoma, taking into account the intraocular pressure at which damage occurred, the family history, the extent of damage to the optic nerve head, visual field, and the presence of systemic risk factors for glaucomatous damage.

Medical management

Very high intraocular pressures need to be lowered immediately with the use of intravenous acetazolamide or mannitol. Oral acetazolamide or glycerol take about half to one hour to control moderately high intraocular pressures. Lowering the intraocular pressure to near-physiological levels allows topical medication to become effective. Long-term use of these systemic medications is not advisable, due to possibly life-threatening side-effects.

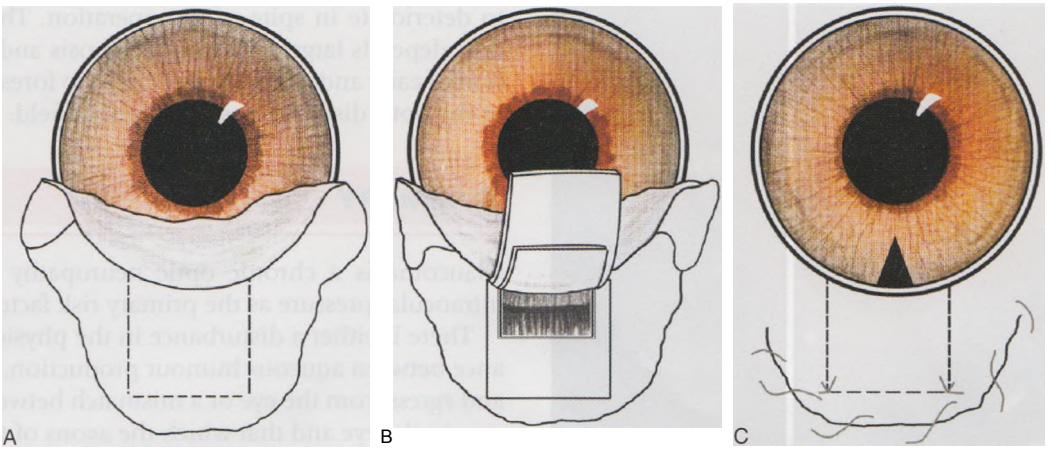
Several groups of drugs are available for the management of glaucomas; the most effective of these are beta-blockers, alpha-2 agonists and prostaglandin analogues. These are used as first-line treatment for a raised intraocular pressure. If the intraocular pressure remains uncontrolled with one of these, another of the drugs mentioned above may be substituted. If the intraocular pressure is lowered by at least 15-20%, but is still above the 'target pressure', an adjunctive drug from another pharmacological group, having a different mechanism of action may be used *(see* Chapter 13). Miotics are essential for the treatment of PACG until an iridotomy is performed.

Increasing the number of topical medications increases the incidence of adverse effects and decreases patient compliance. The maximal tolerated medical therapy is one that allows the patient to have a good quality of life. If, however, this does not control the intraocular pressure adequately, laser trabeculoplasty as described earlier, or surgery may be required.

Surgical treatment

Surgery is commonly undertaken when medical therapy fails to arrest visual field loss, as in a non-compliant patient, in a patient who cannot report for repeated review, or if the intraocular pressure is so high that it is unlikely to be controlled by medication alone. Surgery may also be advised as primary therapy, as it maintains a steady, low intraocular pressure round the clock.

Glaucoma-filtering operations are employed to control the intraocular pressure by the establishment of a 'filtering bleb'. This bleb is composed of spongy tissue, through the interstices of which intraocular fluid is able to make its way into the subconjunctival tissue



Fig, 19.23 Steps of trabeculectomy. (A) Limbus-based conjunctival flap is raised; (B) a 5 5 mm lamellar scleral flap is dissected up to the limbus, and a 2 x 1 mm trabecular block excised; (C) the scleral flap is sutured, titrating the flow of aqueous.

where it is absorbed, instead of the normal drainage into the trabecular meshwork. In a corneoscleral incision the lips of the wound are in good apposition and healing rapidly takes place. This is much less likely to occur if there is a gap between the lips of the wound which becomes filled with loose scar tissue resulting in a filtering cicatrix. Various operations have been based upon this principle, the most favoured today is trabeculectomy. Non-penetrating filtering surgeries that allow the drainage of aqueous through a window in the Descemet's membrane are also being evaluated.

Trabeculectomy involves the creation of a lamellar scleral flap. Under this flap, a piece of sclera which includes a short length of the canal of Schlemm is excised, thus producing two new entrances into the canal itself. Such an operation also forms a filtering channel to the subconjunctival space and its efficacy depends upon two routes of drainage of the aqueous—through the canal of Schlemm and by a transcleral route to the subconjunctival spaces (Figs 19.23 and 19.24). If the wound heals and excessive scar tissue seals the flap over the drainage hole, the pressure in the eye again rises. A repeat trabeculectomy is usually done with the addition of antifibroblastic agents such as 5-FU or mitomycin-C, which are used to slow down the healing process. If the surgeon feels that the wound may heal too rapidly and the risk of excessive fibrosis is high, as in young patients, people of African origin, those with intraocular inflammation or a history of previous eye surgery, then one of these medications is often applied during the primary trabeculectomy. 5-FU is applied in a dose of 50mg/ml and mitomycin-C in a dose of 0.2-0.3 mg/ml for 2-3 minutes.

Complications: In the early postoperative period shallowing of the anterior chamber and hyphaema may be seen. Late complications include bleb failure, blebitis or bleb leak.

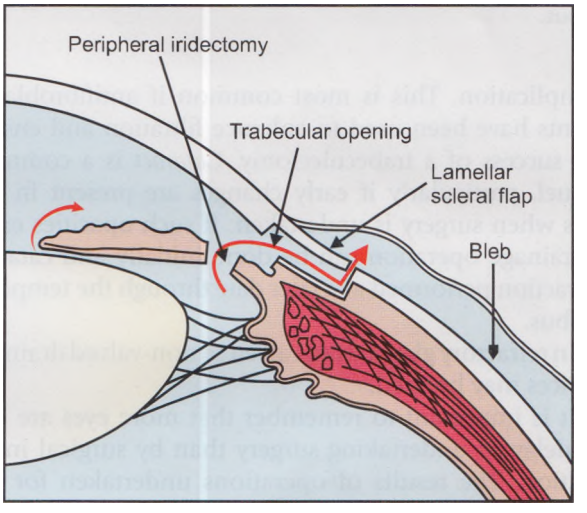


Fig. 19.24 Diagrammatic representation of a trabeculectomy showing the aqueous flow through the trabecular opening under the lamellar scleral flap into the subconjunctival space.

Trabeculectomies are successful in the treatment of primary glaucomas, and the filtering bleb that results is a diffuse elevation of the conjunctiva showing microcystoid changes at the limbus (Fig. 19.25).

These operations—particularly when most effective—are not without their dangers. Post-operative *shallow anterior chambers* are relatively frequent, and can lead to accelerated cataractogenesis and may also cause failure of filtration. Reformation of the anterior chamber with balanced salt solution, air or viscoelastics should be undertaken as early as possible. The occurrence of such shallow chambers can be decreased by the intraoperative application of releasable sutures. The presence of a draining bleb covered with thin conjunctiva may lead to the subsequent development of *secondary infection* which is a serious



Fig. 19.25 Filtering bleb after trabeculectomy, showing a diffuse elevation of the conjunctiva and microcystoid changes at the limbus.

complication. This is most common if antifibroblastic agents have been used to enhance filtration and ensure the success of a trabeculectomy. *Cataract* is a common sequel, particularly if early changes are present in the lens when surgery is undertaken. If such opacities exist, a drainage operation can be done initially and cataract extraction performed at a later date through the temporal limbus.

In refractory glaucomas, valved ornon-valved drainage devices may be used.

It is important to remember that more eyes are lost by delay in undertaking surgery than by surgical intervention. The results of operations undertaken for the control of glaucoma can only control the factor of intraocular pressure. If the deterioration in vision is due essentially to a raised intraocular pressure, its surgical relief will usually prevent further loss; if the intraocular pressure is low and the deterioration is essentially due to a frail lamina cribrosa, the vision will probably continue to deteriorate in spite of the operation. The prognosis thus depends largely on early diagnosis and the institution of early and adequate treatment to forestall cupping of the optic disc and loss of the visual field.

SUMMARY

Glaucoma is a chronic optic neuropathy with raised intraocular pressure as the primary risk factor.

There is either a disturbance in the physiological balance between aqueous humour production, flow within and egress from the eye or a mismatch between the pressure in the eye and that which the axons of the ganglion cells or optic nerve can withstand.

The glaucomas are broadly classified as open or closed angle glaucomas. Open angle glaucomas can be managed medically, but surgery may be necessary if not adequately controlled. Angle closure glaucomas need an initial laser iridotomy followed by medical or surgical therapy. Tonometry, optic nerve head imaging and serial visual fields are parameters used to monitor the effect of treatment.

The most devastating effect of glaucoma is that if not treated, the visual loss is irreversible. It is often a silent disease, so that proper screening and early diagnosis are critical. Several risk factors have been identified; presence of a family history being very important as the disease is now being recognized as hereditary.

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20

Diseases of the Retina

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The retina is a component of what is clinically viewed as the fundus. The neurosensory retina is transparent, the background colour being provided by the retinal pigment epithelium and vascular choroid, as described in Chapter 12. The retina is divided into a number of zones for convenience of recording clinical findings and to permit a precise diagnosis of retinal disorders. The retinal equator is considered to lie in line with the exit of the four vortex veins and the retina posterior to this is called the posterior pole. Examination of the posterior part of the retina is undertaken with the use of a direct ophthalmoscope and by slit-lamp indirect biomicroscopy if additional magnification or a binocular view is required. The retinal periphery lies anterior to the equator, and a generalized view can be obtained by indirect ophthalmoscopy or a more magnified view with stereopsis by the use of a three-mirror contact lens.

The *macula lutea* is an area of the retina approximately 5.5 mm in diameter that is rich in cones, situated about 2 disc diameters (DD) temporal to the optic disc (1 DD, 1.5 mm). The central 1.5mm of the macula is termed the fovea, which has a small, central depression approximately 0.35 mm in diameter called th*efoveola.* The vision is most acute at the foveola, where only cones are found; each cone directly relays to a single ganglion cell. The foveal avascular zone extends over a central area about 0.4-0.6 mm in diameter.

The *retinal vessels* are derived from the central artery and vein, which usually divide into two branches at or near the surface of the disc to form a superior and an inferior trunk *(see* Fig. 1.10A). Each trunk usually divides into two, one of which sweeps up (or down) towards the temporal side, the other up (or down) towards the nasal side—the superior and inferior temporal and nasal arteries and veins. These divide dichotomously into innumerable branches, the mode of division being subject to great variations, but the nasal branches run more radially than the temporal, which make a decided sweep to avoid the macula. There are normally no anastomoses between these vessels. The arteries are distinguished from the veins by being brighter red and narrower. The veins have a purplish tint and are often more convoluted, though sometimes the arteries may also be tortuous. Ophthalmoscopically what is seen is the blood column and not the vessel wall, which is normally transparent. All the retinal vessels may have a bright silvery streak running longitudinally down the centre, which is more prominent with the arteries and is due to reflection of light from the convex cylindrical surface. Choroidal vessels, when visible *(see* Chapter 18), are broader and ribbon-like, without any central streak and they anastomose freely, whereas the retinal vessels do not anastomose at all. These are most visible in albinos and in high myopes.

In normal conditions, no pulsation can be seen in the retinal arteries. In some 80-90% of people, however, retinal *venous pulsation* may be seen at or near the edge of the disc or, indeed, wherever the veins take a very sharp bend; due to the effect of the intraocular pressure. The venous pressure is lowest near the disc, and there is a certain amount of obstruction to the flow of blood as the vessels pass through the narrow neck at the lamina cribrosa. With each arterial pulsation, the intraocular pressure is suddenly slightly raised so that the increased pressure on the outside of the walls of the veins tends to make them collapse. This causes a sudden increased obstruction to the outflow of blood from the eye during systole, but the venous circulation recovers itself during the arterial diastole. The venous pulsation can be increased or made manifest, if absent, by increasing the intraocular pressure by slight pressure with the finger on the globe. This pressure is diastolic and therefore has been called the *negative venous pulse.*

The *macula lutea* is situated about 3 mm or 2 DD to the temporal side of the edge of the disc, a little below the level of the horizontal meridian. It is a small, circular area of a deeper red than the surrounding fundus, and in its centre there is nearly always a *foveal reflex,* seen as an intensely bright spot of light and is due to reflection of light from the walls of the foveal depression. The macular region is supplied by twigs from the superior and inferior temporal arteries, and by small branches coming straight from the disc. There are no retinal blood vessels at the fovea itself, and for a short distance around the centre known as the *foveal avascular zone;* about 0.4-0.6 mm in diameter. Occasionally, small arteries (cilioretinal) originating from the ciliary system run inwards to enter the eye (near the edge of the disc) and then bend sharply outwards towards the macula.

The peripheral retina is the area bounded by the equator and the ora serrata. The ora serrata marks the end of the choroid and retina and is grey to brownish-black in colour. The pars plana extends anteriorly from the ora serrata.

EXAMINATION OF THE FUNDUS

The details of the fundus should be examined systematically. The patient is instructed to look straight ahead and the examiner approaches the eye with an ophthalmoscope or +78 D or +90 D lens from the temporal side so that the disc or optic nerve head is brought into view. The shape and colour of the disc, the arrangement of the vessels, their pulsations if any the colour of the choroidal reflex (its uniformity or tessellation), and gross abnormalities (white or pigmented spots, etc.) are readily noted. The patient is then directed to look up, to the right, to the left and down. In this manner the periphery of the fundus is brought into view.

The macula is examined next. It may be brought into view by telling the patient to look into the light;

but it is best to fix the temporal edge of the disc and pass horizontally outwards for a distance of about 2 DD (a convenient unit in ophthalmoscopic topography), when the macula will be found. Finally, the periphery of the fundus is investigated with an indirect ophthalmoscope or three-mirror lens. With full dilation of the pupil it is possible to see almost up to the ora serrata, especially if the sclera over the ciliary region is slightly indented with a thimble depressor after the eye has been lightly anaesthetized. All findings should be recorded on a retinal chart (Fig. 20.1).

The use of a red-free light enhances the visibility of haemorrhages and blood vessels in the retina as well as defects in the nerve fibre layer, which may be seen as slits or wedges fanning upwards and downwards from the optic nerve head.

The general appearance of the fundus varies considerably in health and some experience is required in differentiating health and subtle disease. Diseases of the retina rarely occur in isolation, and are commonly associated with changes in the adjacent structures such as the choroid, vitreous and optic nerve. The retina is frequently affected by systemic diseases and these manifestations are termed retinopathies.

Retinal affections in general give rise to the following symptoms, only some of which need be present in individual cases. There is usually some diminution in visual acuity. There may be a concentric constriction of the field of vision or scotomata may be present corresponding with the areas affected. There may be metamorphopsia, micropsia or macropsia. The light sense is diminished and photophobia may be present. Pain is almost invariably absent, although discomfort may be experienced.

THE (SYSTEMIC) VASCULAR RETINOPATHIES

The vascular retinopathies occurring as part of a systemic disorder—hypertension, diabetes and late toxaemia of pregnancy—are usually associated with pronounced changes in the retinal vessels, reflecting the vascular status of other tissues such as the brain. The retinal

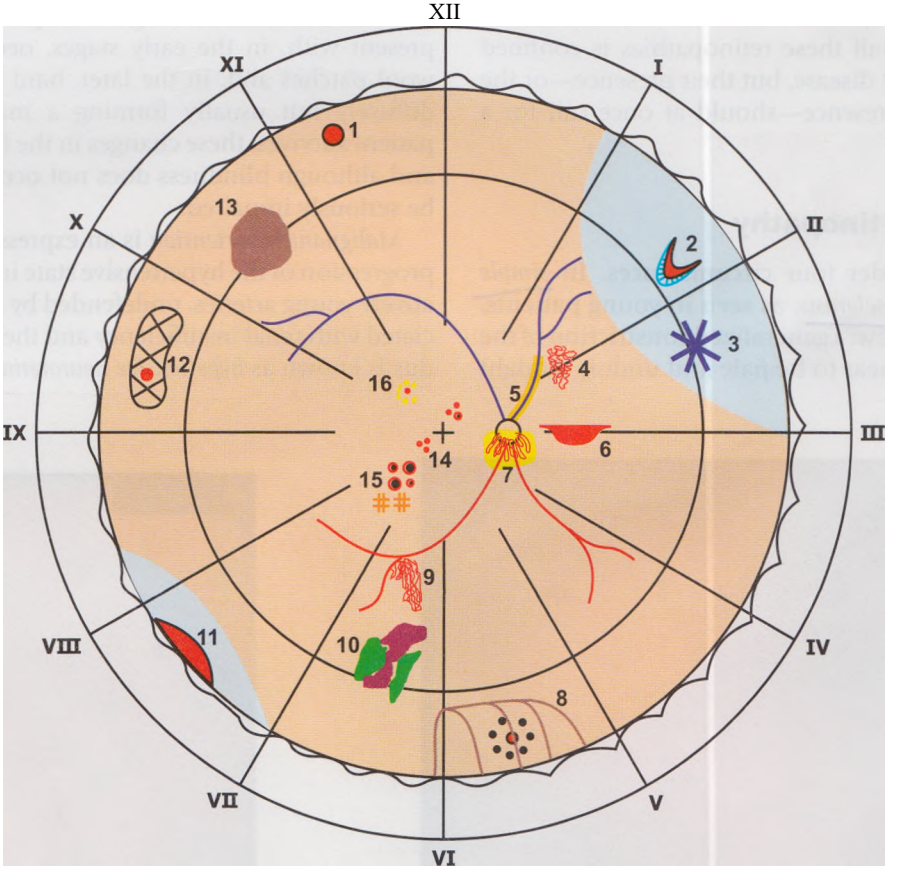


Fig. 20.1 Retinal diagram of common lesions. 1, retinal hole; 2, horseshoe-shaped flap tear with rolled posterior edge; 3, retinal fixed fold in a detached retina; 4, new vessels on retina; 5, venous sheathing; 6, preretinal haemorrhage; 7, new vessels on the disc; 8, circumferential scleral buckle with round hole surrounded by diathermy; 9, elevated new vessels with proliferative tissue; 10, old blood in the vitreous (green) along with fresh haemorrhages (red); 11, retinal dialysis with surrounding retinal detachment; 12, lattice degeneration with atrophic hole; 13, choroidal pigmentation such as a naevus; 14, macular oedema; 15, retinal haemorrhage; and 16, exudates.

changes probably originate from a state of anoxia which results in an increased permeability of the capillaries, the formation of multiple microaneurysms and local degenerative changes in the tissues of the retina.

The most common change is due to swelling of the nerve fibres, giving the appearance of cloud-like, 'soft' aggregates with ill-defined margins—*soft exudates* or cotton-wool patches, usually seen in the superficial layers of the retina. They are commonly small, but may form accumulations larger than the disc, and, since they disappear rapidly, they frequently change their shape. They are formed by the arrest of axoplasmic flow at the edge of an ischaemic area where nerve fibres cross the boundary. Other degenerative changes in the neural elements result from the extravasation of fluid. Extravasated fluid is rich in fibrin and proteins which readily coagulates, and a characteristic retinal manifestation is their deposition as masses of *hard exudates*.. These hyaline or lipid deposits appear as discrete, yellowish or white deposits, and are generally seen as a cluster around a group of leaking microaneurysms. In the macular region they tend to be thrown into radiating folds following the arrangement of the nerve fibres to form a fan- or star-shaped figure *(macular star).*

The treatment of all these retinopathies is confined to that of the general disease, but their presence—or the suspicion of their presence—should at once call for a medical review.

Hypertensive retinopathy

This may occur under four circumstances. In *simple hypertension without sclerosis,* as seen in young patientsT the retinal signs are few: a generalized constriction ofthe Irterioles which appear to be pale and unduly straight with acute-angled branching, additional superficial, flame-shaped haemorrhages and cotton-wool spots may occur and hard exudates are absent (Fig. 20.2). In *hypertension with involutionary sclerosis,* occurring in older patients, the picture of *arteriosclerotic retinopathy* appears. The vascular signs just described are augmented by localized constrictions and dilatations of the vessels with thickening of the vessel wall and the deposition of hard exudates and sometimes haemorrhages without any oedema. Changes at the arteriovenous crossings are diagnostic—nipping and a perpendicular placement of the veins—Gunn sign. Although the vascular changes are bilateral, the retinopathy may remain confined to one eye due to carotid artery insufficiency on that side.

In *arteriolar (diffuse hyperplastic*) *sclerosis* occurring in younger patients, the relatively youthful arterioles respond to the hypertension by proliferative and fibrous changes mainly affecting the media. In the kidneys there is usually a chronic glomerulonephritis and the classical ophthalmoscopic picture is known as 'albuminuric' or 'renal' retinopathy. The vessels show evidence of hypertension. They are narrow and tortuous with nicking at the arteriovenous crossings; multiple haemorrhages are present with, in the early stages, oedema and cotton-wool patches and, in the later, hard exudates scattered diffusely but usually forming a macular star. If the patient survives, these changes in the fundus may regress and although blindness does not occur, the vision may be seriously impaired.

Malignant hypertension is an expression of accelerated progression of the hypertensive state in a patient with relatively young arteries, undefended by sclerosis. It is associated with renal insufficiency and the picture of the fundus is known as *hypertensive neuroretinopathy,* dominated

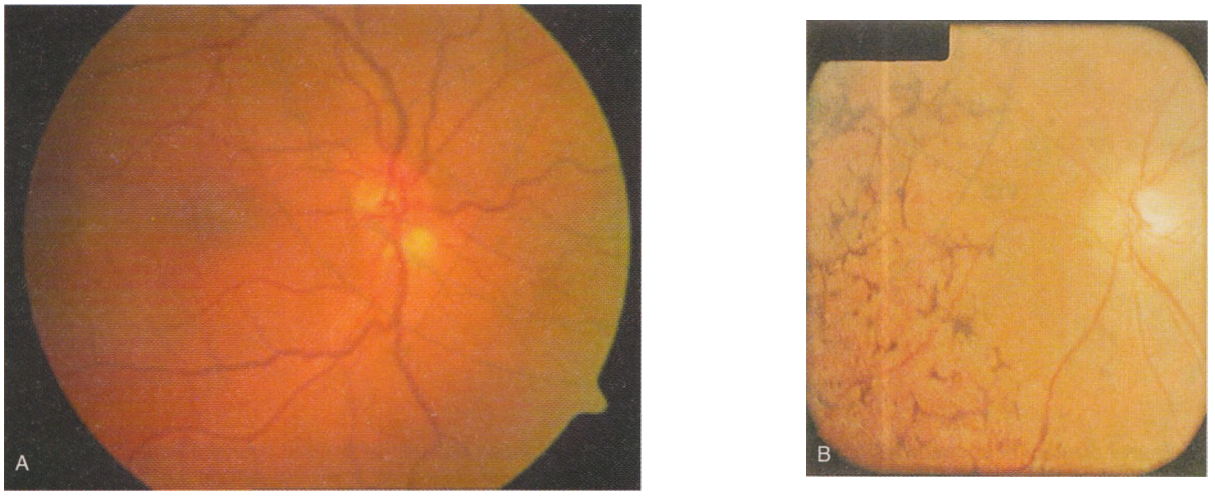


Fig. 20.2 (A) Hypertensive retinopathy grade II. (B) Disc pallor, arteriolar attenuation and pigmentary changes in a patient with retinitis pigmentosa.

by the appearance of oedema (Fig. 20.3). The entire retina may be clouded by a generalized oedema which may be particularly accentuated at the disc, resulting in a marked degree of disc oedema with multiple cotton-wool patches; hard exudates may be so profuse that the patches form enormous masses among which a macular star is often prominent. Vision is usually seriously affected. In such cases, particularly when disc oedema is marked, the prognosis is grave unless the hypertension can be controlled by medical or surgical methods. If general treatment is successful, the ophthalmoscopic appearances may ameliorate dramatically and the vision improves but the ultimate prognosis is unsatisfactory.

The first attempt to relate the retinal vascular changes to survival in the hypertensive population was by Keith, Wagner and Barker in 1939. They divided hypertensive patients into four groups on the basis of the ophthalmoscopic characteristics of each group. This grouping correlated directly with the degree of systemic hypertension and inversely with the prognosis for survival.

- Grade 1: Mild to moderate narrowing or sclerosis of the smaller arterioles.
- Grade 2: Moderate to marked narrowing of the retinal arterioles; exaggeration of the light reflex; changes at the arteriovenous crossings.
- Grade 3: Retinal arteriolar narrowing and focal constriction, prominent arteriovenous crossing changes, retinal oedema, cotton-wool spots, flame-shaped haemorrhages.
- Grade 4: All the features of Grade 3 are seen, as well as papilloedema.

This classification is still in use today and is widely accepted, although there is some difficulty in defining the criteria for Grades 1 and 2.

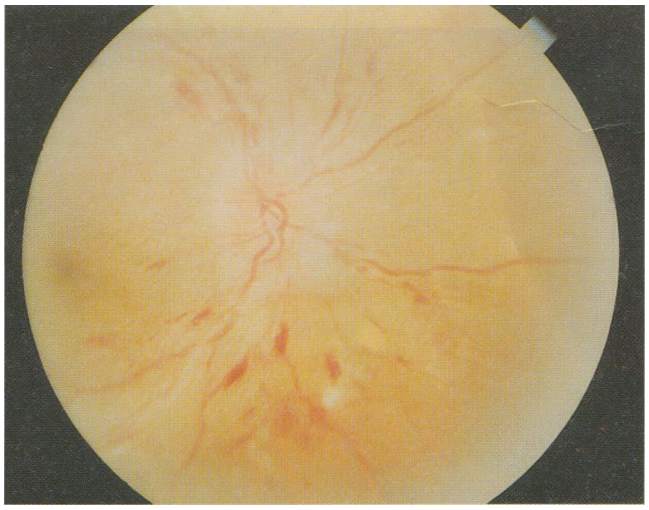


Fig. 203 Hypertensive retinopathy grade IV. There is oedema of the optic disc and marked attenuation of the retinal arterioles, flame-shaped haemorrhages and cotton–wool spots.

Diabetic retinopathy

Diabetes mellitus is a common disease and occurs in one of two forms: Type 1, previously referred to as insulin-dependent diabetes mellitus or IDDM, and Type 2, previously termed as non-insulin dependent diabetes mellitus or NIDDJVL This disease results in generalized macro- and microvascular complications. Microvascular complications due to microangiopathy have been directly linked to glycaemic control and affect the kidneys, eyes and peripheral nerves. Macrovascular complications are more common in diabetic patients than the normal population but are not necessarily directly linked to the level of hyperglycaemia and affect the heart, brain and limbs. A characteristic picture is seen in the fundus, however, in the elderly; the ophthalmoscopic picture may be complicated by arteriosclerosis and hypertension or even renal disease. Almost all patients with Type I diabetes develop a retinopathy in about 15 years. In those with Type II diabetes, the risk of diabetic retinopathy increases with the duration of diabetes, accompanying hypertension and smoking. Diabetics have a 20-25 times greater risk of blindness as compared to the normal population. As therapy of the retinopathy will at best stabilize vision or decrease the rate of visual loss, it is important to screen all diabetics annually by examining the fundus after dilating pupil so as to institute therapy as early as possible. Strict glycaemic control helps to stabilize the retinal changes.

Pathogenesis: Histopathological examination of eyes with diabetic retinopathy shows a loss of intramural pericytes, thickening of the basement membrane and progressive closure of the retinal capillaries. The initial loss of pericytes leads to the formation of dilatations of the vessels seen as microaneurysms and a breakdown of the blood-retinal barrier, allowing leakage of the vascular contents into the surrounding tissues. Oedema is present around such areas, as well as hard exudates and small, localized deep haemorrhages known as dot and blot haemorrhages. In addition, there is an increased aggregation of platelets, causing capillary non-perfusion. Extensive closureof the capillaries leads to ischaemia of the retina. The body attempts to re-establish blood supply by opening up shunt vessels, 'intraretinal microvascular abnormalities' (IRMA), or by elaborating vasoproliferative substances such as vascular endothelial growth factor, that lead to neovascularization at the border between well and poorly perfused retinal areas. This neovascular tissue is more friable, bleeds easily and incites a fibroblastic response.

The causal factors have not been identified but certain risk factors are known to play a role in the development of diabetic retinopathy. Poor control of diabetes mellitus is associated with an earlier onset of diabetic retinopathy, as well as a progression of previously controlled retinopathy. The frequency of the incidence of diabetic

retinopathy increases with the length of time the patient has had diabetes, even though the general disease is mild or has been well controlled, and hence it usually occurs in elderly patients and has become much more common since the use of insulin, which has prolonged the life span of diabetics. Retinopathy is common but not invariable after the disease has lasted 10 years and affects the majority of patients after 20 years. It thus affects both the young and old, for it is the diabetic age and not the chronological age that is important. Uncontrolled systemic hypertension, a poor renal status and smoking are other risk factors that adversely influence diabetic retinopathy.

The presence of retinopathy does not bear any relation to the prognosis of diabetes or the expectancy of life. Visual damage, however, is frequently extensive and permanent, a calamity since the disease is bilateral.

Ophthalmoscopically, the earliest changes of *background diabetic retinopathy* characteristically affect the smaller blood vessels. Small dot and blot haemorrhages are common, and degeneration of the vessel walls leads to the development of microaneurysms, sometimes in vast numbers, which appear as minute round dots occasionally arranged like clusters of grapes at the ends of small vascular twigs; these are an early sign of background diabetic retinopathy (Fig. 20.4A and B). Oedema is not marked, but all over the posterior pole there tend to gather hard, white or yellow, waxy-looking patches of exudates with welldefined,'often serrated margins, which occasionally coalesce into extensive plaques. The fully developed ocular picture with microaneurysms is often associated with evidence of glomerulosclerosis in the kidney (Kimmelstiel-Wilson nephropathy). The management consists of good metabolic control of the diabetes, together with any attendant renal problems or systemic hypertension.

Diabetic macnlopathy: Macular oedema occurs in a large number of eyes and, with central hard exudates, is the commonest cause of diminution of vision in diabetic retinopathy. Both are caused by leakage from dilated capillaries. Clinically significant macular oedema (CSME) is defined as oedema or hard exudates present within 500 nm of the foveal centre, or oedema of more than one disc area in extent, any part of which is within 1 DD of the foveal centre. The leakage can be focal or diffuse, resulting in *jocal* or *diffuse maculopathy. Ischaemic maculopathy* is the result of ischaemic changes at the macula (Fig. 20.5). A mixed histological picture of oedema and ischaemia af'fRe macular area is fairly common. The patient may complain of decrease in vision, but could also have normal vision. Clinically CSME is best recognized by slit-lamp biomicroscopy using a +78 D or +60 D lens, as a loss of the foveal reflex and thickening at or around the macula. Treatment is by photo-coagulcP tion using lasers with long wavelengths, such as krypton and diode. Fluorescein angiography identifies the areas of leakage which can then be photocoagulated directly if focal, or by light intensity burns in a grid pattern of 100-250 micron spots over the posterior pole avoiding the foveal avascular zone (Fig. 20.6 and Table 20.1). Three to four sessions may be required 6-8 weeks apart to stabilize vision if the oedema is diffuse. Fluorescein angiography also helps to diagnose an ischaemic macujppathy, in which case photocoagulation is not helpful and should not be attempted. ^ *c[l(\£p. (*Ca'O *0*

Circinate retinopathy is due to chronic de&ema involv- ' ing a considerable area of the retina at and around the macula, with massive changes in the retina itself. It occurs in elderly people and may form part of a diabetic or hypertensive retinopathy. A girdle of bright white patches with crenated borders appears around the

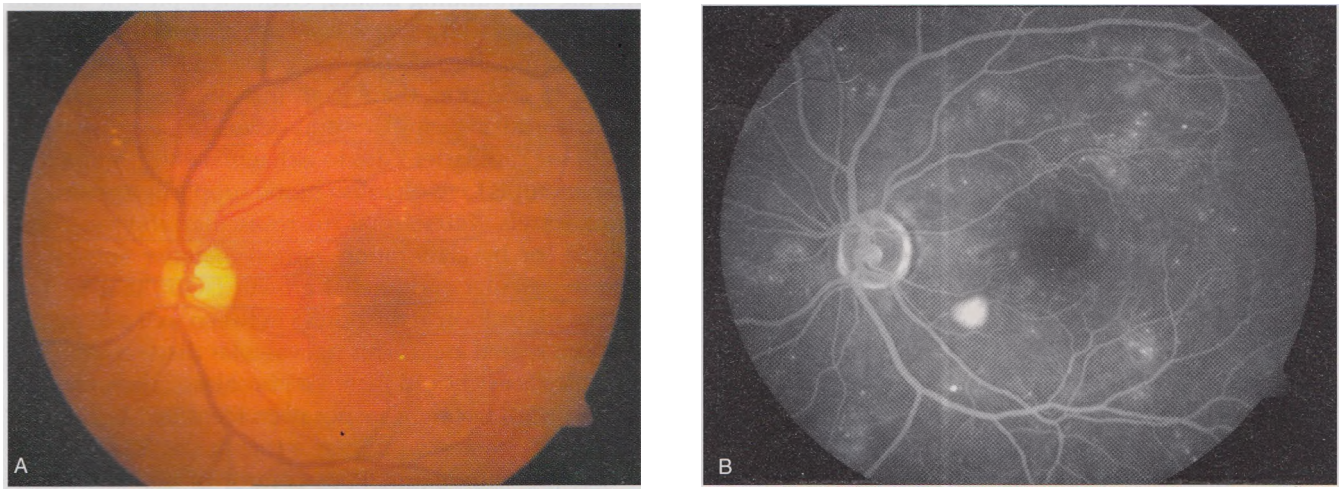
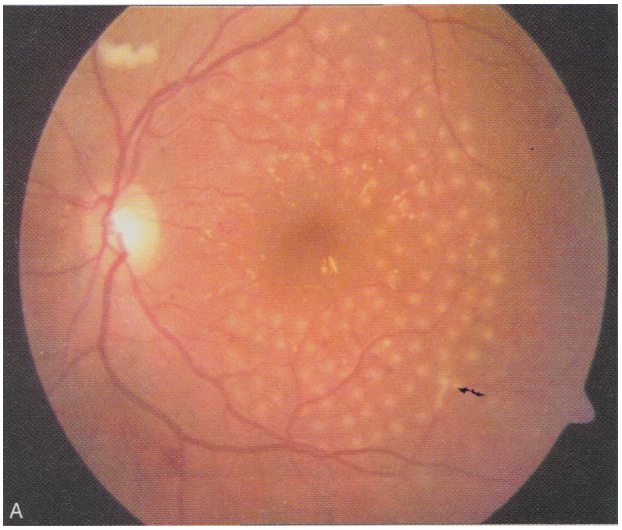


Fig. 20.4 Early background diabetic retinopathy. (A) Hard exudates and dot-blot haemorrhages are seen scattered over the posterior pole. (B) Fluorescein angiogram illustrating multiple leaks corresponding to areas of microaneurysms and exudation. (By courtesy of P Venkatesh)



Follow up of macular edema on OCT

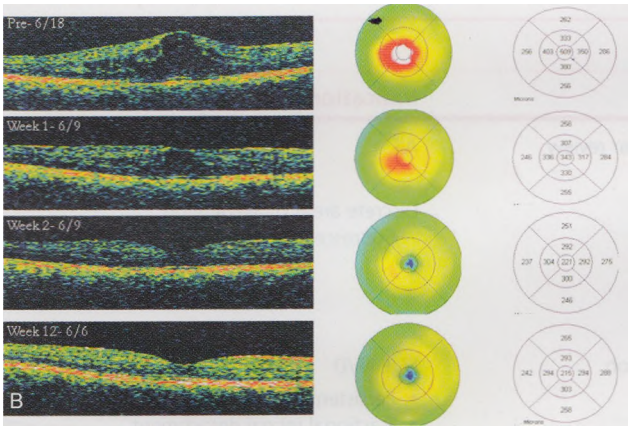


Fig. 20.5 Macular grid.

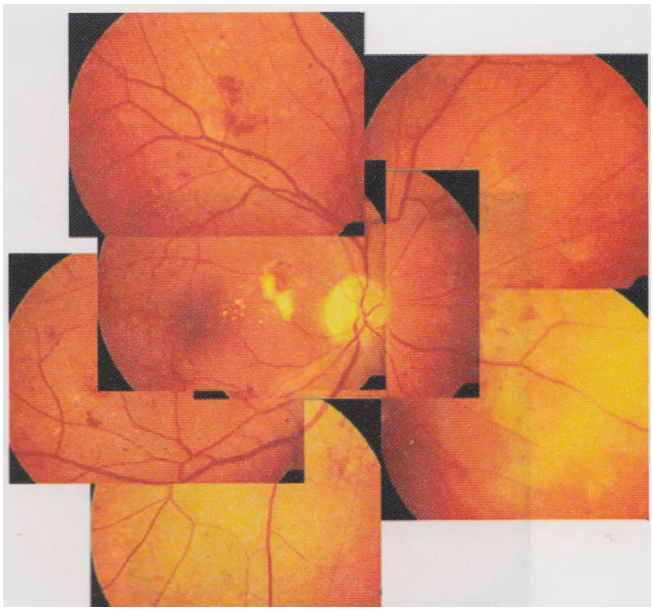


Fig. 20.6 Appearance of laser burns several hours after macular grid for diabetic maculopathy. (By courtesy of P Venkatesh)

macula, made up of aggregations of macrophages full of lipids (Fig. 20.7). The diameter of the girdle, which is usually an imperfect circle, ellipse or horseshoe-shaped open towards the temporal side, is generally considerably greater than a disc diameter, and follows the larger temporal branches of the superior and inferior temporal vessels. The vessels pass over the spots. The macula shows yellowish-wnite areas, slight pigmentation and usually oedema. The patches develop slowly and are usually well advanced before they are noticed. The disease is unilateral in about half the cases. Central vision is much rediicec[. but the peripheral fieldTemainsTull. The patches sometimes disappear slowly and some visual improvement follows. Treatment may be effective if the source of vascular leakage can be localized and destroyed by photocoagulatTon. Intravitreal steroids and anti-VEGF (vascular endothelial growth factor) agents are also being used as therapeutic alternatives in patients with diabetic macular oedema that is resistant to laser photocoagulation (Table 20.1)7

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Preproliferative diabetic retinopathy: Ischaemic changes superimposed on background diabetic retinopathy produce a preproliferative diabetic retinopathy. The fundus shows intraretinal microvascular abnormalities or shunt vessels, and evidence of ischaemia such as more than 8-10 areas of cotton-wool spots (Fig. 20.8). Dilatation and irregularities of the veins and attenuation of the arterioles is also present. These changes indicate progression towards the more devastating form of proliferative diabetic retinopathy. Such patients should be reviewed frequently with fluorescein angiography and photocoagulated at the first sign of new vessels in the retina. Panretinal photocoagulation should be undertaken^ loITowaip^is not possible.

Proliferative diabetic retinopathy: About two-thirds of Type 1 diabetics are likely to develop proliferative diabetic retinopathy over three decades. The neovascularization arises from the optic nerve head; there is neovascularization of the disc (NVD) and along the large vessels, as well as neovascularization elsewhere fNYE) (Fig. 20.9). It appears in areas of capillary closure and the accompanying fibrous tissue varies in extent. Such fibrovascular tissue may lie flat on the retina or attach itself to the posterior vitreous face leading later to vitreous traction, retinal separation and the tearing of blood vessels. This is the commonest cause of spontaneous vitreous haemorrhage in adults. Extension of the neovascular process into the anterior segment with neovascularization of the jris_(rubeosis iridis) and angle and subsequent neovascular glaucoma can also occur.

~The treatment available for proliferative diabetic retinopathy is photocoagulation of the ischaemic areas to reduce the metabolic demand and decrease or prevent

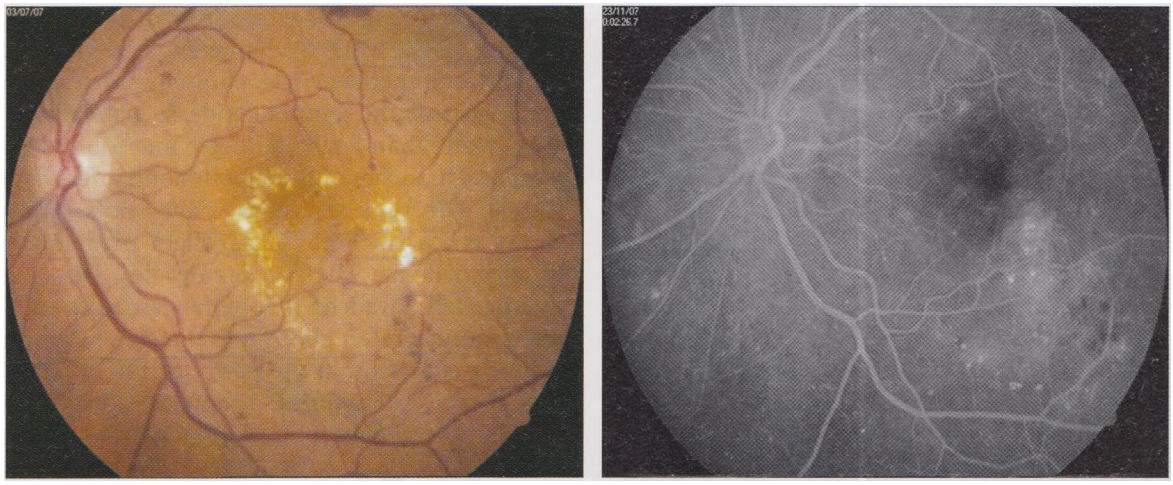


Fig. 20.7 Circinate retinopathy. Rings of hard exudates can be seen at the posterior pole. (By courtesy of P Venkatesh)

Table 20.1 Management of diabetic retinopathy

Type of retinopathy	Therapy	Indications
Background	Control of diabetes; regular review	All
Maculopathy		
• CSME	Focal photocoagulation	Discrete areas of leakage on fluorescein angiography
Diffuse leak around macula	Grid laser/IVTA	
• Circinate	Focal photocoagulation	
Preproliferative retinopathy	Frequent review	
Proliferative retinopathy	Panretinal photocoagulation	NVE/NVD
Advanced diabetic eye disease	Vitreoretinal surgery with photocoagulation	• Persistent vitreous haemorrhage • Tractional retinal detachment

CSME, clinically significant macular oedema; NVE, neovascularization elsewhere; and NVD, neovascularization of the disc.

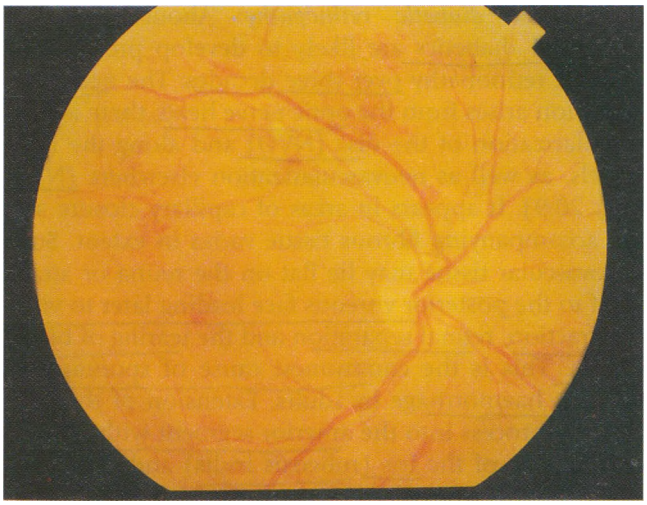


Fig. 20.8 Preproliferative retinopathy. Extensive flame-shaped haemorrhages and soft exudates along with microvascular anomalies are scattered over the posterior pole.

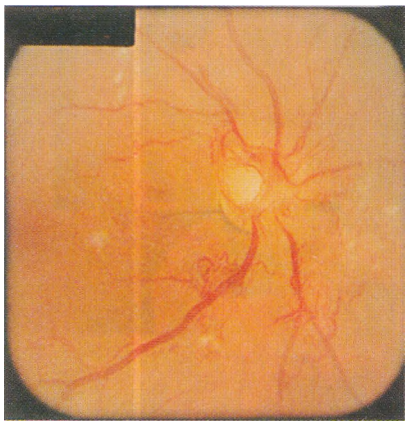


Fig. 20.9 Proliferative diabetic retinopathy. There is neovascularization of the disc with cotton-wool spots.

the release of vasoproliferative factors by conversion of hypoxic foci into anoxic areas and leaking vascular anomalies into inert scars (Table 20.1). This relieves the retina of oedema and hard yellow exudates, improves its function and also causes the regression of new vessels, inhibiting further haemorrhages. Patients who have neovascularization affecting more than one-third of the disc surface, greater than half a disc diameter of neovascularization elsewhere or vitreous haemorrhage are believed to be at high risk for severe visual loss and require panretinal photocoagulation. This is done using a retinal laser lens, which gives a large field of view (Fig. 20.10). A circular area of a radius of *1×h* DD with the fovea at its centre is left untouched. Photocoagulation burns with the argon, frequency-doubled YAG 532 or the diode laser are applied outside the vascular arcade above and below the macula using spot burns of 200 microns each (Fig. 20.11). In all meridians, photocoagulation is extended anteriorly to the equator using spot burns of 500 microns. Burns are applied to blanch the retinal pigment epithelium, and these preferentially obliterate the deeper layers. A total of 2000-3000 bums are needed to complete the treatment in each patient, administered in 2-4 sessions.

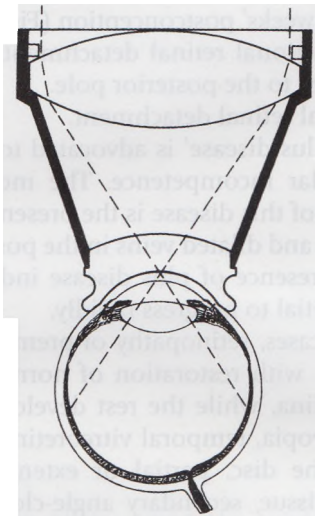
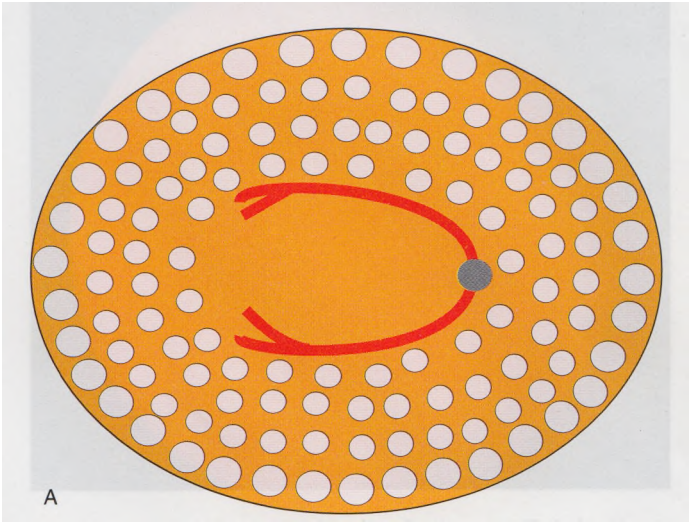


Fig. 20.10 Retinal laser contact lens.

In diabetics, the long-term visual results of panretinal photocoagulation for eyes with new vessels in the disc are most encouraging. Neovascularization of the iris usually regresses after laser therapy, but neovascular glaucoma is the major cause of visual failure along with tractional retinal detachment. Successful visual results require long-term follow-up with repeated photocoagulation of recurrent neovascularization and macular leaks.

Adjunctive modes of inhibiting vascular endothelial growth factor allow greater success in controlling the neovascularization. Several anti-VEGF agents, such as bevacizumab (Avastin) and ranibizumab (Lucentis), have been developed and are being used in diabetic retinopathy. Triamcinolone acetonide in an intravitreal dose of 1/2/4 mg has been evaluated in the treatment of diabetic macular oedema.

In more advanced fibroproliferative retinopathy causing a tractional retinal detachment or with vitreous haemorrhage that does not clear, vitreoretinal surgery is the treatment of choice *(see* Chapter 21). Early vitrectomy is more beneficial for those with Type 1 diabetes who are younger and more prone to severe proliferative retinopathy. Early removal of the vitreous, which acts as a scaffolding for new blood vessel growth, prevents the development of additional neovascularization. A tractional retinal detachment is treated by excising as much



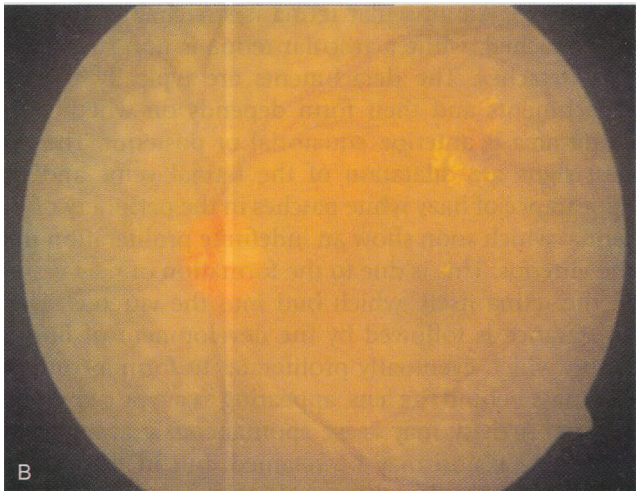


Fig. 20.11 (A) Panretinal photocoagulation for proliferative diabetic retinopathy. (B) Appearance of laser burns after one sitting of panretinal photocoagulation in a diabetic patient. Macular grid is also visible. (By courtesy of P Venkatesh)

fibrovascular tissue from the retinal surface as possible and sealing any retinal breaks with laser and an internal tamponade.

A peculiar feature sometimes met with in diabetes is *lipaemia.* It occurs especially in young patients when the triglyceride concentration in the blood exceeds 2000 mg/100 ml. This condition occurs in growth-onset diabetes associated with marked acidosis. The ophthalmoscopic appearances are striking and are known as *lipaemia retinalis.* The retinal vessels contain fluid which looks like milk, the arteries being pale red and the veins having a slight violet tint. The fundus, in general, has a relatively normal coloration.

Retinopathy of prematurity

The retinal manifestations of this disease are generally noted some weeks after birth in premature infants who have been given high concentrations of oxygen, and is usually confined to those with a birth weight of under 1.5 kg and/or a gestational age of 32 weeks.

Pathogenesis

Retinal vessels extend up to the nasal edge of the retina by the eighth month of gestation, but the temporal periphery becomes vascularized later, by about a month after birth. These immature vessels are prone to damage in the presence of oxygen which leads to vasoconstriction, especially in premature infants. Retinopathy of prematurity has been shown to follow excessive oxygenation in the nursing of premature infants during the early stages of their lives. As a result, the retinal arteries and eventually the veins are obliterated, inciting a phase of neovascularization. The retinal and vitreous changes in retinopathy of prematurity can be explained by proliferation and contraction of tissue originating in the shunt area. An avascular retina is stretchable, and may stay attached, while a vascular retina is non-stretchable and detaches. The detachments are typically traction detachments and their form depends on whether the shunt area is anterior, equatorial or posterior. The earliest signs are dilatation of the retinal veins and the appearance of hazy white patches in the periphery of the retina, which soon show an indefinite proliferation into the vitreous. This is due to the formation of new vessels in the retina itself, which bud into the vitreous. Their appearance is followed by the development of fibrous tissue, which eventually proliferates to form a continuous mass behind the lens, appearing as a type of pseudoglioma. Activity may cease spontaneously at any stage and some vision may be retained, but in many cases it progresses so that the retina is detached and the eye becomes microphthalmic. In this case, of course, vision is lost. The condition is usually bilateral.

Five stages of retinopathy of prematurity are included in the new international classification for the acute phases.

- Stage 1: A discrete line of demarcation separates the anterior, immature, avascular retina from the mature, vascularized retina posteriorly. A thin, greyish line is seen concentric to the ora serrata with some abnormal vessels present posterior to it.
- Stage 2: The demarcation line is transformed into an elevated ridge separating the avascular and vascular retina. The ridge is vascularized and some neovascular tufts can be seen posterior to it (Fig. 20.12).
- Stage 3: Fibrovascular tissue develops at the ridge with extraretinal neovascularization extending into the vitreous. The posterior retina now shows tortuous, dilated retinal vessels. Retinal and vitreous haemorrhages are common. This stage is seen to occur at about 35 weeks' postconception (Fig. 20.13).
- Stage 4: Tractional retinal detachment extends from the periphery to the posterior pole.
- Stage 5: Total retinal detachment.

The term 'plus disease' is advocated to indicate progressive vascular incompetence. The most prominent manifestation of this disease is the presence of tortuous retinal arteries and dilated veins in the posterior pole. In general, the presence of plus disease indicates activity, with the potential to progress rapidly.

In 80% of cases, retinopathy of prematurity resolves spontaneously with restoration of normal vascularization of the retina, while the rest develop some sequelae such as myopia, temporal vitreoretinal fibrosis with dragging of the disc, partial or extensive retrolental fibrovascular tissue, secondary angle-closure glaucoma

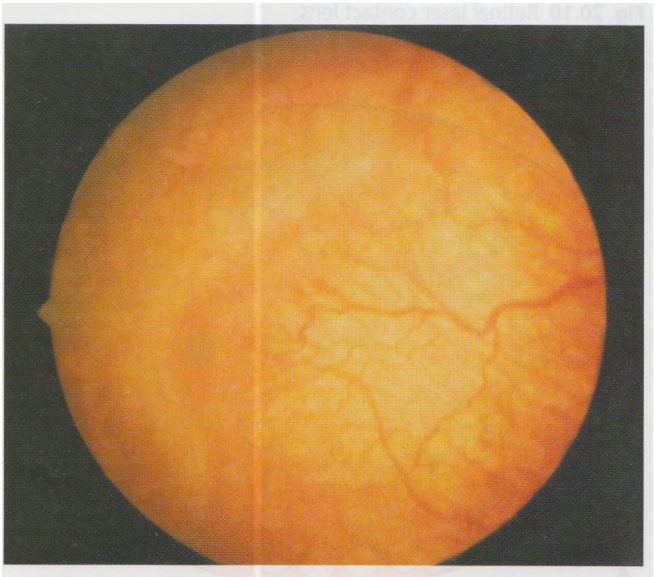


Fig. 20.12 A fibrovascular frond without any demarcation line. As one follows the blood vessels anteriorly, they disappear beyond the neovascular area. (By courtesy Harsh Kumar and Michael J Shapiro)

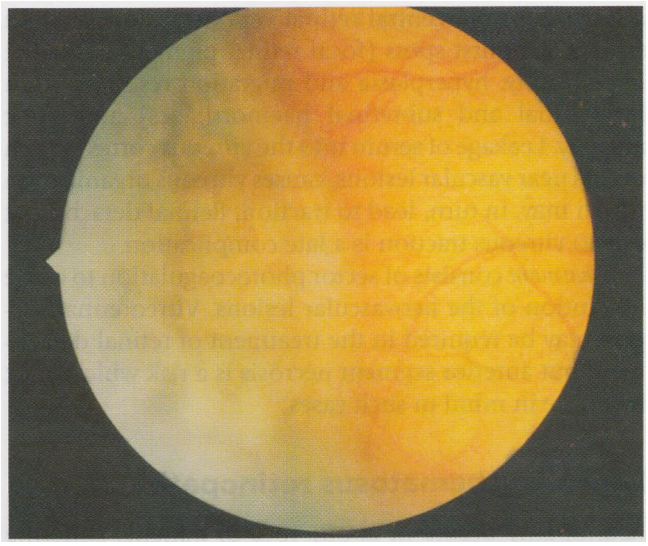


Fig. 20.13 Laser spots in the avascular retina anterior to the ridge. (By courtesy Harsh Kumar and Michael J Shapiro)

and total retinal detachment. Retrolental fibroplasia as a term is now reserved for the non-acute, late cicatricial changes that are seen in severely affected infants.

Management

Prophylaxis is most important. All babies weighing less than 1500g at birth or having a gestation period of less than 32 weeks should be screened with indirect ophthalmoscopy for retinopathy of prematurity, between 32 and 36 weeks postconception. In the management of premature infants weighing less than 1200 g, the $Pa0_2$ level of blood from the umbilical artery should be monitored, levels of 50-100 mmHg being regarded as unlikely to produce constriction of immature retinal vessels. Unsatisfactory guides include 'pinkness', oxygen given at less than 40% in the tent and vascular constriction as seen by the ophthalmologist. Before the child is discharged from the hospital the temporal periphery of each retina should be examined with the indirect ophthalmoscope to look for threshold disease, i.e. a ridge with extraretinal fibrovascular proliferation and posterior venous dilatation and arteriolar tortuosity.

If minor signs of retinopathy of prematurity are noticed, examination should be repeated at the ages of 1, 3 and 6 months and every 4 months up to the age of 4 years, with the aim of diagnosing early retinal holes or localized detachment of the retina. Treatment by photocoagulation or cryotherapy of one eye should be considered only when *definitely progressive* 'plus disease' or bilateral proliferative lesions are noted in the vitreous. The presence of mild intravitreal neovascularization warrants delay in the consideration of photocoagulation therapy, since spontaneous resolution occurs in a high percentage of patients (80%). Once the condition has developed fully, the visual prognosis is poor and treatment is relatively ineffective. Removal of the fibrous mass requires a lensectomy and vitrectomy and may be helpful in some cases.

Acquired immune deficiency syndrome

Many persons with acquired immune deficiency syndrome (AIDS) have retinal manifestations. Cotton-wool spots are seen in about 50% of cases, although their aetiology is uncertain. Areas involved by cotton-wool spots are free of infectious agents and immunoglobulin deposition, and it is now believed that these are directly virus-related (HIV). Patients are open to infection from cytomegalovirus, *Toxoplasma* and herpesvirus, as well as other opportunistic organisms.

Retinopathy in toxaemia of pregnancy

This occurs late in pregnancy, exceptionally before the sixth month and practically always in the ninth month. It has many of the characteristics of hypertensive retinopathy. Initially there is narrowing of the retinal arteries, usually the nasal branches first, which in any event are the smaller; and this is followed by spasmodic contractions. As the blood pressure rises, oedema appears making it resemble hypertensive retinopathy in its most marked forms. The exudation may be so profuse and generalized as to cause a severe retinal detachment.

The occurrence of this disease puts a peculiar responsibility on the ophthalmologist and any visual symptoms occurring in the later stages of pregnancy must be thoroughly investigated. Constriction, particularly of the nasal branches of the retinal artery, should at once call for extreme care in the general treatment of the case; the occurrence of arterial spasms together with an increase in weight, indicating the systemic retention of fluid, are ominous signs. The advent of retinopathy should call for a termination of the pregnancy, since its continuance will probably result in the loss of vision and perhaps of the life of the mother as well as in the birth of a stillborn foetus. Timely induction of labour, however, as well as adequate general care, usually lead to recovery, provided gross organic changes have not occurred in the retina; even the retinal detachment will resolve in these circumstances.

The retinopathy of a *phaeochromocytoma* has similar features in that it usually affects a healthy retinal vascular system and the changes are reversible provided they have not been present for too long a period.

Sickle cell retinopathy

Sickle cell haemoglobin is an abnormal haemoglobin found mainly but not exclusively in people of African origin. When it is deoxygenated it becomes insoluble and distorts the normally discoid red cell into a characteristic sickle shape. Such sickled red cells tend to obstruct

capillaries and this leads to infarction, particularly in the periphery of the retina.

A variant called sickle cell C disease does not occur as frequently as sickle cell anaemia or the sickle cell trait, but it is the most important haemoglobinopathy in ophthalmology because its clinical manifestation is predominantly in the eye, consisting of retinopathy, angioid streaks, papilloedema, cataract, glaucoma, and circumscribed dilatation and constriction of conjunctival capillaries.

Pathogenesis: Normal adult haemoglobin is a tetramer formed from haemoglobin units. Each of the four globin units is a polypeptide chain of 140 amino acids. Two of the globin units are so similar as to be called 'a', whereas the other two are called '(3'. Normal adult haemoglobin is designated a2 (32, different genes being responsible for the production of the a- and the |3 polypeptide chains. In sickle cell haemoglobin the molecule is identical to normal haemoglobin, except that in the sixth position of the p polypeptide chains, the amino acid valine is present instead of glutamic add. In haemoglobin C, the amino acid lysine will have been substituted for the glutamic acid in the sixth position of the |3 polypeptide chains. Patients with sickle cell haemoglobin C disease (SC disease) lack a normal gene capable of producing normal 3 polypeptide chain genes. They therefore have no normal adult haemoglobin, their haemoglobin consists of HbS and HbC produced by the ($3^{s}$and (3^{C} polypeptide chains, respectively.

The fundus shows both proliferative and non-proliferative changes. The former begins with occlusion of the peripheral arterioles leading to neovascularization and vitreous haemorrhage. Fibrovascular proliferation creates formations like 'sea fans', particularly in the superotemporal periphery of the retina (Fig. 20.14A and B). The retinopathy consists of vascular tortuosity, central retinal artery occlusion, central retinal vein occlusion, angioid streaks, sunburst spots (focal retinal pigment epithelial hypertrophy, hyperplasia and migration resulting from intraretinal and subretinal haemorrhages) and optic atrophy. Leakage of serum into the vitreous cortex, which occurs near vascular lesions, causes vitreous organization which may, in turn, lead to traction. Retinal detachment due to vitreous traction is a late complication.

Treatment consists of sector photocoagulation to cause involution of the neovascular lesions. Vitreoretinal surgery may be required in the treatment of retinal detachment but anterior segment necrosis is a risk which must be borne in mind in such cases.

Lupus erythematosus retinopathy

Retinopathy occurs in about 10% of patients suffering from lupus erythematosus. Cotton-wool spots in the posterior retina associated with flame-shaped haemorrhages occur, sometimes with papilloedema. If there is renal involvement the picture may be complicated by the superimposition of a hypertensive retinopathy.

Other associations are keratoconjunctivitis as part of a Sjogren syndrome, nodules in the sclera and episclera, anterior uveitis and a butterfly skin eruption over the nose and cheeks involving the lower lids. Such patients demonstrate the LE cell phenomenon whereby leucocyte nuclei undergo spontaneous denaturation and phagocytosis. Antinuclear factors are demonstrated by immunofluorescence and are present in 95-100% of patients.

The tissue lesions of this disease are due to deposition of antigen-antibody complexes. IgG and complement have been demonstrated in the glomeruli of lupus erythematosus patients.

Systemic lupus erythematosus affects young women nine times more commonly than men. It may be due to an

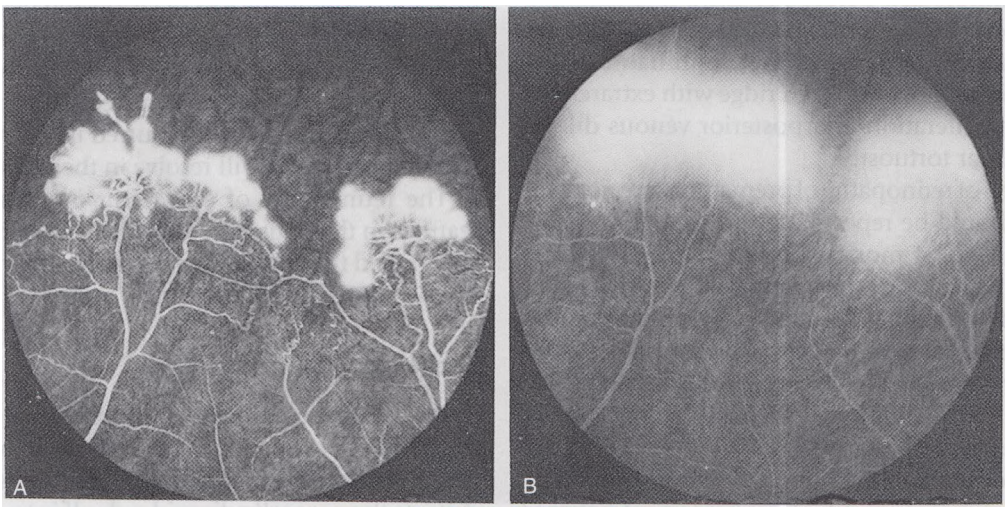


Fig. 20.14 (A and B) Fluorescein angiogram of sickle cell retinopathy showing the neovascular fronds leaking dye in the late phases.

innate tendency to produce auto-antibodies because the defective T-lymphocytes fail to exercise their restraining influence on B-lymphocyte function.

VASCULAR DISORDERS OF THE RETINA

Obstruction/Occlusion of the retinal arteries

An obstruction, complete or partial, permanent or temporary, may affect either the retinal arteries or veins.

Obstruction of the arterial circulation

Obstruction of a retinal artery is usually due to an embolus; superadded spasm often completes the occlusion. It may occur without obvious general vascular disease or, when widespread, there may be associated arteriosclerosis, hypertension or Buerger disease. Obstruction by an embolus (Fig. 20.15) is often secondary to a plaque of atheroma situated at the bifurcation of the common carotid artery in the neck, or occasionally to a diseased mitral or aortic valve.

The obstruction may affect the central artery itself when the entire retina is involved, or a peripheral branch when the effects are localized. *Central retinal artery occlusion (CRAO)* is nearly always at the lamina cribrosa, where the vessels normally become slightly narrowed. Such an accident causes sudden and complete retinal ischaemia and this tissue rapidly dies. The eye becomes suddenly blind, although when the causative factor is minute emboli, premonitory obscurations of vision may occur. Examination of the fundus reveals a very typical picture (Fig. 20.16A). The larger arteries are reduced to threads, the smaller are invisible but the veins are little altered except on the disc where they are contracted. Within a few hours the retina loses its transparency, becoming opaque and milky-white, especially in the neighbourhood of the disc and macula. At the fovea centralis, where the retina is extremely thin, the red reflex from the choroid is visible and appears as a round cherry-red spot, presenting a strong contrast to the cloudy white background.

When obstruction to the blood flow is not complete, the flow may be partially restored in the course of a few days, in which case gentle pressure upon the globe may break up the column of venous blood into red beads separated by clear interspaces. The beads move in a jerky fashion through the vessels, sometimes in the normal direction of blood flow, sometimes in the opposite direction (the 'cattle-truck' appearance). If the veins are easily emptied of blood or arterial pulsation is produced by slight pressure on the eyeball, it is evidence of incomplete blockage.

The white appearance of the retina takes several weeks to clear up but eventually the membrane regains its transparency and appears normal; it is, however, completely atrophic apart from the outer layers which receive their nourishment from the choroid. The vessels are contracted or reduced to white threads although some of them refill at a later stage due to the establishment of a feeble collateral circulation through an anastomoses with the ciliary system round the disc. The disc is atrophic. There is no direct pupillary reaction and light perception is lost.

In some cases a certain degree of central vision persists in spite of apparent complete occlusion of the central artery. This is due to the presence of cilioretinal arteries which, when present, always supply the macular region and naturally escape occlusion; or to a macular branch of the central artery given off proximal to the block. The remainder of the field of vision is lost. In rare cases a cilioretinal artery alone becomes blocked.

In *branch retinal artery occlusion (BRAO),* only the area supplied by this branch is affected. In the early stages the corresponding scotoma is usually somewhat indefinite, but later settles down to form a permanent sector-shaped defect.

Treatment seldom helps, but attempts should be made to relieve spasm or drive an embolus into a less important branch if the patient is seen early. Massaging the globe is probably the most effective method but paracentesis

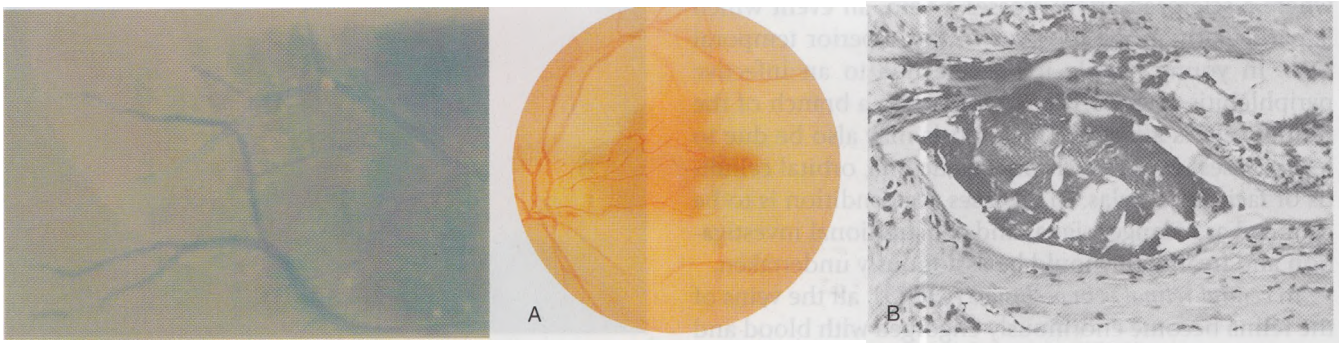


Fig. 20.15 Embolus seen in the retinal arteriole at the point of branching. (By courtesy of GS Sihota)

Fig. 20,16 (A) Central retinal artery occlusion with a cherry-red spot and sparing of a temporal cilioretinal vessel. (B) Embolic occlusion of the central retinal artery. (By courtesy of Wolter)

has been employed for this purpose; to be effective such measures must be adopted without delay. Inhalation of amyl nitrite produces vasodilatation. Branch occlusion may be relieved in this way. The normal result of an occlusion of the central artery, however, is blindness.

Obstruction of the venous circulation

Venous stasis retinopathy is a well-defined clinical entity that consists of unilateral disc oedema with variable retinal vascular changes in young healthy adults. The individual is usually 20-40 years of age and the initial symptom is a vague, unilateral fogginess of vision. The retinal vascular abnormality may be minimal or present as markedly engorged, dilated, tortuous veins and haemorrhages at the posterior pole extending into the retinal periphery. Visual acuity remains good and vitreous haemorrhage is never present. Neuro-ophthalmological examination is negative and fluorescein angiography shows venous stasis with delayed venous drainage. There is generally no permanent visual defect. Systemic corticosteroids are occasionally used but the disease can safely be followed without neurodiagnostic studies in a healthy young adult where there are no abnormal systemic or neuro-ophthalmological findings. Steroids should be withheld unless there is macular oedema. The fundus picture simulates that of central venous thrombosis and probably results from phlebitis affecting the central vein within the optic nerve head. The cause is unknown although increased levels of circulating IgM have been reported in a large number of patients. The essential difference between venous stasis retinopathy and central venous thrombosis is that in the former there is a stasis of the venous circulation in the absence of ischaemia of the retina.

Venous thrombosis usually occurs in elderly people with cardiovascular disease. In these cases the obstruction is usually in the central vein just behind the lamina cribrosa where the vein shares a common sheath with the artery so that the two are affected by the same sclerotic process. At other times in arteriosclerotic patients, the block may be peripheral, usually at a bifurcation or where a sclerosed artery crosses a vein, an event which is particularly prone to occur in the superior temporal vein. In young people it may be due to an infective periphlebitis (Fig. 20.17) in which case a branch of the central vein is affected. Thrombosis may also be due to local causes, such as a chronic glaucoma, orbital cellulitis or facial erysipelas. In all cases the condition is to be regarded as a danger signal and constitutional investigation and treatment should be assiduously undertaken.

In *central retinal vein occlusion (CRVO),* all the veins of the retina become enormously engorged with blood and extremely tortuous, and the retina is covered with haemorrhages (Fig. 20.18). Sight is much impaired, though not as rapidly as in obstruction of the central artery. In many cases bunches of tortuous new vessels are formed upon the optic disc (Fig. 20.19A and B); in others a collateral circulation is effected by similarly tortuous new vessels in the retina. Eventually the affected retina becomes atrophic with fine pigmentary changes. The prognosis is rendered worse by the fact that secondary glaucoma ensues in 2-3 months in a considerable number of cases, due to neovascularization at the angle of the anterior chamber.

In *branch retinal vein occlusion (BRVO)* when a single branch of the central vein is blocked, the oedema and haemorrhages are limited to the area supplied by the

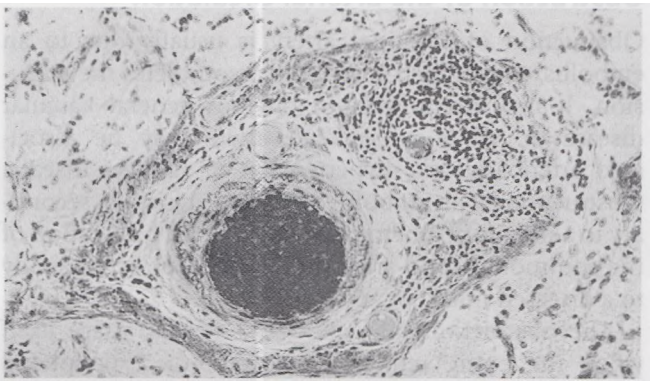


Fig. 20.17 Inflammatory venous occlusion at the disc. Section through the central vessels, close to the actual venous occlusion. The central retinal artery is normal, but the lumen of the vein (above right) is extremely narrowed by dense lymphocytic infiltration of the wall. (By courtesy of Klien)

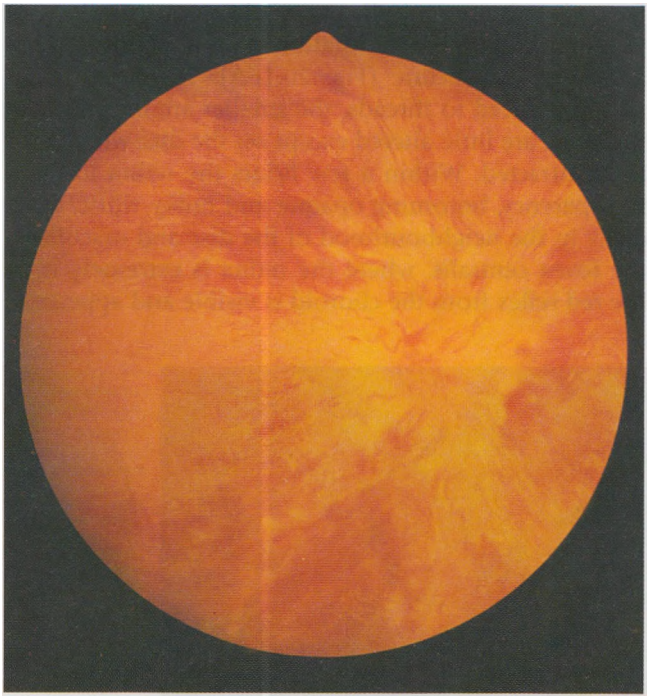


Fig. 20.18 Picture of a fresh central retinal vein occlusion showing dilated tortuous veins and extensive haemorrhages. (By courtesy of AH Paul)

vein. In these cases the visual defect is partial but not exactly sectorial as in the case of occlusion of a branch of the artery. The prognosis for central vision is better, but unfortunately blockage of the superior temporal vein frequently involves the macula (Fig. 20.20A). Eyes with intact or complete perifoveal capillary arcades have a better visual prognosis than eyes with incomplete arcades as demonstrated by angiography (Fig. 20.20B). Secondary glaucoma rarely occurs in branch thrombosis.

No *treatment* is effective in cases of venous occlusion once the blockage has become complete. If there is widespread capillary occlusion, panphotocoagulation of the retina (or cryoapplications if the media are hazy) may forestall neovascular glaucoma and rubeosis iridis. Widespread capillary occlusion is associated with cotton-wool spots, delayed arteriovenous transit time, large vessel leakage and retinal oedema. In branch occlusion, destruction of areas of poor perfusion (as seen by closure of retinal capillaries in an angiogram) may relieve persistent oedema and inhibit neovascularization. Photocoagulation should not be done until most of the intraretinal blood is absorbed, which takes 1-2 months after the onset of occlusion.

Coats disease

This presents a characteristic monocular ophthalmoscopic picture seen usually in boys who are otherwise apparently healthy. There is usually a large, raised, yellowish-white area of exudation or several smaller areas posterior to the vessels (Fig. 20.21), detachment of the retina; cataract or glaucoma may occur in the late stages. There is always microscopic evidence of haemorrhage between the retina and choroid and in the deep

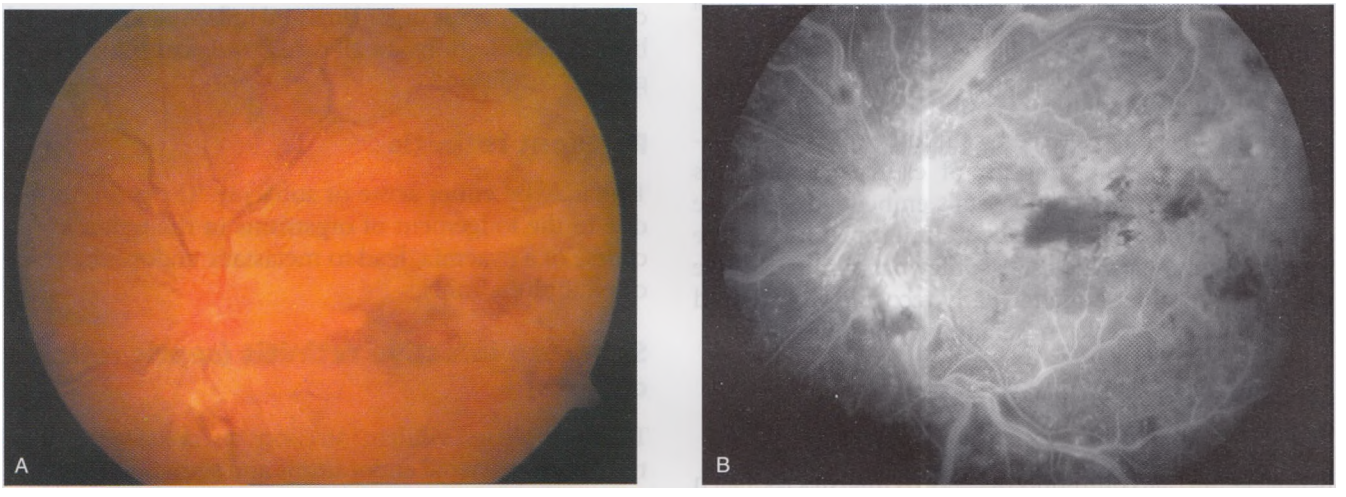


Fig. 20.19 (A and B) Old central retinal vein occlusion with neovascularization of the disc. (By courtesy of P Venkatesh)

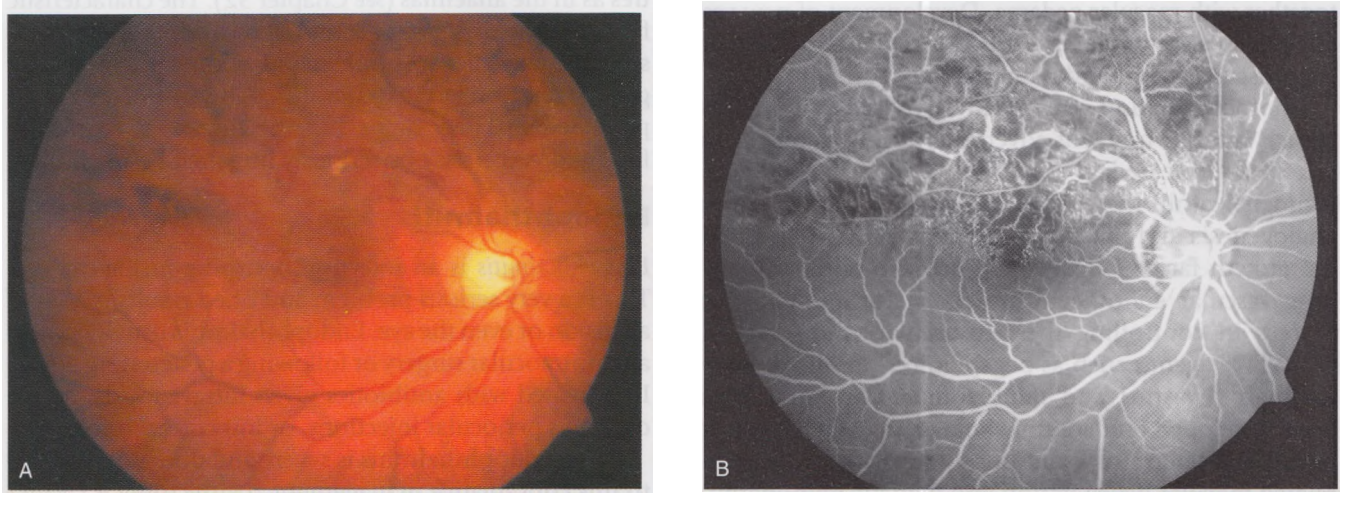


Fig. 20.20 Branch retinal vein occlusion. (A) Occlusion of the superotemporal retinal vein. There are surrounding haemorrhages and retinal oedema. (B) Fluorescein angiography shows areas of hypofluorescence and an incomplete perifoveal arcade. (By courtesy of P Venkatesh)

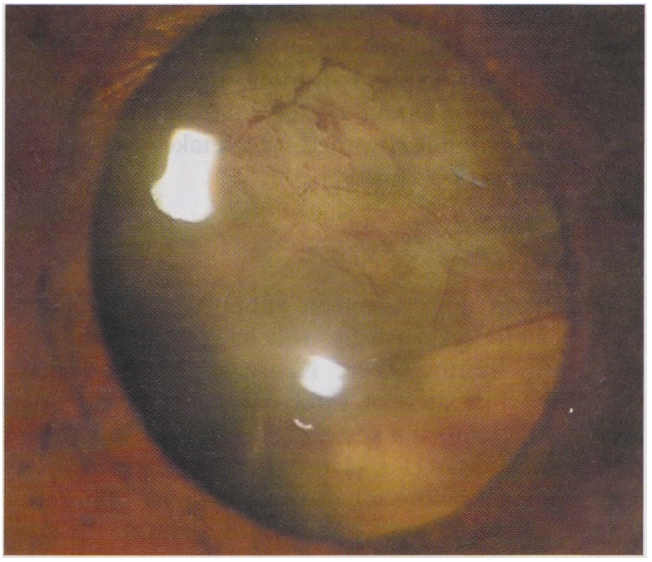


Fig. 20.21 Coats disease showing subretinal exudation and retinal angiomatosis.

layers of the retina, and the ophthalmoscopic appearance is usually characterized by a number of small aneurysms and a varying amount of exudate, sometimes with masses of cholesterol crystals embedded in it. The choroid is at first healthy. A very similar picture may be produced in angiomatosis. A somewhat similar disease may occur in older patients. Early recognition followed by prophylactic laser/cryotherapy may be beneficial.

Medical therapy in retinal vascular diseases

Retinal ischaemia commonly occurs in retinal diseases such as diabetic retinopathy and retinal venous occlusions, leading to the subsequent development of neovascularization on the disc (NVD) or elsewhere in the retina (NVE) together with macular oedema. Development of new vessels is also a feature in age-related macular degeneration (neovascular form) and retinopathy of prematurity.

Photocoagulation remains the standard treatment of choice, but has frequent adverse effects. Pro-angiogenic factors are released in response to an ischaemic environment within the eye, the principal factor regulating angiogenesis and macular oedema is vascular endothelial growth factor (VEGF). Adjunctive modes of inhibiting vascular endothelial growth factor allow greater success in controlling the neovascularization. Several anti-VEGF agents, such as pegaptanib (Macugen), bevacizumab (Avastin) and ranibizumab (Lucentis), have been developed and are now being successfully used in pharmacotherapy of conditions like neovascular age-related macular degeneration and diabetic retinopathy.

Steroids can down-regulate inflammatory stimuli by modulating the response of the vascular endothelial growth factor (VEGF) gene, whose antigens are present on human retinal pigment epithelium (RPE). They thus may play a role in regulating edema. Triamcinolone acetonide in an intravitreal dose of 1/2/4 mg has been evaluated in the treatment of retinal diseases such as diabetic retinopathy, exudative age related macular degeneration, cystoid macular edema, venous occlusion, Eales' disease etc. In the setting of macular degeneration, neovascularization disrupts the blood-brain barrier function of the RPE, and it has been shown that Triamcinolone acetonide can induce RPE proliferation and stabilization.

INFLAMMATION OF THE RETINA (RETINITIS)

Most of the inflammations of the retina are associated with inflammation of the choroid, the inflammatory process involving both tissues to form a chorioretinitis. These may be divided into purulent inflammations caused by pyogenic organisms and inflammations caused by specific infections. In all cases, *treatment* is that of the general condition.

Purulent retinitis

This may be either acute or subacute. The acute forms, due to the lodgement of organisms in the retina in the course of a pyaemia, lead to metastatic endophthalmitis or panophthalmitis.

Subacute infective retinitis (septic retinitis of Roth)

This occurs in less virulent infections of a metastatic nature, typically in bacterial endocarditis and sometimes in puerperal septicaemia. The posterior part of the fundus is generally affected, where numerous recurrent haemorrhages of embolic origin appear, some of which have white centres as in the anaemias *(see* Chapter 32). The characteristic feature is the presence of round or oval white spots (Roth spots), many of which are cytoid bodies. There is little general reaction in the retina although some oedema and papilloedema may occur, but the disease is frequently fatal and vision may be seriously impaired before death.

Endophthalmitis

Endophthalmitis is an infection occurring inside the eye. This is a very serious problem and often results in loss of all vision or even the eye. Endophthalmitis usually occurs after intraocular surgery or following a penetrating injury. It is treated with antibiotics given intravenously, as eye drops, as periocular injections, or intravitreal injections.

If the endophthalmitis is severe and does not respond to this conservative management, a vitrectomy is carried out. Vitrectomy is done to remove infectious material inside the eye, decrease the bacterial load and allow

antibiotics to be in direct contact with the infected tissues. The visual prognosis in any case of endophthalmitis is guarded; severe visual loss can occur if the endophthalmitis is not treated early enough and adequately.

Acute retinal necrosis (ARN) syndrome

The disease is characterized by blurred vision, an anterior uveitis, whitening of the peripheral and sometimes the posterior retina in multifocal and coalescent patches, retinal haemorrhages and vasculitis involving both the central artery and vein. Two-thirds of the cases are unilateral. Retinal detachment occurs in 75% of patients, usually within 3 months of the onset of symptoms secondary to holes within the necrotic retina and in association with vitreous traction. A herpes-type DNA virus has been identified as a probable aetiological agent. The affected persons, however, are generally in good health. Intravenous acyclovir has been shown to induce some regression of the retinal lesions (*see also* Chapter 13).

Cytomegalovirus infection

Human cytomegalovirus infection is characterized by distended tissue cells in which nuclei contain large acidophilic inclusion bodies. The majority of the population is infected and has no symptoms, but in patients with impaired immune function the disease may become manifest, as in patients who have received organ transplants followed by massive doses of immunosuppressive agents or who suffer from AIDS.

The eye may be affected by an isolated macular lesion or by a severe chorioretinitis with exudates

Syphilis

Most syphilitic retinal affections are secondary to choroidal inflammations but certain ill-defined changes may occur primarily in the retina. *Congenital syphilitics* occasionally show a dusty discrete pigmentation of the retina at the periphery where a multitude of black and white spots appear ('pepper-and-salt' fundus). In the more definite forms, there are larger atrophic and pigmented areas at the periphery (anterior retinitis), a condition often seen with interstitial keratitis.

In *acquired syphilis* endarteritis may be prominent with whitish exudates along the course of the vessels. A diffuse retinitis may occur, particularly in the secondary stage of the disease wherein the retina, especially in the central area, becomes grey and cloudy. This is almost always accompanied by a severe vitritis. As the condition subsides the typical picture which develops consists of an atrophic optic disc, attenuated vessels, and a generally depigmented retina with the pigment aggregated in corpuscles, particularly at the periphery, in a distribution resembling pigmentary retinal dystrophy.

The subjective symptoms are defective central vision, night blindness, irregular and concentric contraction of the field with or without central, paracentral, or ring scotomata and metamorphopsia. Treatment is as prescribed for cerebral syphilis.

Sarcoidosis

The characteristic histological lesion in sarcoidosis is an epithelioid cell granuloma, similar to a tubercle without caseation. The mediastinal lymph nodes are a common site of such lesions but the lungs, liver, spleen, skin and eyes together with the parotid glands are also affected. The ESR is usually elevated and there is a slight leucopenia. The serum albumin-globulin ratio is disturbed and the serum angiotensin-converting enzyme (ACE) levels are raised. Hypercalcaemia may be present. The tuberculin test is usually negative but the Kveim reaction, which is a test for skin sensitivity to sarcoid material, may be useful. X-rays of the chest may show bilateral lymph node involvement in the hilar region of the lungs and this may lead eventually to pulmonary fibrosis. Occasionally the bones of the hand are affected so that the phalanges show cystic areas.

A widespread retinopathy may develop consisting of 'candle-wax' like deposits of exudates along the vessels and small, whitish areas which have been shown to be granulomata. The optic nerve head may be oedematous and also affected by nodular granulomata leading to atrophy. There may be patches of chorioretinitis and periphlebitis in association with posterior uveitis. Of patients with ocular sarcoid, 25% show evidence of posterior segment involvement during their illness. When the retina is involved there is often an associated affection of the central nervous system.

Toxoplasmosis

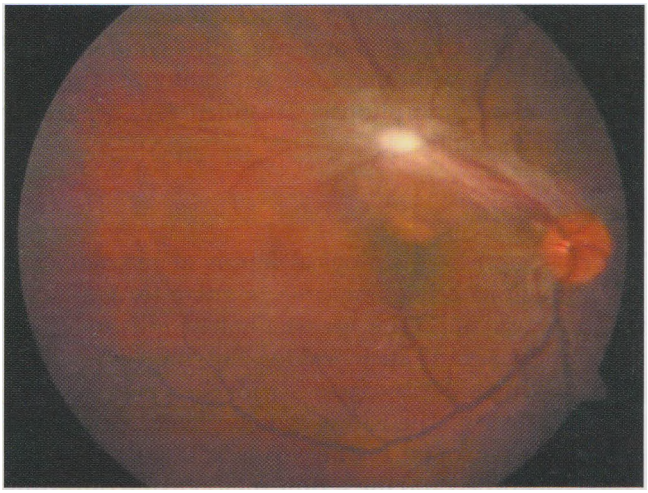
(See Chapter 32).

Toxocariasis

When tissues other than the skin are invaded by nematode larvae the condition is referred to as visceral larva migrans. *Toxocara canis* and *Toxocara catis* are roundworms and are common causes of ocular disease.

Children eat infected material so that the eggs of the worm hatch in the duodenum and larvae then penetrate the intestinal wall, enter the venous circulation and migrate across the pulmonary capillary bed to reach the respiratory tree. Some are again swallowed to reach the jejunum. If the infection is heavy, the children suffer from fever, anorexia, eosinophilia and hepatomegaly. The larvae may lodge in the eye without systemic signs.

The larvae produce an intraocular granuloma consisting of eosinophils and IgE, which is situated centrally or



Fig, 20,22 *Toxocara* granuloma.

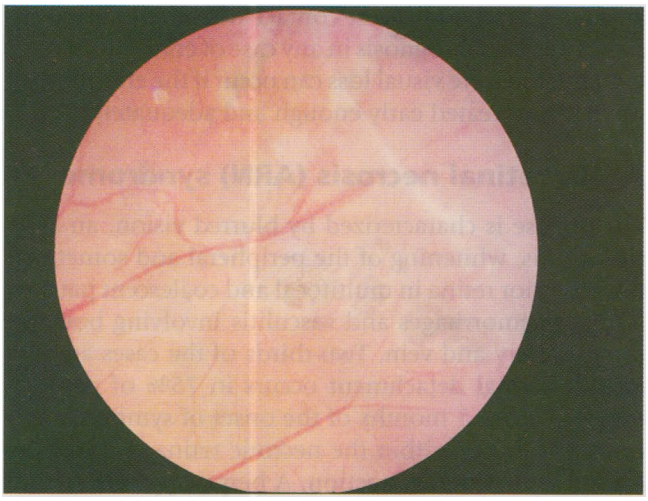


Fig. 20.23 Eales disease. Photograph of the peripheral retina showing an area of healed perivasculitis, with retinal sheathing, a fibrovascular vitreoretinal frond and scars of previous photocoagulation.

peripherally in the retina as a white lesion. It protrudes into the eye from the retinal tissues (Fig. 20.22) and occasionally an endophthalmitis develops.

During the acute stage antibody titres rise in the blood stream and a skin test with antigens may produce a reaction. No eggs are found in the stool because no adult worms develop systemically. A skin test is carried out with an antigen of the adult worm. Testing with larval antigens is more sensitive as is the enzyme-linked immunosorbent assay (ELISA).

Vitritis may respond to topical steroids which may be supported by thiabendazole and systemic steroids. Tractional detachments of the retina are common and in such cases vitrectomy and/or scleral buckling may have a part to play.

Ascaris lumbricoides may also produce ocular inflammation as a result of larval migration.

Periphlebitis retinae

This is a relatively common disease which manifests itself clinically by inflammation of the veins and progressive ischaemia in the periphery of the retina. This leads to a proliferation of new vessels on the retinal surface or as fronds, and repeated haemorrhages into the vitreous. It occurs typically in apparently healthy young adults, usually males *(Eales disease*) (Fig. 20.23).

Retinitis from bright light (photoretinitis)

This occurs after exposure of the eyes to bright sunlight, as in looking at an eclipse of the sun with inadequately protected eyes ('eclipse blindness'), or exposure to the flash of the short-circuiting of a strong current. Practically all the visible rays, ultraviolet and many infrared rays pass unimpeded to the retina and these are absorbed by the pigmentary epithelium. Pathological changes are produced by the resultant heating effect. The lesion is, in fact, a bum of the retina, generally seen in the paramacular area.

The symptoms are persistence of the after-image, progressing later into a positive scotoma, and metamorphopsia. Ophthalmoscopically, there may be no signs at first, or a pale spot is seen at the fovea with a brownish-red ring round it. Later there are usually deposits of pigment and small, grey punctate spots around the fovea, or even the formation of a retinal hole.

Prognosis must be guarded; although improvement often occurs, some defect usually remains and the scotoma may persist permanently.

No treatment is effective. Glasses impervious to visible short wavelength radiation should be used prophylactically on such occasions or preferably the light source may be viewed by reflection from a mirror or not at all.

Light-induced maculopathy due to the strong focused light of the operating microscope has been recorded in patients who have undergone cataract surgery with posterior chamber lens implantation. The macula presents an oval area of mild yellow-white discoloration on the second postoperative day, which gradually becomes mottled and pigmented. In most patients the lesion is just above or below the foveola, so that central vision returns to normal leaving a paracentral scotoma.

DEGENERATIONS OF THE RETINA

Myopic chorioretinal degeneration

Pathological myopia is associated with a highly myopic refractive error, usually more than 6 D of myopia, with an elongated axial length and chorioretinal degeneration. Peripapillary atrophy, temporal crescent, macular atrophy,



Fig. 20.24 Fundus in myopia showing significant tessellation, slightly tilted disc, peripapillary atrophy and atrophy involving the central macula. (By courtesy of P Venkatesh)

Foster-Fuchs spot, lacquer cracks, lattice degeneration and diffuse chorioretinal atrophy are seen in various degrees and combinations in these cases (Fig. 20.24).

Age-related macular degeneration

Age-related macular degeneration (ARMD) is one of the leading causes of blindness in the world and presents as two forms: 'dry' or atrophic and 'wet' or exudative. The atrophic form is more common than the exudative, with about 90% of patients being diagnosed with atrophic ARMD. The exudative form of the disease usually leads to more serious vision loss and is responsible for 90% of the blindness due to this disease. Macular degeneration is more common in people over 65 years of age, Whites and females.

Pathogenesis

ARMD is caused by sclerosis of the arteries that nourish the retina. This deprives the sensitive retinal tissue of oxygen and nutrients that it needs to function and thrive. The atrophic form possibly results from the thinning of macular tissues, amorphous deposits and pigmentation in the macula. Exudative macular degeneration occurs when new vessels form a choroidal neovascular membrane to improve the blood supply to oxygen-deprived retinal tissue. These new vessels are friable and leak blood and fluid causing damage to the surrounding tissue. Hereditary factors, age, nutrition, smoking, hypertension and exposure to sunlight are all risk factors.

ARMD can produce a gradual diminution of vision in those with the atrophic type or a sudden painless loss of vision in the exudative variety. Common complaints are distorted vision, seeing straight lines such as the side of a doorway appear wavy, bent or fuzzy. There may be shadowed areas in the central visual field causing difficulty in reading. Macular degeneration does not cause complete blindness as it does not affect peripheral vision.

Ophthalmoscopically, the dry type is characterized by drusen and loss of pigment in the retina and pigment epithelium (Fig. 20.25A). Drusen are small, yellowish deposits on Bruch's membrane derived from metabolic products of the visual receptors and retinal pigment epithelium deposited as mucopolysaccharides and lipids on Bruch's membrane. Exudative ARMD appears as an elevation of the neurosensory retina or pigment epithelium beneath which abnormal blood vessels, fluid and haemorrhage are present (Fig. 20.25B).

Management

The exact causes of ARMD are still unknown. Zinc supplements and anti oxidant vitamins may help to lower the risk for or halt the progression of dry ARMD. Laser photocoagulation is effective in sealing leaking or bleeding subretinal vessels in some eyes with exudative macular degeneration. This does not restore lost vision, but it may prevent further loss. Early diagnosis is critical

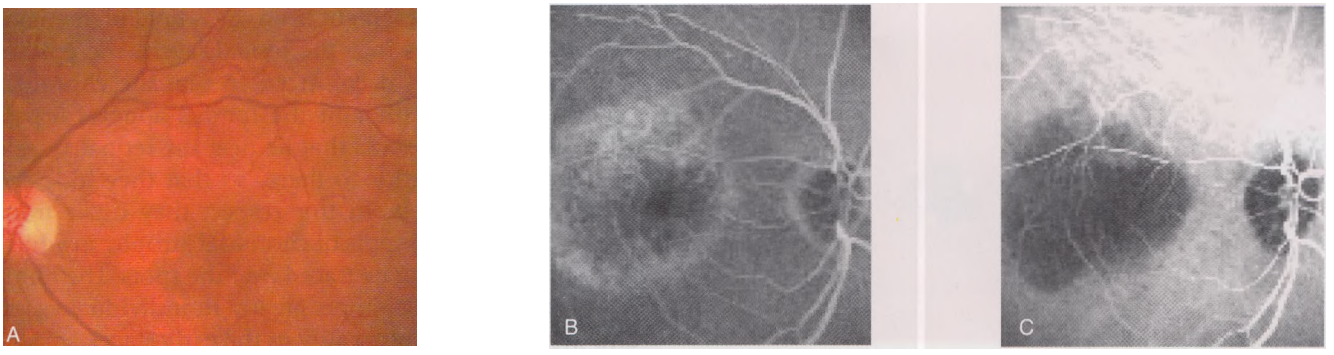


Fig. 20.25 (A) Dry type of age-related macular degeneration, showing an absent foveal reflex and yellowish-white drusen below the macula; (B) wet type of age-related macular degeneration seen on fluorescein angiography; (C) indocyanine green angiography. (By courtesy of D Talwar)

for the management of exudative macular degeneration, and patients can detect early changes in the second eye by monitoring their central vision at home with an Amsler grid. Patients with central visual loss may benefit from the use of low vision aids. Transpupillary thermotherapy and photodynamic therapy using lasers and submacular and macular translocation surgery are currently being evaluated for the treatment of ARMD. The risk of developing a choroidal neovascular membrane in the second eye is higher if large drusen with hyperpigmentation are present and the patient is hypertensive.

Macular holes

Macular retinal holes can occur due to ocular injuries, with age and as a sequel to intraocular inflammation. The vitreous gel has a firm attachment to the macula. If the vitreous degenerates as with ageing or trauma, it separates from the retina, occasionally leading to traction on the macula, causing first an elevation and later a loss of the retinal layers, partial in lamellar holes and a loss of the entire sensory retina in full-thickness holes. They gradually affect central vision, while lamellar holes cause distorted and blurred vision. Full-thickness macular holes lead to a complete loss of central vision. The edge of a macular hole can be identified using slit-lamp biomicroscopy and a +78 D or +60 D lens. Lamellar holes commonly show yellowish deposits at the base of the hole and do not have a surrounding retinal detachment (Fig. 20.26). Full-thickness holes generally have a surrounding ring of retinal detachment sometimes extending far away from the macular area into the periphery. Some macular holes seal spontaneously and require no treatment. In many cases, vitreous surgery is required to ease the vitreous traction and an internal tamponade with gas to close the hole and restore useful vision.



Fig. 20.26 Lamellar macular hole showing a sharp retinal edge without surrounding detachment and yellowish–white deposits at the base. (By courtesy of GS Sihota)

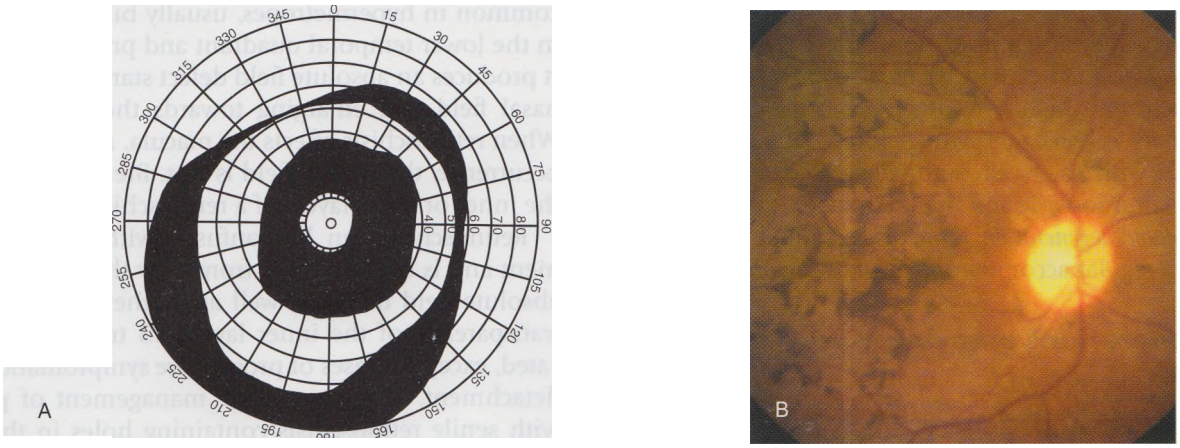
Pigmentary retinal dystrophy (retinitis pigmentosa)

This is a slow, degenerative disease of the retina, almost invariably occurring in both eyes, beginning in childhood and often resulting in blindness in middle or advanced age. The degeneration affects primarily the rods and cones, particularly the former, and commences in a zone near the equator of the eye gradually spreading both anteriorly and posteriorly. The macular region is not affected until a late stage.

The symptoms are characteristic, the most prominent being defective vision in the dusk (night blindness, *nyctalopia).* This symptom may be present several years before pigment is visible in the retina and is due to the degeneration of the rods, which are primarily responsible for vision in low illumination. The visual fields show concentric contraction, especially marked if the illumination is reduced. In early cases a partial or complete annular or ring scotoma is found corresponding to the degenerated zone of retina (Fig. 20.27A). As the disease progresses the field becomes gradually smaller until at last it is reduced to a restricted area around the fixation point. Even though the central vision may be retained for a long time, such patients with 'tubular vision' have great difficulty in getting about, for they are in much the same situation as a person looking down two long tubes, seeing only the thing they are actually looking at and nothing around it. Loss of central vision does not usually occur until 50 or 60 years of age, although cataractous changes may cause earlier deterioration. Associated ocular anomalies include a higher incidence of glaucoma and rarely keratoconus.

Ophthalmoscopic examination shows a characteristic picture (Fig. 20.27B). Initially the equatorial region is affected and the posterior pole and the periphery are normal, but as the disease progresses the entire retina may become involved. In the zone affected, the retina is studded with small, jet-black spots resembling bone corpuscles with a spidery outline. The retinal veins, never the arteries, often have a sheath of pigment for part of their course. As the pigment from the retinal pigmentary epithelium migrates into the retinal layers, the epithelium itself becomes decolorized so that the choroidal vessels become visible and the fundus appears tessellated. The pigment spots that lie near the retinal vessels are seen to be anterior to them, so that they hide the course of the vessels. In this respect they differ from the pigment around spots of choroidal atrophy in which the retinal vessels can be traced over the spots. The number of pigment spots differs greatly in individual cases, and they are often very scanty in the early stages.

The retinal blood vessels, both arteries and veins, become extremely attenuated and thread-like. As the disease progresses and the ganglion cells become degenerate,



Fig, 20.27 (A) Ring scotoma in a case of pigmentary dystrophy. (B) Retinitis pigmentosa with bone corpuscle formation, attenuated retinal arterioles and a yellowish disc.

optic atrophy sets in and gradually increases. The disc exhibits the characteristics of primary optic atrophy, but is not quite typical of this condition for, although pale, it has a wax-like yellowish appearance and is often termed as 'consecutive optic atrophy'. In the later stages a progressive posterior cortical cataract is formed, leading ultimately to complete opacification of the cortex.

The electroretinogram (ERG) and particularly the electro-oculogram (EOG) in such cases are markedly subnormal or completely extinguished early in the disease before subjective symptoms or objective signs appear, a point of great prognostic importance in assessing the future of a young child in an affected family. In secondary retinitis pigmentosa, a sequel to an inflammatory retinitis, on the other hand, often ophthalmoscopically indistinguishable from the primary condition, the response is only slightly subnormal unless the condition is very advanced. Congenital syphilis may produce a similar picture, although the distribution of the pigment spots is seldom typical.

The condition is abiotrophic in nature and is genetically determined. In the majority of families it appears as a recessive trait and consanguinity of the parents is not infrequent. Occasionally it shows a dominant heredity when the disease may be transmitted through several generations; this is the mildest form of the disease. Exceptionally it is sex-linked and clinically the prognosis for vision is poor. No advice can therefore be given as to the likelihood of transmission in any particular case unless the individual pedigree has been investigated.

Other defects elsewhere may be associated with the condition, the most common of which is a syndrome of obesity, hypogonadism, mental defect and polydactyly (*Laurence-Moon-Biedl-Bartum syndrome),* deafness (Usher syndrome) cardiac conduction defects and abetalipoproteinaemia.

Treatment is eminently unsatisfactory since, despite many claims, nothing appears to have a decided influence upon the course of the disease.

Retinitis pigmentosa sine pigmento is a variant of the disease with the same symptoms, but without visible pigmentation of the retina. It is probably only the early stage of the more common dystrophy. It is progressive and leads to optic atrophy, thus differing from *congenital stationary night blindness,* which is a rare hereditary disease without ophthalmoscopic signs, remaining station-ary throughout life.

Retinitis punctata albescens is an allied condition in which, with the same history and symptoms, the retina shows hundreds of small white dots distributed fairly uniformly over the whole fundus. A stationary form exists; but other cases are progressive and almost certainly represent atypical varieties of the pigmentary dystrophy. In the first case the ERG is normal; in the second, subnormal or extinguished.

Angioid streaks

Dark brown or pigmented streaks which anastomose with each other and may be mistaken for blood vessels are sometimes seen ophthalmoscopically. They differ in distribution from any normal set of vessels, are usually situated near the disc at a deeper level than the retinal vessels, and are very irregular in contour. They are due to changes in the elastic tissue of Bruch's membrane, and are frequently associated with more widespread degeneration of a similar nature, as in the elastic tissue of the skin (*pseudoxanthoma elasticum)* or of the arterial walls. Vascular and degenerative choroidal lesions elsewhere in the fundus, particularly a choroidal neovascular membrane at the macula, are common developments. Paget disease of bone, Ehlers-Danlos syndrome and sickle cell disease may be associated with angioid streaks.

Benign peripheral retinal degenerations

There are a number of retinal degenerations which do not threaten the retina or lead to retinal breaks. Such lesions

are called *snowflakes,* because of their dotted white appearance, which soon come close to the ora serrata. *Paving stone degeneration* caused by focal chorioretinal atrophy is present in a high percentage of normal eyes; *reticular pigmentary degeneration,* which looks rather like a honeycomb with each cell outlined by pigment; *equatorial drusen* commonly found in elderly people and *peripheral microcystoid degeneration,* which is present in all adult eyes and is a regular accompaniment of the ageing retina.

Degenerations associated with retinal breaks

Lattice retinal degeneration

Lattice retinal degeneration is recognizable by white arborizing lines arranged in a lattice pattern occurring in the upper peripheral fundus near the equator with the long axes parallel to the ora serrata. Retinal thinning is a constant feature and abnormal pigmentation is often present. The degeneration is slowly progressive and retinal tears are common in association with vitreous liquefaction.

White without pressure

Pale, discrete areas of the retinal periphery without the application of any external pressure are thought to be the result of vitreous traction which could result in the formation of retinal break.

Focal pigment proliferation or clumping

This occurs in the equatorial region or near the ora serrata. The pigment may be in the retina, choroid or both. In the equatorial region focal pigment proliferation may be found with a retinal tear. Posterior vitreous detachment (PVD) is commonly associated with adhesions to the area of affected retina.

Diffuse chorioretinal degeneration

This is often found in myopic eyes. The choroid is depigmented and the retina thin and this may lead to the development of a retinal hole. Chorioretinal scars from old inflammatory processes, particularly if they are peripherally situated, are prone to produce retinal tears.

Cystoid retinal degeneration of the peripheral retina

This type of degeneration is present in varying degrees in all eyes but tends to increase with age and, in the very old, may predispose to retinal detachment.

Retinoschisis

Senile retinoschisis is characterized by splitting of the retina at the level of the outer plexiform layer. It is more common in hypermetropes, usually bilateral, occurring in the lower temporal quadrant and progressing slowly. It produces an absolute field defect starting in the upper nasal field and enlarging towards the fixation point. When retinoschisis affects the macula, an extremely rare occurrence, the central field is lost. Breaks may occur in the inner or outer layers of a retinoschisis.

Retinoschisis can be confused with retinal detachment and is differentiated from it by the presence of an absolute field defect as well as by the immobility and transparency of the inner layer. No treatment is indicated, except in cases of progressive symptomatic retinal detachment. The appropriate management of patients with senile retinoschisis containing holes in the outer layer is periodic observation because so few of them develop progressive detachment. When schisis is accompanied by rhegmatogenous retinal detachment, scleral buckling with encirclement is the operation employed.

Juvenile retinoschisis

Juvenile retinoschisis is a hereditary disorder in which there is a splitting of the retina in the nerve fibre layer with the development of nerve fibre layer breaks. This may be associated with cystoid changes in the fovea manifesting as retinal folds radiating from the foveal centre in a petalloid pattern.

DETACHMENT OF THE RETINA

The neuroepithelium and the pigmentary epithelium of the retina normally lie in apposition, the potential space between them representing the original primary optic vesicle. It is understandable that the two layers can be readily separated and such an event is called a *detachment* or (since only the inner layer of the embryonic retina is involved) a *separation* of the retina. Retinal detachment occurs when subretinal fluid accumulates in the potential space between the neurosensory retina and the underlying retinal pigment epithelium. Depending on the mechanism of subretinal fluid accumulation, retinal detachments traditionally have been classified into rhegmatogenous, tractional and exudative.

Detachments of the retina are divided into two classes from the clinical point of view—*secondary detachments* due to an obvious mechanical cause when the detachment is a subsidiary event—*exudation* or *traction* because of another disease process in the eye; and *rhegmatogenous detachments* due to the development of a break in the retina, in which case the state of this tissue is of primary importance.

Secondary detachments may be due to the retina being pushed away from its bed by an accumulation of fluid or a neoplasm. The fluid may be blood (as from a choroidal haemorrhage) or exudate (exudative choroiditis

or retinopathy, angiomatosis, toxaemia of pregnancy). If such an exudate is absorbed, the detached retina may well become spontaneously replaced. Tumours of the choroid have a similar effect, partly by lifting up the retina mechanically, partly by the transudation of fluid due to the circulatory disturbances caused by the mass of the neoplasm. For this reason such detachments habitually cause an extensive separation of the retina, particularly in the lower part of the eye where the fluid tends to gravitate. Alternatively, a secondary detachment may be due to the retina being mechanically pulled away from its bed by the contraction of fibrous tissue in the vitreous, *tractional detachment,* such as occurs in plastic cyclitis, proliferative retinopathy or the retinopathy of prematurity. The prognosis in such cases is, of course, not so good.

The term rhegmatogenous is derived from the Greek word *rhegma* (a discontinuity or a break). A rhegmatogenous retinal detachment occurs when a tear in the retina leads to fluid accumulation with a separation of the neurosensory retina from the underlying retinal pigment epithelium. This is the commonest type of retinal detachment.

Retinal breaks are frequently very difficult to find, but it is extremely important to find them. In the first place, the presence of a break designates a detachment as rhegmatogenous; in the second, cure depends on its occlusion. The shape of such breaks varies. Breaks can be *round holes,* horseshoe-shaped *tears* or *retinal disinsertion at the ora (dialysis).* Retinal tears are usually horseshoe- or arrow-shaped with a lid-like tongue pulled inwards by the vitreous (Fig. 20.28A); they are most frequent at the periphery and commonest in the upper parts of the retina where the vitreous drags if it is adherent. Others are atrophic and rounded (Fig. 20.28B), being less peripheral and sometimes occurring at the macula. Occasionally, extensive tears occur. Those involving more than a quadrant of the circumference are called *giant retinal tears.* A disinsertion of the retina from the ora serrata causes a large tear known as retinal dialysis. A dialysis may be large, in which case the choroid is seen through it and the edge of the detached retina is sharply defined (Fig. 20.28C).

Pathophysiology

Rhegmatogenous detachment of the retina is always due to the formation of a 'break' in the retina which allows fluid from the vitreous to seep through and raise the neurosensory retina from the retinal pigment epithelium. If the vitreous gel is healthy and solid such a detachment rarely occurs; if it is fluid or partially detached, and particularly if it is adherent to the retina in some portions so that with movements of the eye it continually drags upon the torn area, a rhegmatogenous detachment readily develops.

Vitreoretinal traction is responsible for the occurrence of most rhegmatogenous retinal detachment. The vitreous becomes more syneretic with age and a PVD occurs. In certain eyes, strong vitreoretinal adhesions are present in certain areas and the occurrence of a partial PVD can lead to the formation of a retinal tear, allowing fluid from the liquefied vitreous to seep under the tear, leading to a retinal detachment.

Predisposing factors

These include myopia, previous intraocular surgery such as aphakia or pseudophakia, a family history of retinal detachment, trauma and inflammation. Retinal necrosis with the formation of retinal breaks can occur in the ARN syndrome and in cytomegalovirus retinitis.

Clinical features

The symptoms of a shallow detachment may be non-specific in the initial stages, for the retina may obtain sufficient nourishment from the fluid which underlies it to retain its functions, which maybe only partially impaired for a considerable period. Sometimes the first symptom

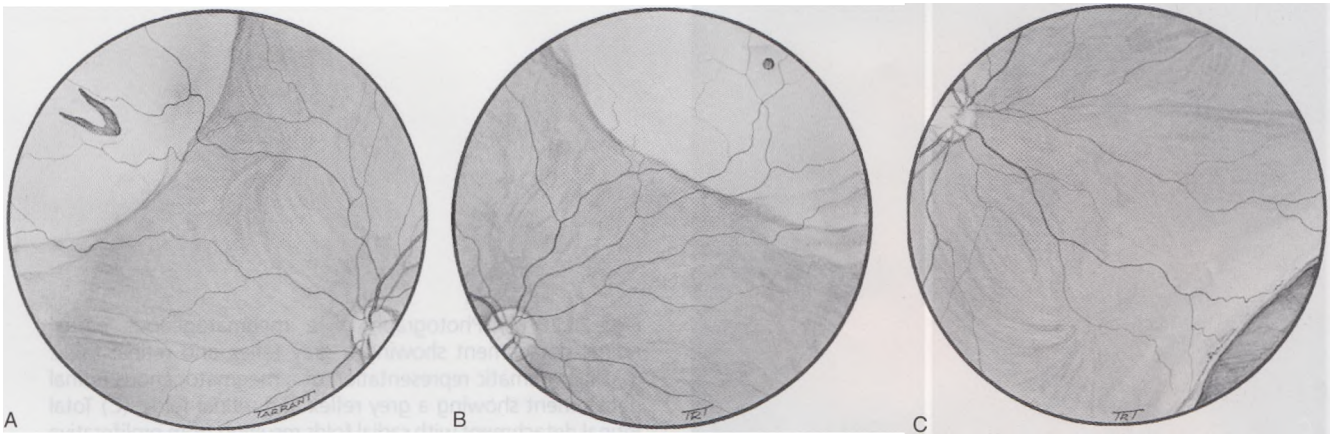


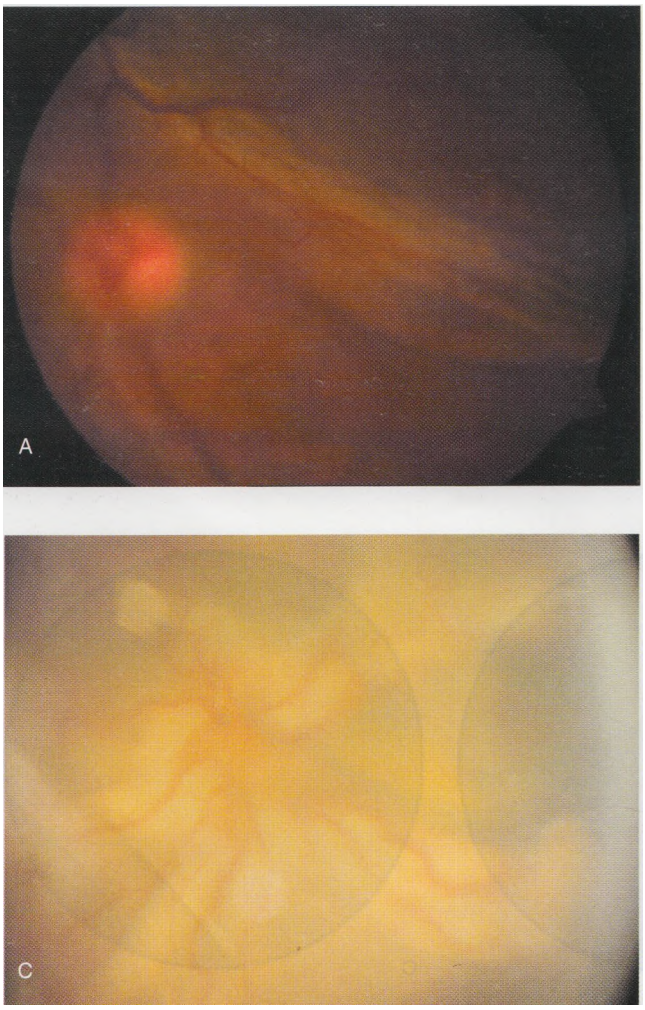
Fig. 20.28 Holes in the retina. (A) Arrow-head rent; (B) round hole; (C) anterior dialysis. (By courtesy of Shapland)

observed is transient flashes of light (photopsia) in a particular part of the visual field, due to slight traction of the retina which irritates the neuro-epithelium. They should always be regarded seriously, particularly if they appear in the nasal field and if followed by an increase in muscae volitantes but they not infrequently occur, especially in myopic eyes, without being followed by detachment. Once a retinal break occurs there is release of pigment or a small haemorrhage which manifests as 'floaters' or small moving spots in the patient's field of vision. These float in the vitreous cavity and cast a shadow on the retina *(muscae volitantes).* Once a retinal detachment occurs and extends posterior to the equator, patients complain of a 'curtain' or 'veil' obscuring their field of vision. The patient experiences a fall in visual acuity when the macula becomes detached, or a large bullous detachment obstructs the fovea.

Diagnosis and management

The clinical picture of a detached retina is characteristic, but the diagnosis may be difficult in the case of shallow detachments. Failure in diagnosis is almost always due to the omission of a thorough routine examination of the eye. The observer often employs the direct method of ophthalmoscopy only, with which a shallow detachment appears little altered from the normal fundus, except for an absence of the normal choroidal pattern. By preliminary examination with the mirror alone, a difference in the nature of the reflex as the eye is turned in various directions will at once arrest attention, while examination with the indirect ophthalmoscope will give a clearer picture.

In the early stages, and sometimes for a long period in shallow detachments, the colour of the detached portion remains relatively normal. Eventually, and sometimes rapidly, the detached portion of retina assumes a different tint from the normal fundus. In the most typical condition it is white or grey, with folds which show a bright sheen at the summits and appear greenish-grey in the depressions (Fig. 20.29A and B). During slight movements of the eye the folds show oscillations and the retinal vessels are seen coursing over the surface, following all the curves of the folds. Owing to the fact that they are separated from the choroid, they cut off the light reflected



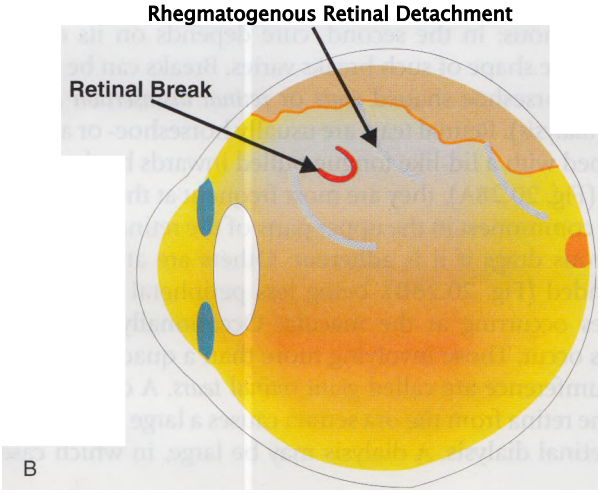


Fig. 20.29 (A) Photograph of a rhegmatogenous partial retinal detachment showing a grey reflex and retinal folds. (B) Diagrammatic representation of a rhegmatogenous retinal detachment showing a grey reflex and retinal folds. (C) Total retinal detachment with radial folds resulting from proliferative vitreoretinopathy. (By courtesy of P Venkatesh)

from this membrane and therefore look much darker than usual, and may be almost black with the vessels showing no central light streak. When the detachment is very extensive, great balloon-like folds may be seen, and these may cut off all view of the disc. Once the retina becomes detached, it assumes a slightly opaque colour secondary to intraretinal oedema and the normal choroidal pattern of vessels is no longer seen. It has a convex configuration, and moves freely with eye movements unless proliferative vitreoretinopathy (PVR) is present.

At the edges of the detachment a considerable degree of pigmentary disturbance may appear, as well as white spots of exudation, haemorrhages and greyish-white lines due to the retinal folds. In total detachment the retina is funnel shaped, remaining attached at the disc and at the ora serrata. Still later it becomes largely bunched behind the lens, the part attached to the disc being pulled out into a straight cord. In these cases the disturbance to the nutrition of the eye leads to the development of a complicated cataract so that ophthalmoscopic examination becomes impossible.

The intraocular pressure is usually lower than that in the fellow eye and this is reversed by retinal reattachment. In certain cases, the intraocular pressure may be higher than the fellow eye. Pigment in the anterior vitreous (tobacco dusting or *Shaffer* sign) is usually present. After a few weeks, a retinal detachment may present with more fixed folds, retinal thinning, intraretinal cysts, subretinal fibrosis and demarcation lines. These lines are present usually at the junction of the attached and detached retina. Even though they represent areas of increased retinal adhesion to the retinal pigment epithelium, it is not uncommon for subretinal fluid to spread beyond the lines.

PVR is the most common complication following a rhegmatogenous retinal detachment. There is a growth of cellular membranes within the vitreous cavity and around the retina, and is noted as stages A, minimal; B, moderate; C, marked and D, massive, and the number of involved quadrants is recorded as 1-4. This scar tissue exerts traction on the retina and may result in recurrence of the retinal detachment, even after an initially successful retinal reattachment procedure. This leads to disappointing visual results.

A retinal break is identified and localized in most eyes with rhegmatogenous retinal detachment; 50% have more than one break. More than half of all retinal breaks are located in the upper temporal quadrant, although any quadrant may be affected. Lincoff proposed rules to localize retinal breaks by observing the configuration of the retinal detachment. A superior retinal detachment extending downwards equally on both sides of the macula is commonly found to have a retinal break present within a clock hour of 12 o'clock. Similarly, an inferior retinal detachment extending upwards equally on both sides of the macula is commonly found to have a retinal break present within a clock hour of 6 o'clock. Asymmetrical distribution of subretinal fluid points to the presence of a retinal break within one to two clock hours of the edge of the more vertically extensive retinal detachment. Bullous detachments are generally caused by superior breaks.

Prophylaxis of retinal detachment is best done by identifying predisposing retinal breaks and other lesions, and treating them with cryotherapy or laser (Fig. 20.30), especially if other risk factors are present. These include symptoms suggestive of vitreoretinal traction, a history of previous trauma, myopia, a positive family history, prior cataract surgery or a detachment in the fellow eye. Even after prophylactic laser treatment, a lifelong follow-up of such eyes is essential. Asymptomatic patients with peripheral retinal degenerations that could lead on to a retinal break, e.g. lattice degeneration, have a low risk of retinal detachment and require only periodic review.

Since more than one hole may exist, a thorough and painstaking examination of all parts of the fundus must be done in every case; this may be time-consuming but is essential. Since many holes are in the extreme periphery, full mydriasis is necessary, and for this purpose the indirect method of ophthalmoscopy, using strong illumination, is more useful and effective than the direct. Sometimes such a lesion is rendered visible only by pressing gently on the sclera near the ora serrata with a strabismus hook or a scleral indentor. The retinal periphery should also be examined using a Goldmann three-mirror fundus lens, which provides a magnified view of the ora and its environs through the slit-lamp microscope. A careful drawing showing the position of retinal holes, pathological lesions, retinal vessels and other landmarks, is made of the fundus. Examination should be carried out with the patient in different postures sitting, supine, lateral, and so on; of these the supine is the most important, since this is the position in which the operation is usually performed. Changes in posture may reveal a retinal tear that has hitherto been hidden by a retinal fold. Accurate localization of the retinal tear or holes in relation to the outside of the sclera is essential; this is done by assessing the tears in

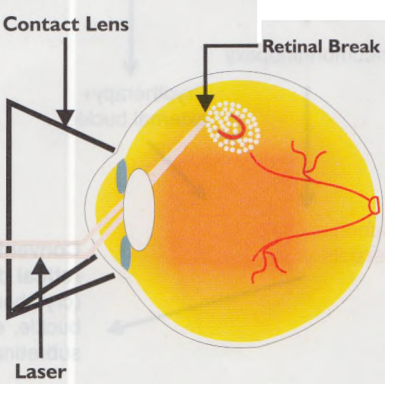


Fig. 20.30 Prophylactic laser therapy using a retinal contact lens to apply at least two rows of laser spots around a retinal tear without detachment.

terms of the clock-face, or the meridian in which the hole lies. Its distance from the ora serrata is judged ophthalmoscopically in terms of optic disc diameters.

Operations for retinal detachment can be successfully performed only after accurate localization of all retinal breaks.

Surgical management

Several different procedures are required for retinal detachment, depending on the extent and duration of the condition and the condition of the retina *(see* Flowchart 20.1).

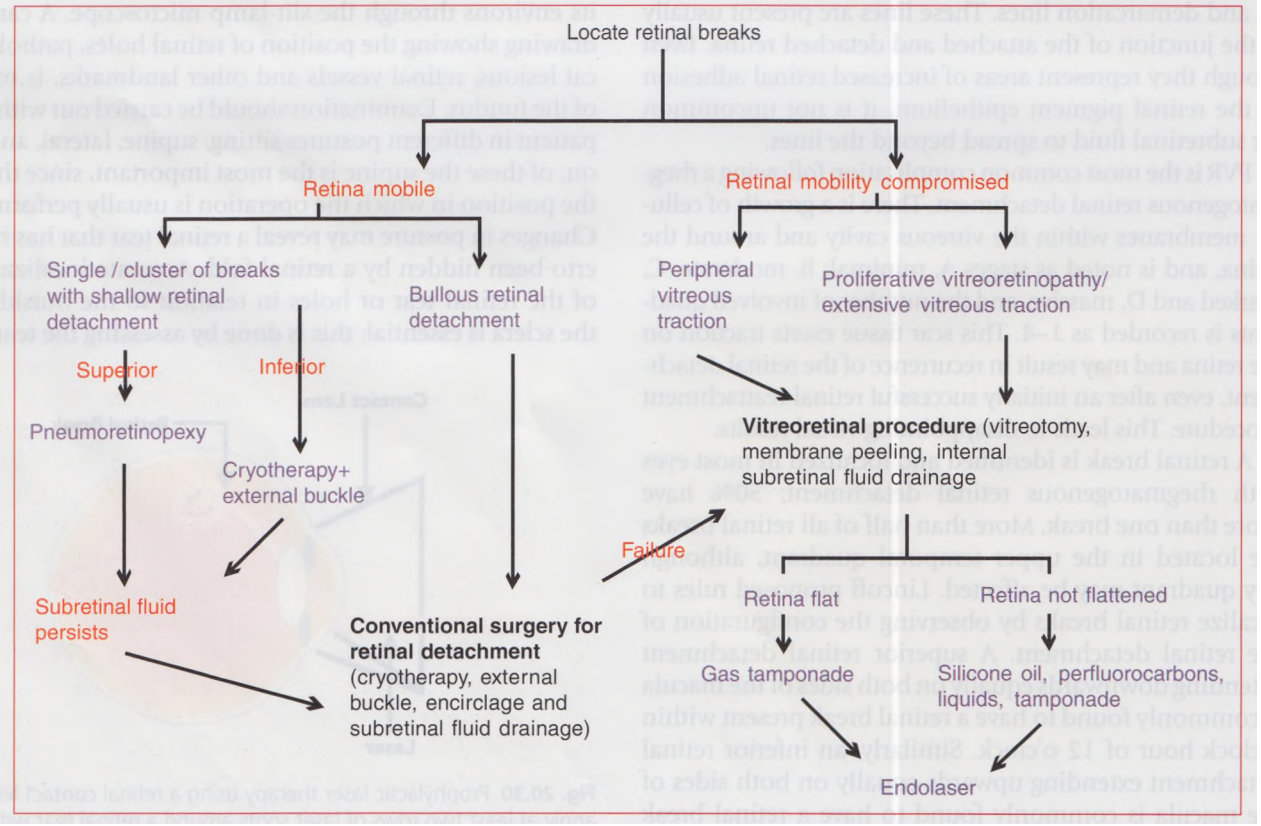
Common principles used in all types of surgery to treat a retinal detachment are as follows:

1. identification of all retinal breaks and areas of vitreous or periretinal traction;
2. induction of aseptic chorioretinal inflammation around the breaks to seal them;
3. release of any vitreous or periretinal traction;
4. drainage of subretinal fluid and
5. ensuring chorioretinal apposition for at least a couple of weeks by either or both of the following:
   - external tamponade—silicone buckle, sponge, tyre, encircling band;
   - internal tamponade—air, gases such as sulphur hexafluoride (SF_6), perfluoropropane (C_3F_8), or liquids such as silicone oil.

These individual components of surgery can be combined in various permutations, depending upon the clinical state of the individual eye and the choice of the surgeon. The surgical options include pneumatic retinopexy, scleral buckling, or vitreoretinal surgery *(see* Chapter 21). The surgical goals are to identify and to close all retinal breaks with minimum iatrogenic damage. This is achieved by good indirect ophthalmoscopy followed by the creation of chorioretinal inflammation using cryotherapy or laser. Subsequently, the retina and choroid are approximated to allow development of chorioretinal adhesions by using methods of external or internal tamponade. In the presence of vitreous traction, viUeous haemorrhage or severe proliferative vitreoretinopathy, vitreoretinal surgery is required.

Cryotherapy or *laser* is commonly used to produce chorioretinal inflammation around the edges of the retinal break. However, the former breaks down the blood-ocular barrier and may stimulate dispersion of retinal pigment epithelium cells into the vitreous cavity, which may contribute to PVR. Following cryotherapy, chorioretinal adhesion takes 2-6 weeks to form. Laser photocoagulation causes less morbidity and is the treatment of choice prophylactically except in very peripheral retinal breaks. It requires close chorioretinal apposition for at least one week, and cannot be used in the presence of a detachment.

Pneumatic retinopexy can be used in eyes with fresh retinal detachments having a single retinal break or a



Flowchart 20.1 Approach to the management of a retinal detachment.

group of breaks that are clustered within 1 clock hour in the superior two-thirds of the fundus. In this procedure, a bubble of gas is injected intravitreally through the conjunctiva and postoperatively the patient is positioned so that the bubble tamponades the retinal break against the pigment epithelium. This closes the break and allows resorption of the subretinal fluid. A chorioretinal adhesion is achieved by applications of laser or cryotherapy to the edges of the retinal break. The success of this procedure is poor in eyes with PVR grade B or greater.

Scleral buckling or *external plombage* (Fig. 20.31) is a procedure in which a soft silicone encircling band or sectoral buckle is sutured to the sclera, and indents the outside of the eye towards the detached retina, thereby relieving vitreous traction on the retinal break. In such cases, subretinal fluid does not need to be drained if the hole is well supported by the buckle and the circulation of the central retinal artery is not compromised. Scleral buckles are usually made of silicone rubber and silicone sponge. In the presence of extensive vitreous traction or multiple retinal breaks, an encircling band of silicone rubber is placed around the eye beneath the rectus muscles and tied after external drainage of some subretinal fluid, so as to produce a circumferential buckle to relieve the pull on the underlying retinal periphery. This encircling procedure may be used prophylactically in the second eye if the first presents with a non-traumatic giant tear.

Drainage of subretinal fluid through an external sclerotomy or internally by a flute needle is indicated in eyes with bullous retinal detachments where chorioretinal apposition is difficult, or when a more marked elevation of the buckle is required. Complications that may result from drainage of subretinal fluid include choroidal haemorrhage, retinal perforation, retinal incarceration, choroidal neovascularization and endophthalmitis. Non-drainage retinal surgery is also effective, but needs close monitoring of the intraocular pressure during surgery and in the immediate postoperative period. To achieve this objective, patients may require adjunctive procedures such as paracentesis or vitrectomy to allow adequate elevation of the buckle without causing a central retinal artery occlusion. In non-drainage surgery, subretinal fluid may take longer to reabsorb, especially in older patients.

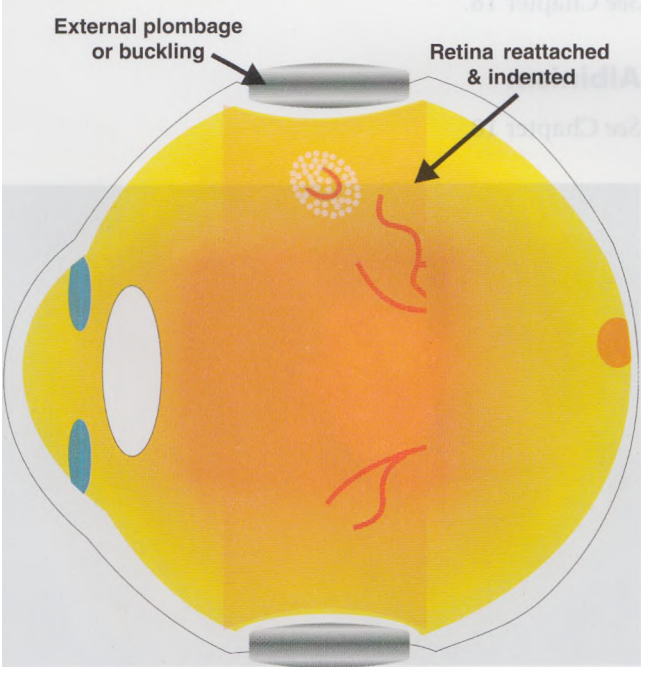


Fig. 20.31 External buckling or plombage with a silicon buckle after cryotherapy around the retinal breaks.

If PVR is present or where vitreous traction is the cause of a persistent detachment, *vitreoretinal surgery* is indicated. Surgery starts with a pars plana, 3-port vitrectomy. Any axial opacities such as vitreous haemorrhage or lens fragments, if present, are removed. A vitrectomy with removal of the vitreous from the margins of the breaks and the vitreous base is performed. Any membranes present over the retina as a feature of PVR are also peeled off or segmented to prevent puckering of the retina and allow good chorioretinal apposition. Internal drainage of the subretinal fluid is done through the retinal break using a soft, blunt, silicone-tipped needle, also called a 'flute' needle. The subretinal fluid is drained through a pre-existing retinal break or through a posterior retinotomy during air-fluid exchange. Stiff retinas as in old retinal detachments need silicone oil or perfluorocarbon liquids to flatten them. Once the retina is flat, endolaser is used to treat the area of retina surrounding any retinal tears or holes. Long-acting gases are injected after removal of silicone oil (air-silicone oil exchange) or silicone oil is left in the eye to tamponade the retina internally.

The gases commonly employed for tamponading the retina are sulphur hexafluoride (SF_5) or perfluoropropane (C_3F_8). Sulphur hexafluoride is an inert gas of high molecular weight, low water solubility and low diffusion coefficient that expands to 2.5 times its original bubble volume in the eye and persists twice as long as an air bubble of comparable initial size. Gases such as sulphur hexafluoride have a higher surface tension than silicone oil and are absorbed in a couple of weeks, but they expand with changing atmospheric pressure. Patients with an intraocular gas bubble should not fly in non-pressurized aircraft.

Silicone oil offers certain advantages over gas in the treatment of selected complicated retinal detachments. It acts as efficiently as gas in tamponading the retina and retains its shape for extended periods so that refilling is not required; furthermore, it dampens the tendency towards re-proliferation. Silicone oil can produce a secondary glaucoma, cataract and a keratopathy and hence needs a planned removal in a second procedure 8-12 weeks later.

Visual rehabilitation is faster with silicone oil than with gas tamponade, and laser therapy of retinal defects

can also be done more easily than with a gas bubble in the vitreous. The qualities of silicone oil prove most valuable in eyes with advanced PVR or giant tears.

Complications of surgery: The common complications of retinal surgery are persisting retinal detachment macular pucker, PVR, recurrent detachment, diplopia due to extraocular muscle damage and anterior segment ischaemia.

Prognosis: The prognosis in rhegmatogenous detachment of the retina, untreated by operation, is unfavourable. The detachment becomes total, the photoreceptors start to degenerate within a couple of weeks, impairing visual recovery and complicated cataract and iridocyclitis follow. Retinal reattachment surgery now has an anatomical success rate of over 95%. The visual prognosis depends on the duration of macular detachment and the presence of proliferative vitreoretinopathy. The prognosis is poor if the holes are large or multiple, when the vitreous, retina and choroid are grossly degenerated especially in the presence of multiple vitreous bands, when there is high myopia and if the detachment has been present for 9 months or more.

The most important cause of failure of retinal reattachment surgery is the proliferation and contraction of membranes on both surfaces of the detached retina and on the posterior surface of the detached vitreous gel. Before the era of vitrectomy, scleral buckling alone was used, which had a reattachment rate of 47%. At present, scleral buckling is combined with vitrectomy or with the use of silicone oil and other substitutes. Most detached retinae can be replaced by such methods. Visual results, on the other hand, are somewhat disappointing. In cases that can be treated without the use of silicone oil there is a 50% chance of achieving a visual acuity of 20/400 or better. When silicone oil is needed the chance of achieving a visual acuity of 20/400 or better after 30 months is just under 20%. As this is only used in long-standing or complicated cases, this reflects the adverse visual prognosis in such detachments. As long as there is perception of light there is always the chance that an anatomical success may result in improved visual function.

The risk of developing a retinal detachment in the fellow eye of such patients ranges from about 15% in phakic eyes, to over a third in aphakic or pseudophakic eyes.

CONGENITAL ABNORMALITIES OF THE RETINA

Congenital pigmentation of the retina

Small, oval, grey spots or groups of polygonal greyish-black spots are occasionally seen in the retina in routine examination of the fundus. They are flat, lie below the vessels, and remain unchanged indefinitely. They are congenital and due to heaps of retinal pigment and epithelium similar to those forming melanomata in the iris (*see* Chapter 18).

Medullated nerve fibres

The medullary sheaths of the fibres of the optic nerve normally appear behind the lamina cribrosa. Occasionally, patches of fibres become myelinated before they have passed through the lamina cribrosa. They appear ophthalmoscopically as white patches, the peripheral edges of which are radially striated, looking as if frayed (Fig. 20.32). Usually the patches are contiguous with the disc; occasionally they are isolated, but rarely far from the disc. The retinal vessels are covered in places by the opaque fibres. When present, the blind spot is enlarged, or a scotoma is present corresponding with the position of the patch. Very rarely, the patch is large and involves the macula, so that central vision is abolished. If glaucoma or optic atrophy causes the fibres to degenerate, the medullary sheaths disappear and no trace of the abnormality remains. They may also undergo selective disappearance in patients with demyelinating disorders such as multiple sclerosis. It is important to be able to diagnose such fibres, since they may be mistaken for exudates, as in hypertensive retinopathy. They not infrequently occur in both eyes. Strictly speaking, they are not congenital, for myelination of the optic nerve progresses from the brain towards the periphery, and is not completed until shortly after birth. No treatment is required.

Coloboma of the retina and choroid

See Chapter 18.

Albinism

See Chapter 18.

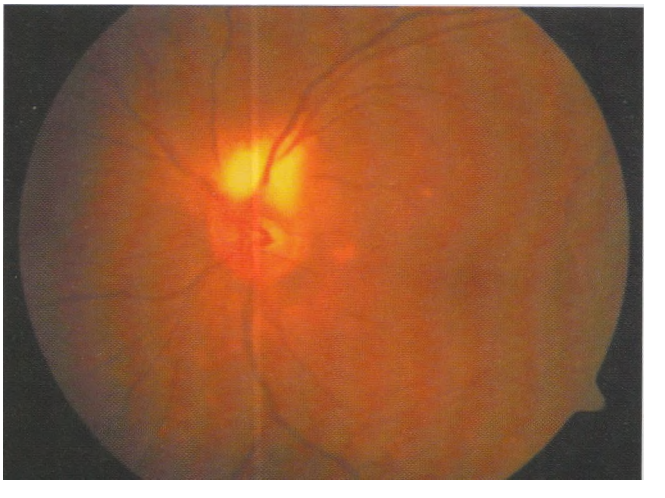


Fig. 20.32 Medullated nerve fibres over the superior part of the optic nerve head.

PHAKOMATOSIS

The phakomatoses comprise a group of diseases with a familial incidence and a congenital basis with a tendency for the development of neoplasias in the central nervous system and elsewhere. In this the retina and optic nerve maybe involved. The following varieties of phakomatosis have prominent retinal features.

Angiomatosis of the retina (von Hippel-Lindau disease)

This is a rare familial disease, which generally becomes manifest in the third and fourth decades of life and is more frequent in males than females. The cerebellum, medulla, spinal cord, kidneys and adrenals are also affected with angiomatoses and cysts. The ocular lesions are often bilateral, slowly progressive, and may precede a fatal cerebellar lesion by 10-15 years.

The ophthalmoscopic appearances vary; the most common is a great tortuosity and dilatation of the vessels together with the presence of peripheral retinal angiomas. Sometimes they are large like balloons; at other times small and miliary *(see* Chapter 32). The condition is progressive and eventually the increased permeability of the vessels leads to the deposition of enormous quantities of exudates, which appear in great masses in the fundus, eventually resembling the exudative retinopathy of Coats *(see* p. 315). Retinal detachment is a frequent sequel.

Treatment is unsatisfactory, but in the early stages cryodestruction or laser photocoagulation of a localized angioma may have a beneficial effect.

Tuberous sclerosis (Bourneville disease)

When this occurs in young individuals, it is associated with nodular lesions in the central nervous system and skin, particularly on the face (adenoma sebaceum). Similar nodular (mulberry) tumours, which are actually retinal astrocytomas, about the size of the disc occur in the retina, particularly near the optic nerve head. The cerebral lesions frequently lead to epilepsy and mental deficiency.

Neurofibromatosis (von Recklinghausen disease)

This may be associated with somewhat similar tumours in the retina, corresponding to those related to the nerves of the lids and orbit *(see* Chapter 32).

HEREDITARY DYSTROPHIES OF THE CENTRAL RETINA AND CHOROID

Hereditary dystrophies of the posterior pole of the eye produce bilateral and usually symmetrical lesions in the absence of general physical disturbance. The fundus picture in individuals of the same family is often similar and examination of relatives may lead to a diagnosis (Table 20.2).

Table 20.2 Classification of hereditary central retinochoroidal dystrophies

Site	Disease
Nerve fibre layer	Sex-linked juvenile retinoschisis
Neuroepithelium	Stargardt disease
(neurosensory retina)	Dominant foveal dystrophy
	Inverse retinitis pigmentosa
	Progressive cone dystrophy
	Familial lipid degenerations
Pigment epithelium	Vitelliform dystrophy of the fovea
	Reticular dystrophy
	Butterfly-shaped dystrophy of the fovea
	Fundus flavimaculatus
	Grouped pigmentation of the foveal area
Choroid	Central areolar choroidal atrophy

Sex-linked juvenile retinoschisis

This is a common bilateral dystrophy of the central retina. The fovea displays a cystoid structure with radiating striation of the superficial retinal layers. In 50% of cases a peripheral retinoschisis is found in the inferior temporal quadrant but does not usually extend up to the ora, unlike a retinal detachment. The ERG is subnormal, while the EOG is normal. It is due to a splitting of the sensory retina, predominantly within the nerve fibre layer.

Stargardt disease

Stargardt disease is a recessive, progressive tapetoretinal dystrophy of the central retina and develops between the ages of 8 and 14 years. In the early stages the fovea appears normal but in the advanced stages a demarcated focus of 'beaten bronze' atrophy is seen in the foveal region. Whitish flecks surround the ovoid zone of atrophy, when differential diagnosis from fundus flavimaculatus, which is often accompanied by a foveal dystrophy, may be impossible. In the final stages the posterior pole shows an extensive chorioretinal atrophy with poor vision. Dark adaptation, the ERG and the EOG are subnormal while the visual fields may become slightly restricted. Fluorescein angiography shows a 'dark choroid' in a large majority of patients. There is no leakage of dye. The final result is the complete disappearance of the visual elements and the pigment epithelium

in the centre of the retina. By the age of 40 only 22% of patients are likely to have a vision of 6/12. Once the visual acuity drops below this level it tends to decrease rapidly and stabilize at 6/60.

Dominant foveal dystrophy

This is a progressive tapetoretinal dystrophy of the central retina. It starts later in life and runs a milder course than Stargardt disease.

Inverse retinitis pigmentosa

Bone corpuscles are visible in the perifoveal area while the retinal periphery is normal. True bone corpuscles are never found in the fovea itself. Histological studies show a progressive degeneration of the neuroepithelium and pigment epithelium. Later there is a general atrophy of the whole retina. The heredity is autosomal recessive.

Progressive cone dystrophy

Progressive cone dystrophy is a dominantly inherited condition characterized by a bilateral progressive loss of visual acuity with extreme photophobia. The visual fields reveal a central scotoma and colour vision is absent. It is due to a primary dystrophy of the retinal cones. Ophthalmoscopy may only show a moderate foveal change but later a bull's eye pattern of depigmentation develops with a central hyperfluorescent spot on fluorescein angiography. Cone components of the ERG are reduced or absent while the rod components are normal. The EOG is unaffected.

Vitelliform dystrophy of the fovea

Vitelliform dystrophy of the fovea is known as Best disease. It is characterized by a sharply delimited, usually bilateral orange-yellow disc in the foveal region resembling the yolk of a fried egg (Fig. 20.33). Visual acuity remains good and the neuroepithelium is unaffected. Serious loss of vision occurs only after transition to an irregular pigmented lesion, after the egg has become 'scrambled' or after haemorrhages. This leads to a polymorphous foveal dystrophy. The vitelliform disc is probably situated in the pigment epithelium and contains homogeneous viscous material. The visual fields are normal with the exception of a central scotoma. Dark adaptation and the electro-retinogram are normal but the EOG is definitely pathological.

Reticular dystrophy of the retinal pigment epithelium

This condition is characterized by a peculiar defined network built up of black pigmented lines consisting of

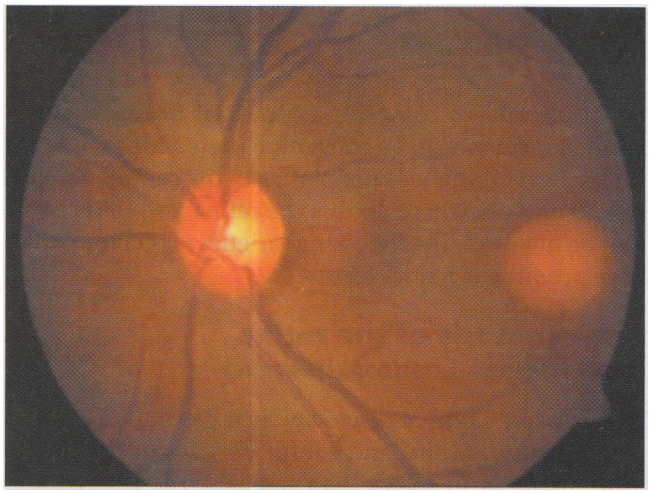


Fig. 20.33 Vitelliform dystrophy of the fovea. A sharply defined yellow disc is seen in the foveal region resembling the yolk of a fried egg. (By courtesy of P Venkatesh)

closely packed pigment granules at the posterior pole. The fovea itself displays a black spot of about one disc diameter situated at the level of the pigment epithelium. The condition is due to an autosomal recessive gene.

Butterfly-shaped pigment dystrophy of the fovea

This is a rare dystrophy with a pigmented butterfly-shaped structure at the level of the pigment epithelium at the fovea. Visual acuity is only slightly diminished. The ERG is normal while the EOG is found to be subnormal in most cases. The condition is inherited dominantly.

Fundus flavimaculatus

Fundus flavimaculatus is a flecked retinal dystrophy affecting both eyes and appears usually in the third or fourth decade of life. White or yellowish-white deep retinal flecks resembling fish tails with fuzzy outlines as seen with the ophthalmoscope are characteristic. The flecks never extend beyond the equatorial retinal zone. Fifty per cent of affected individuals have macular involvement. The central vision falls when the macula is affected. Dark adaptation and the ERG are normal but the electrooculogram is mostly pathological, indicating a diffuse involvement of the retinal pigment epithelium. Histological examination reveals a primary abnormality of the pigmentary epithelium due to an accumulation of lipofuscin-like substance while the neuroepithelium, Bruch's membrane and choroid are normal. It is now considered to be part of Stargardt disease.

Grouped pigmentation of the foveal area

This condition has rarely been described. Round pigmentary spots are present in the foveal area. Visual

acuity is normal or slightly diminished. The visual fields, dark adaptation and the electro-retinogram are normal.

The hyaline dystrophies

The hyaline dystrophies have been described under several names—Doyne honeycomb dystrophy or Hutchinson—Tay choroiditis. They are due to an enzymatic defect in the pigment epithelium. Initially tiny, round, white flecks appear in the posterior pole of the eye. White colloid bodies on the nasal side of the optic disc may be regarded as pathognomonic of this affection. The dystrophy is first seen between the ages of 20 and 40 years and is initially without symptoms. The colloid bodies increase and coalesce and eventually visual acuity may be disturbed. In advanced stages a central scotoma is found. Dark adaptation, the electro-retinogram and the electrooculogram are normal. Fluorescein angiography shows multiple round fluorescent spots with sharp borders. There are also abnormal areas seen with fluorescein angiography, indicating a disturbance in the pigment epithelium overlying the drusen. Histopathological examination reveals a deposition of a mosaic of colloid excrescences on the cuticular lamina of Bruch's membrane and an absence or deficiency of the pigment epithelium over each hyaline deposit. Inheritance follows a regular dominant pattern.

Pseudo-inflammatory foveal dystrophy (Sorsby)

This is a rare hereditary dystrophy characterized by bilateral inflammatory signs in the posterior pole. Haemorrhages, exudates, oedema and pigmentary proliferation are manifestations of this disease starting between the ages of 30 and 50 years. Later a generalized choroidal atrophy develops. There is degeneration in the elastic layer of Bruch's membrane and a choroidal atrophy on histological examination. The defects in Bruch's membrane are regarded as a primary causal agent. Inheritance is usually autosomal dominant.

Central areolar choroidal atrophy

Central areolar choroidal atrophy is a disease primarily affecting the posterior pole in predisposed individuals over the age of 40 years. A progressive atrophy of the choroidal vessels is found and the choriocapillaris, pigment epithelium and outer retinal layers gradually disappear. A central yellowish-white area of chorioretinal atrophy evolves and eventually central vision is lost. Colour vision is affected. Dark adaptation, the electro-retinogram and the EOG are mostly normal. Fluorescein angiography shows intense fluorescence in the area of the visible choroid where the retinal pigment epithelium has disappeared. Histopathologically there is a central area of chorioretinal atrophy. Heredity is usually autosomal recessive but autosomal dominant inheritance has been described.

Leber congenital amaurosis

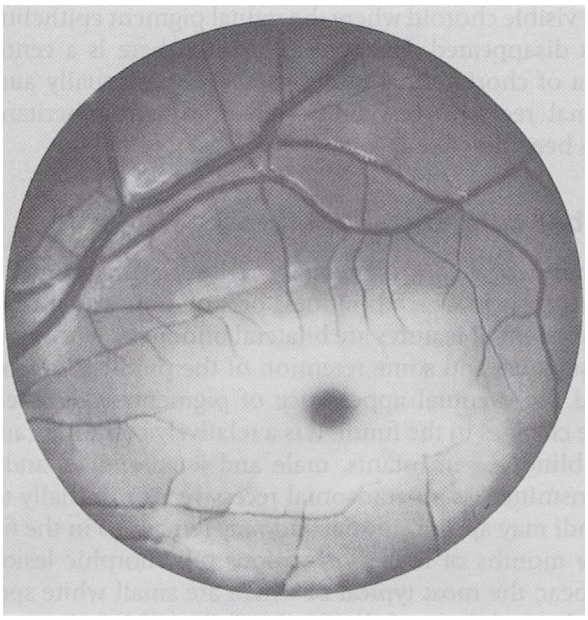
Leber described a pigmentary retinitis with congenital amaurosis in which blindness occurred in early infancy. The essential features are bilateral blindness, with coarse nystagmus and some retention of the pupillary reflexes and the eventual appearance of pigmentary degenerative changes in the fundi. It is a relatively common cause of blindness in infants, male and female alike, and is transmitted as an autosomal recessive trait. Initially the fundi may appear normal and may remain so in the first few months of life. Soon various polymorphic lesions appear, the most typical of which are small white spots in the periphery of the fundus followed by pigmentation. These are at first punctate of the 'pepper-and-salt' variety, which later aggregate until eventually the typical bone corpuscular form of pigmentary dystrophy develops. The optic discs become pale, the retinal vessels attenuated and the macula affected. The ERG is absent and the EOG defective.

A juvenile form of the disease affecting vision in the sixth or seventh year of life leading to blindness at the age of 30 years has also been described.

Lysosomal storage disorders

Three familial syndromes characterized by lipid degeneration and the formation of large vacuolated 'foam' cells may affect the retina. In two of them the ganglion cells of the central nervous system and retina only are affected (Tay-Sachs disease and Batten-Mayou disease), while the other has a more general distribution (Niemann-Pick disease).

Amaurotic family idiocy (Tay-Sachs disease): This is an autosomal recessive abnormality which occurs most commonly in Jewish children, and commences during the first year of life. The apparently healthy child becomes gradually blind, with muscular wasting and weakness, and mental apathy progressing to idiocy. Death follows in from 1 to 2 years. The ophthalmoscopic picture is very characteristic, resembling that of embolism of the central artery. There is a round, white area at the macula, with a cherry-red spot at the fovea (Fig. 20.34). In the later stages there is optic atrophy, which is always bilateral. The disease is due to an absence or deficiency of hexosaminidase A enzyme leading to storage of ganglioside G_{m2} in the central nervous system including the ganglion cells of the retina.



Fig, 20.34 Cherry–red spot.

The heterozygote may be detected by decreased enzyme activity in the serum. Prenatal diagnosis is possible by amniocentesis.

Maculocerebral familial degeneration (Batten-Mayou disease): This has an autosomal recessive inheritance, commencing at about 6 or 8 years. Defective vision with a central scotoma is accompanied by a weak intellect, and later convulsions and spasticity. Ophthalmoscopically the discs are pale and the vessels small. At the macula there are yellowish-grey spots and granular pigmentation, and there may be pigmentation in other parts of the retina of the 'salt-and-pepper' type. The ophthalmoscopic picture varies in different cases. Thirty per cent of lymphocytes in the peripheral blood are vacuolated. Autofluorescent material is deposited intracellularly throughout the body—possibly ceroid and lipofuscin. The syndrome is eventually fatal and there is no method of prenatal diagnosis.

Lipid histiocytosis (Niemann-Pick disease): This has similar but much more widespread changes of lipid storage; the spleen and liver are particularly affected. Sphingomyelin and cholesterol accumulate in the reticuloendothelial and nervous systems and in the parenchymal cells of many organs. Late in the course of the disease the retina may be involved, when changes similar to those in Tay-Sachs disease may be found. Conjugate gaze palsies are common.

SUMMARY

The retina is a light sensitive membrane which lines inside of the eye behind the ora serrata. It exists in a double layer with the transparent inner neurosensory retina which converts the light stimulus sensed by its photoreceptors into a signal which can be transmitted along the visual pathway to the brain and the outer pigment epithelium which maintains the photoreceptors and absorbs stray light.

Diseases that affect the retina include those that are the result of systemic diseases which affect its vasculature such as hypertensive retinopathy, diabetic retinopathy, retinopathy of prematurity, etc.; diseases that more directly result from local effects on retinal vessels such as retinal arterial and venous occlusion; inflammatory disorders due to infectious agents, immune system related diseases or toxic effects; retinal degenerations which are usually hereditary; retinal breaks and retinal detachment; and neoplastic diseases.

SUGGESTED READING

1. Machemer R, Michelson G, Maumann G. Atlas of Ophthalmology. Online multimedia database endorsed by the International Council of Ophthalmology. Online Journal of Ophthalmology. Retrieved August 12, 2010, from www.atlasophthalmology.com.
2. The National Eye Institute (NEI), a part of National Institute of Health (NIH), USA. The David G Cogan Ophthalmic Pathology Collection: A study and teaching collection of clinical ophthalmic cases and their pathology. Retrieved August 12, 2010, from http://cogancollection.nei.nih.gov/.

Chapter 21

Diseases of the Vitreous

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The *vitreous humour* is a transparent gel that provides a clear optical medium, structural integrity to the eye, as well as a pathway for nutrients utilized by the lens, ciliary body and the retina. The vitreous is clear and avascular, filling the space bound by the lens, retina and optic disc, it occupies approximately 80% of the volume of the globe. The internal limiting membrane, on the inner surface of the retina, separates it from the vitreous and there exists a potential space, the *subhyaloid space,* between the two. The vitreous consists largely of water (99%), a network of collagen fibrils, large molecules of hyaluronic acid, peripheral cells (hyalocytes), and mucopolysaccharides, forming a gel-like material. It has all the properties of a hydrophilic gel, undergoing turgescence and deturgescence and readily becoming liquefied when its protein base becomes coagulated, a transformation which occurs with age and on the slightest insult, either mechanical or chemical. It is attached to adjacent tissues, especially the posterior lens surface in youth, as *Weigert ligament,* a very strong attachment at the vitreous base around the ora serrata, a weak attachment at the optic nerve head, paravascular attachments and a weak oval attachment at the paramacular area.

Examination of the anterior vitreous can be carried out with a slit-lamp by rotating the slit 45° and rotating the slit or illumination arm at the minimum angle of separation from the viewing pathway. The vitreous should be observed for cells and any opacities. As the patient moves his eye, any settled opacities rise up into the path of observation.

CHANGES IN THE VITREOUS WITH AGE

Clocjuet canal, which contains the primary *vitreous* at birth, runs straight from the lens to the optic disc. The *secondary vitreous* eventually becomes liquefied and shrinks. Between 40 and 70 years of age in most individuals and earlier in myopes, vitreous liquefaction or *syneresis* occurs, the vitreous mass gradually shrinks and collapses, causing its separation from the retina, a condition known as posterior vitreous detachment (PVD). Condensations of the vitreous fibrils are present within this liquefied vitreous and are visible as *floaters.* When they float into the optic axis, especially against a bright background, they can be seen as *muscae volitantes* in various shapes and sizes.

VITREOUS DETACHMENT

Vitreous detachment occurs in three forms: posterior, basal and anterior.

Posterior vitreous detachment

Posterior vitreous detachment occurs posterior to the vitreous base and is a senile phenomenon (although commoner in diabetics and occurring at an earlier age in myopes) appearing spontaneously, producing a sudden onset of *photopsiae (see* Chapter 9) and floaters. The photopsiae are due to vitreoretinal adhesions and are provoked by ocular movement. They are commonly noticed in the temporal field although they should normally be projected in the meridian opposite to the site of retinal traction. Patients complain of a ring-like opacity, *Weiss ring,* which is the detached attachment of the vitreous to the edges of the optic nerve head.

The upper part of the vitreous commonly collapses first. The incidence of retinal complications is low. The condition is benign unless it is associated with other pathological findings, such as retinoschisis, a rhegmatogenous retinal detachment or diabetic retinopathy.

Patients with posterior detachment of the vitreous must be carefully examined, and reassured if there is no evidence of retinal tear, peripheral retinal degenerations, or vitreoretinal adhesion or traction.

Anterior and basal vitreous detachments

These occur secondary to trauma and are often accompanied by vitreous haemorrhage.

OPACITIES IN THE VITREOUS

Vitreous opacities are extremely annoying as they cast a shadow on the retina and appear as black spots moving in and out of the visual field, especially when reading. They are commonly mistaken for small flying insects, and are termed *muscae volitantes* or floaters. Most floaters are merely compressed cells or strands of the vitreous gel which have clumped together so that they are less transparent than the rest of the vitreous. They may be due to the following conditions:

1. developmental opacities which are located in the canal of Cloquet and are remnants of the hyaloid system or
2. degenerative changes, some of which are described below.
   - *Asteroid hyalosis,* usually found in the elderly, is characterized by the unilateral appearance of spherical or disc-shaped white bodies in the vitreous cavity. These are calcium-containing lipid complexes attached to the collagen fibrils and suspended throughout the vitreous. They may be commonly seen in diabetes. It is unilateral in the majority of cases and affects both sexes, is asymptomatic but may make examination of the fundus difficult with the ophthalmoscope. Treatment is rarely required unless vision is affected, in which situation a vitrectomy may be considered.
   - *Synchysis scintillans:* This degenerative condition leads to deposition of cholesterol crystals in the vitreous. These are also found in the anterior chamber and subretinal space. It affects damaged eyes which have been subjected to trauma or inflammatory disease in the past. The crystals are multicoloured, glittering particles which settle in the lower part of the vitreous cavity due to gravity but can be thrown up by eye movements to form a shower of iridescence. The vitreous in such cases is liquefied and no treatment is indicated.
   - *Amyloid degeneration:* Amyloidosis is a rare systemic disease and amyloid material is deposited in the collagen fibres of the heart, thyroid, pancreas, peripheral nerves and muscles. It is a heredofamilial syndrome transmitted as a Mendelian dominant producing generalized weakness, loss of weight, peripheral neuropathy and symptoms related to the affected organs. It runs a long, tedious course. The clinical features consist of diplopia, diminution of vision, external ophthalmoplegia, vitreous opacities, retinal haemorrhages and exudates. Both eyes are involved and the vitreous becomes opaque. The earliest lesion originates in the wall of a retinal vessel which has a cloudy margin and this slowly invades the vitreous body from behind forwards. Diagnosis is confirmed by biopsy of the conjunctiva, rectum, skin or sternal marrow. The vitreous opacities themselves are linear with footplate attachments to the retina and posterior surface of the lens and this is a helpful diagnostic feature. Vitreous amyloidosis may be treated surgically by pars plana but the prognosis must always be guarded.

There are many other causes of vitreous opacities. A senile or myopic eye produces opacities due to condensed vitreous fibres floating in areas of liquefaction. Vitreoretinal degeneration may form a part of other syndromes such as retrolental fibroplasia, Wagner disease, Ehlers-Danlos syndrome and Marfan syndrome. They can also be formed by the inflammatory cells of cyclitis, haemorrhage secondary to diabetes, retinal vasculitis or subarachnoid haemorrhage and occasionally by neoplastic cells.

VITREOUS BANDS AND MEMBRANES

Vitreous bands or *membranes* often form after posterior vitreous detachment and originate from hyalocytes, fibrocytes, migratory retinal pigment epithelial cells in the presence of a retinal hole, or endothelial cells of the

capillaries. If such a band is adherent to the retina and is producing photopsia, retinal oedema or haemorrhage then the traction is likely to give rise to retinal breaks or a detachment.

In some diseases, a *preretinal* or *epiretinal membrane* lines the inner surface of the retina; if it is thin it looks like a sheet of cellophane, and if thick it resembles a sheet of tissue. As the membrane contracts the retina wrinkles producing a macular or extramacular pucker. Epiretinal membranes may progress to threaten central vision and cause a significant visual handicap, as evidenced by metamorphopsia and may then be removed by vitrectomy with dissection of the membranes. They are commoner in older people and are often bilateral though asymmetrical. Pars plana vitrectomy combined with epiretinal membrane stripping is effective, particularly in treating macular pucker, though the complication of cataract would seem to be an unavoidable risk.

Signs of traction in the peripheral fundus are retinal areas of white-without-pressure, detachment of the ora serrata or a U-shaped retinal tear with an operculum. In the posterior fundus they consist of oedema of the retina, haemorrhage, macular cystoid changes, heterotopia of the macula and tenting of the retina.

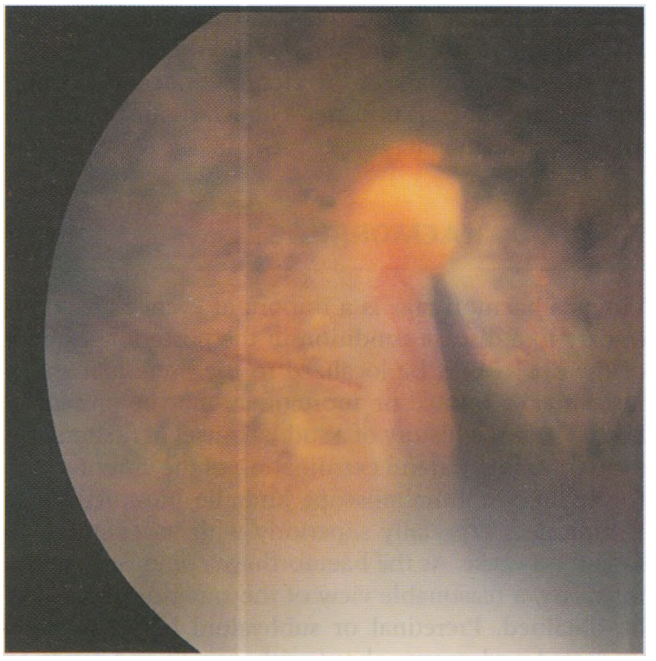


Fig. 21.1 Posterior hyperplastic primary vitreous showing a leash of vascularized fibrous tissue extending from the back of the lens to the optic nerve head. Extensive chorioretinal degeneration and a pigmentary retinopathy can also be seen.

PERSISTENT HYPERPLASTIC VITREOUS

This condition is seen in two forms—anterior or posterior. There is a failure of the structures within the primary vitreous to regress. Shortly after birth a unilateral, white pupillary reflex is noticed in the full-term infant, which may later be associated with other abnormalities such as cataract *(see* pp. 267-268), glaucoma, long and extended ciliary processes, microphthalmos and intraocular haemorrhage.

The retrolental tissue contracts over time to pull the ciliary processes inwards. Later the lens becomes opaque and glaucoma intervenes. Ultrasonography and computed tomography are helpful in diagnosing this condition. If diagnosed at an early stage it may be possible to aspirate the lens followed by excision of the retrolental membrane and a vitrectomy. Visual prognosis is poor.

The posterior form of persistent hyperplastic vitreous includes a persistent hyaloid artery with a large stalk issuing from the optic disc (Fig. 21.1). Advanced cases may have an extensive tractional retinal detach-ment for which little can be done.

VITREORETINAL DEGENERATION

Wagner disease is a bilateral condition transmitted as an autosomal dominant trait. The fundus shows narrow and sheathed vessels, pigmented spots in the periphery or along the retinal vessels, and choroidal and optic atrophy. The vitreous is liquefied with condensed membranes. During adolescence the vitreous shrinks and if attached to the retina may produce a tear. Cataract is a late complication. Extensive liquefaction of the central and posterior portions of the vitreous body takes place leaving a thin layer of formed cortex on the surface of the retina.

The management consists of regular examinations for retinal tears which should be treated with photocoagulation or cryotherapy. In the presence of severe vitreous traction, vitreoretinal surgery is indicated.

Stickler or Wagner-Stickier syndrome is also known as hereditary progressive arthro-ophthalmopathy and is a variant of Wagner syndrome. This is an autosomal dominant connective tissue disorder affecting the ears, eyes and joints. Patients complain of stiff, painful, prominent and hyper-extensible large joints. They may also have a cleft palate, bifid uvula and sensorineural deafness. Ocular involvement includes a progressive myopia, spontaneous retinal detachments and cataracts. Blindness is frequent in the first decade.

Goldmann-Favre vitreoretinal degeneration

This condition produces progressive loss of vision due to retinoschisis, pigmentary degeneration resembling retinitis pigmentosa, followed by cataract and retinal detachment. The affliction is bilateral and familial, being transmitted as

an autosomal recessive trait. Retinoschisis is both central, affecting the macula, and peripheral. When the pigmentary changes are marked, the electroretinogram is extinguished. The vitreous undergoes liquefaction. There is no satisfactory treatment.

VITREOUS HAEMORRHAGE

Vitreous haemorrhage is a important event as it is secondary to a disease condition in the posterior segment of the eye. It may be localized to the preretinal space, intravitreally located or, more often, may be present in both. There is a history of a sudden onset of floaters and a fall in vision. Careful examination of the vitreous with the indirect ophthalmoscope and the bio-microscope is indicated, especially superiorly with indentation, to look for a cause. As the haemorrhage commonly settles inferiorly, a reasonable view of the superior retina may be obtained. Preretinal or subhyaloid blood remains unclotted and moves about with gravity and tends to acquire a boat-shaped configuration which is red in colour. Blood in a lacuna of the vitreous tends to separate whereas blood in the gel clots and moves bodily with the gel itself. Blood of long-standing duration in the vitreous loses colour and settles inferiorly, as a white opaque mass.

Ultrasonography with a B-scan is particularly helpful. Fresh haemorrhage within the vitreous cavity gives rise to scattered point-like echoes of varying amplitude. Sedimentation of haemorrhage within the fluid vitreous produces a flat sheet of very high-amplitude echoes. Posterior vitreous detachment is indicated by point-like echoes confined to the gel compartment or retrohyaloid space. Extensive fibrovascular membranes on the retinal surface may be detected by ultrasound in proliferative diabetic retinopathy. Diabetic traction detachment appears as an angular retinal elevation that is immobile on dynamic testing.

The common causes of vitreous haemorrhage are proliferative diabetic retinopathy (Fig. 21.2), retinal tears, branch retinal vein occlusion, retinal vasculitis and peripheral retinal neovascularization. Trauma is the commonest cause in the young.

Early surgical intervention is required in eyes having a traumatic etiology or those associated with a retinal detachment. Other causes can be managed conservatively with the head elevated so as to minimize the dispersion of blood within the gel. If the blood sinks under the influence of gravity it may be possible to discover a cause which should be treated. If the vitreous fails to clear after a week the patient should be mobilized and seen at 2-monthly intervals. If the haemorrhage does not clear in 6 months, vitreoretinal surgery should be considered, if the electrophysiological parameters show a functional retina, and ultrasonography indicates a reasonable chance of anatomical success. Active treatment is particularly indicated if the fellow eye is similarly affected.

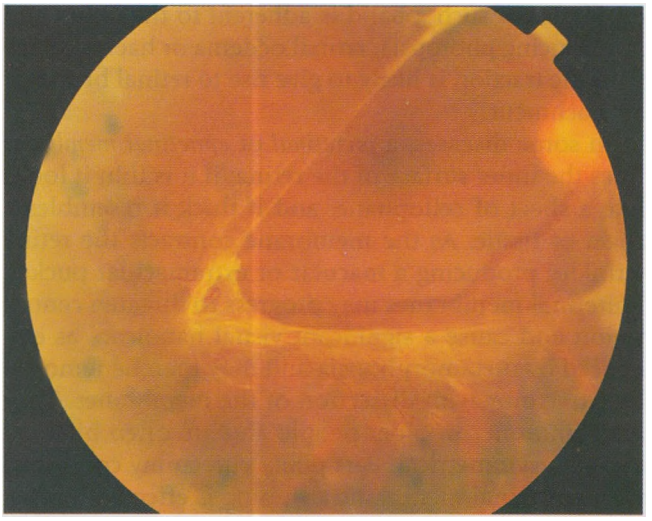


Fig. 21.2 Proliferative diabetic retinopathy. Haemorrhage generally occurs from the preretinal fibrovascular fronds. The picture shows extensive panretinal photocoagulation scars and persistent vitreoretinal fibrovascular bands.

Vitreous haemorrhage and retinal tears

Retinal tears crossing a blood vessel can lead to vitreous haemorrhage. This tends to occur in myopes and in those who have predisposing degeneration of the retina. It produces localized flashes and floaters before the onset of the haemorrhage itself and may be precipitated by mild ocular trauma.

Vitreous haemorrhage and posterior vitreous detachment

Bleeding in association with posterior vitreous detachment is due to retinal traction and may occur in the vitreous gel, or a preretinal haemorrhage may be found which sinks to the lower part of the globe. Vitreous haemorrhage due to a *posterior vitreous detachment* usually clears spontaneously. If a bleeding vessel can be seen it should be photocoagulated.

Vitreous haemorrhage and retinal vein occlusion

Venous obstruction occurs at the lamina cribrosa or at the arteriovenous crossings and is prone to occur when the patient is hypertensive or arteriosclerotic. Venous collaterals form at the optic disc between the retinal and ciliary circulations and between branches of the

obstructed vein and the adjacent patent venules, particularly in tributary occlusion. About 3 months after the occlusion, capillary microaneurysms and fibrovascular proliferation may occur and vitreous haemorrhage may arise from the delicate new vessels. Photo-coagulation has a part to play in the prevention of this syndrome.

Vitreous haemorrhage in Eales disease

Eales disease is an idiopathic, inflammatory peripheral retinal vasculopathy which presents with recurrent vitreous haemorrhages in young males. It has been suggested that a hypersensitivity reaction of the retinal vessels to tuberculoproteins may be the cause of the vasculitis. The peripheral retinal vasculitis leads to obliteration of the affected vessels, particularly the shunt capillaries of the peripheral retina, which in turn produces hypoxia and finally vasoproliferation. The vasculitis is seen clinically as a 'sheathing' of the vessels, which leak copiously on fluorescein angiography. Haemorrhages, soft exudates and retinal oedema are common at the junction of perfused and non-perfused zones of the retina. Later, obliteration of the vessels occurs, seen as solid white lines and these are surrounded by arteriovenous shunt vessels and neovascularization on the retina or extending into the vitreous. Eventually recurrent vitreous haemorrhages occur. Initially these clear spontaneously, but after a few recurrences, the haemorrhage organizes, and is associated with a tractional retinal detachment and secondary glaucoma.

Treatment consists of systemic steroids which may be helpful in the early vasculitic stage. Abnormal vessels under traction should be treated with photocoagulation. Vitreoretinal surgery may be necessary in cases of marked vitreous traction threatening the macula.

Vitreous haemorrhage due to sickle cell retinopathy

Sickle cell C disease has its clinical manifestations predominantly in the eye (*see* p. 311).

Vitreous haemorrhage due to ocular trauma

Vitreous haemorrhage in the young commonly follows contusion or a perforating injury. The haemorrhage is usually intravitreal and the blood is clotted. An intraocular foreign body must be excluded by fundus examination (Fig. 21.3) and investigations such as X-ray and ultrasonography and removed if present. An open globe injury needs immediate repair, with the vitreous haemorrhage being tackled 10 days later, when a posterior vitreous detachment would make the surgery easier. The patient should be advised rest and the head elevated for 5-6 days. After a concussional injury, vitrectomy may be postponed for 6 months to allow for spontaneous clearing of the vitreous haemorrhage provided there is no underlying retinal detachment. The patient should have serial ultrasonography during waiting period to ensure there is no retinal detachment. This is because in the presence of accompanying retinal detachment early vitreoretinal surgery is advised.

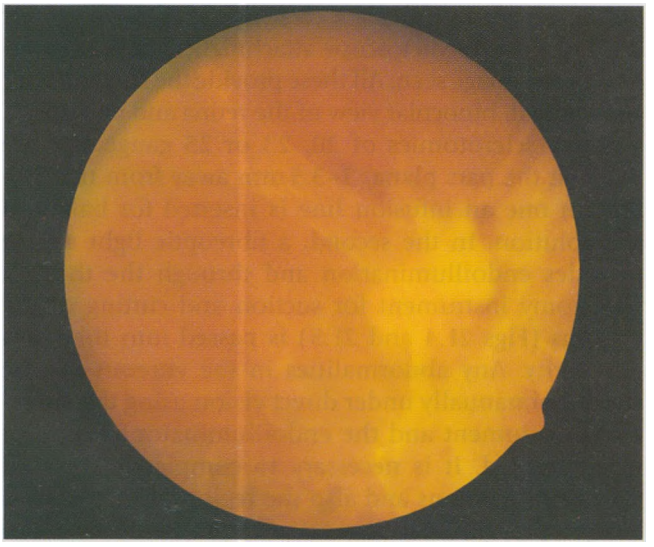


Fig. 21.3 Foreign body lying on the retinal surface, encapsulated by fibrous tissue and accompanying vitreoretinal fibrotic bands.

VITREOUS SURGERY

An abnormality leading to opacification of the vitreous body or the development of vitreoretinal scar tissue may require vitreous surgery. Common indications for vitreous surgery include vitreous haemorrhage, complications from diabetic retinopathy such as tractional retinal detachment, complicated retinal detachment, preretinal membrane fibrosis, injury with or without an intraocular foreign body, macular hole, endophthalmitis and complications of prior intraocular surgery.

The principles of vitreous surgery are:

- to remove any vitreous abnormalities, e.g. haemorrhage, traction bands;
- to restore retinal anatomy by removal of epiretinal membranes or drainage of subretinal fluid;
- to treat abnormal retinal vessels or breaks by endophotocoagulation or cryotherapy and
- to provide tamponade to maintain chorioretinal apposition, internally by silicon oil and gases, or externally by an encirclage or plomb (buckle).

A vitrectomy is performed through a surgical microscope allowing coaxial illumination and fine movements byX-Y coupling. Special planoconcave lenses are placed

on the cornea to provide a clear image of the posterior third of the eye. Microscope attachments allow re-inversion of the image seen. All these provide the surgeon with a magnified, binocular view of the retina and vitreous.

Three sclerotomies of 20, 23 or 25 gauge size are made at the pars plana, 3-3.5 mm away from the limbus. In one an infusion line is inserted for balanced salt solution. In the second, a fibreoptic light source provides endoillumination and through the third, a vitrectomy instrument for suction and cutting of the vitreous (Figs 21.4 and 21.5) is passed into the vitreous cavity. Any abnormalities in the vitreous can be cleared bimanually under direct vision using the vitrectomy instrument and the endoilluminator as support when needed. It is necessary to completely clear all the central vitreous and also the region of the vitreous base to prevent later fibrovascular proliferation. Once the visibility of the retina is restored, the cause for the vitreous disturbance is treated. Endophotocoagulation with a fibre optic probe delivering diode laser may be required to seal a retinal break or treat areas of retinal neovascularization. Endodiathermy can be utilized to coagulate bleeding vessels.

Vitrectomy is seldom carried out as an isolated procedure, but is often associated with surgery for vitreoretinal proliferation, complicated retinal detachments or foreign bodies in the eye. In the presence of vitreoretinal proliferation it is important to relieve all traction on the retina. Vitreous bands can be cut using the vitrectomy instrument or special miniature vitreoretinal scissors. Epiretinal membranes are removed by gentle peeling with a vitreoretinal pick and forceps, or by cutting them with vitreoretinal scissors, to allow the retina to fall back into place. Small foreign bodies are dissected of their fibrous capsule with a vitreoretinal pick or forceps and then removed by intravitreal foreign

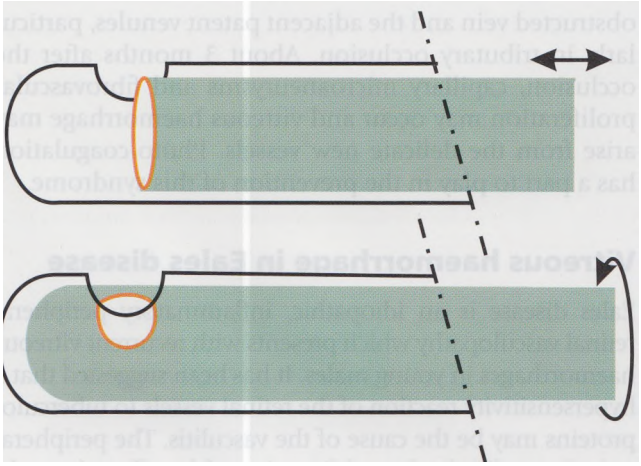


Fig. 21.4 Vitrectors cut either by a guillotine action (as in the figure above) or a rotary action (as below).

body forceps. An intravitreal magnet is occasionally employed. Maintenance of chorioretinal apposition to allow chorioretinal adhesions to occur and to prevent recurrence of fibrovascular proliferation in the vitreous necessitates an internal tamponade with gases or liquids.

Clinical situations in which internal tamponade is required, with the best possible option.

Gas	• Primary vitreoretinal surgery for a detachment
	• Macular hole surgery
Gas/liquid	• Retinal detachment with PVR
	• Giant retinal tear
	• Infectious retinitis
Liquid	• Severe proliferative diabetic retinopathy
	• Chronic uveitis with hypotony
	• Complicated paediatric detachment

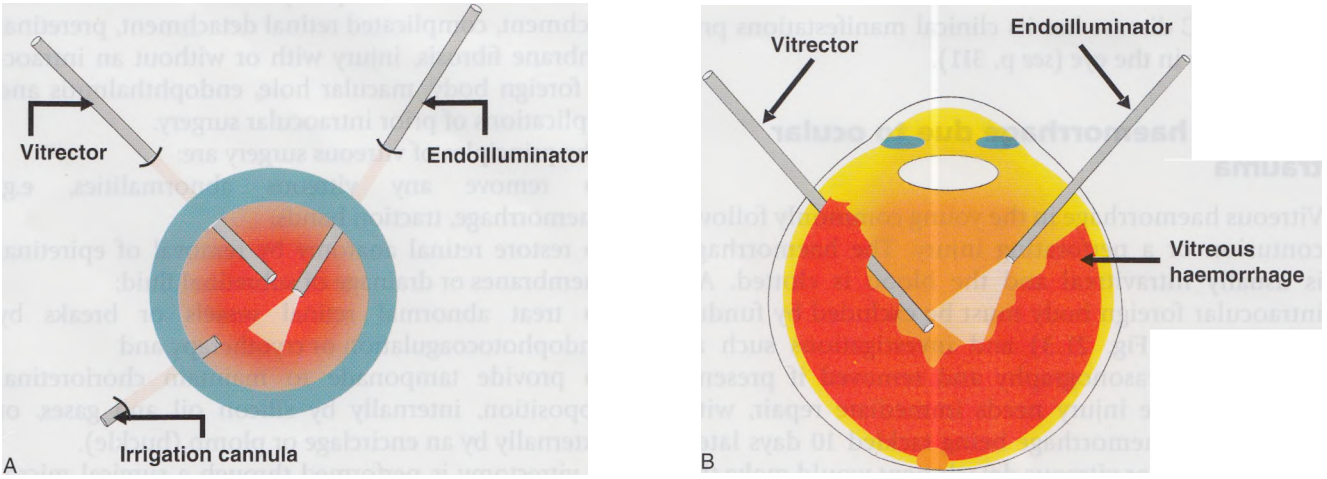


Fig. 21.5 Vitrectomy. (A) Three sclerotomies allow the placement of a vitrector, endoilluminator and irrigation cannula. (B) Cross-sectional view of a vitrectomy undertaken to clear a vitreous haemorrhage.

Combining agents available for tamponade allow support to the superior and inferior retina simultaneously without the need for positioning of the patient and also permits drainage of the subretinal fluid through the break. The disadvantages are a more rapid emulsification of the liquids and more frequent inflammation. Some of the combinations studied are semifluorinated alkanes with silicone oil, fluorosilicone and silicone oil, and 30% F_6H_8 with 70% polydimethylsiloxane 1000.

Visual prognosis after vitreous surgery is often guarded and depends upon the basic disease process and the degree of damage to the retinal receptors. Meticulous surgery has greatly increased the chances of anatomical success.

SUMMARY

The vitreous is a transparent gel which constitutes 80% of the volume of the globe and provides a clear optical medium behind the lens, ft is strongly attached at the vitreous base on the ora serrata, along an annular attachment known as Weigert's ligament to the posterior lens surface and has weak attachments to the optic disc, retinal vessels, macula, and regions of retinal scars and lattice degeneration. Diseases include detachment, haemorrhage, degeneration and inflammations which are usually accompanied by involvement of adjacent retina and choroid in various degrees.

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Diseases of the Optic Nerve

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OVERVIEW

Anatomy

The optic nerve consists of approximately 1.2 million axons that arise from the retinal ganglion cells (*see* p. 11) and has four parts: (i) the *intraocular portion* (1 mm), i.e. the optic nerve head visible as the optic disc on fundus examination; (ii) *intra-orbital portion* (25-30 mm); (iii) *intracanalicular portion* (5-9 mm) and (iv) *intracranial portion* (10-16 mm), which goes up to the optic chiasma. The axons are second-order neurones and though termed as a 'nerve' the optic nerve is actually a tract identical to other white matter tracts of the brain. Eighty per cent of the fibres of the optic nerve originate from the macular region, which represents 90% of the retinal ganglion cells. Hence, diseases of the macula and optic nerve can mimic each other.

Microscopically, the optic nerve possesses oligodendrocytes, astrocytes and microglia, whereas true peripheral nerves possess Schwann cells, fibroblasts and macrophages. As with white matter of the brain, the optic nerve has no powers of regeneration. The axons of the optic nerve acquire myelin sheaths proximal to the lamina cribrosa and do not possess a neurilemma. Like other parts of the central nervous system, the optic nerve is covered with pia, arachnoid and dura mater as soon as the nerve leaves the eyeball.

Normal physiology of axoplasmic transport and flow

Apart from the *neural* signals, axons permit the transfer of intracellular organelles such as mitochondria, chemicals and proteins from the neuronal cell body to the distal terminal and *vice versa.* In the case of the optic nerve, the neuron soma is the ganglion cell body in the retina. The unmyelinated axons traverse the retina in the retinal nerve fibre layer, exit the eye through the optic nerve head, acquire myelin sheaths outside the globe and travel

as the optic nerve. They then partially decussate and pass as the optic chiasma and later the optic tract to terminate in the lateral geniculate body. *Orthograde axoplasmic transport* (from the eye to the brain) has a slow component (proteins and enzymes) that progresses at 0.5-3.Omm/day, an intermediate component (mainly mitochondria) and a rapid component (subcellular organelles) that moves at 200-1000 mm/day. *Retrograde axoplasmic transport* of lysosomes and mitochondria (from the brain to the eye) also occurs at an intermediate rate.

Blood circulation of the optic nerve

See p. 14, Chapter 1.

Aetiopathogenesis of optic nerve diseases

The optic nerve could be affected by disorders that produce (i) swelling, oedema or accumulation of excess fluid in and around the nerve; (ii) ischaemia, by affecting the blood supply; (iii) inflammation within or around the nerve; (iv) degeneration or atrophy of the axons by direct compression or toxic effects; (v) direct injury by penetrating trauma or indirect injury by concussional and rotational forces and/or (vi) abnormal embryogenesis *in utero* leading to congenital anomalies.

Clinical features

Diseases affecting the optic nerve give rise to visual disturbances but can sometimes be asymptomatic and remain unnoticed (as in early *papilloedema).* There are certain retinal disorders that can masquerade as optic nerve diseases producing similar symptoms of decreased vision, central field defect and disturbance of colour perception. Central serous retinopathy (CSR) is a classic example. Localization of a lesion producing visual disturbance to the optic nerve can almost always be made by careful clinical examination including visual acuity, colour vision, pupillary reactions, visual field and ophthalmoscopic appearance of the optic nerve head. Sometimes visual disturbance in diseases affecting the optic nerve may be more subtle and may affect aspects of visual function other than visual acuity such as loss of contrast sensitivity, diminished stereoacuity and decrease in brightness of objects. Retinal diseases affecting the macula generally have normal pupillary reactions and an abnormal photostress test (*see* p. 102).

Differential diagnosis

This can be made by categorizing the patient on the basis of

- whether one or both eyes are affected;

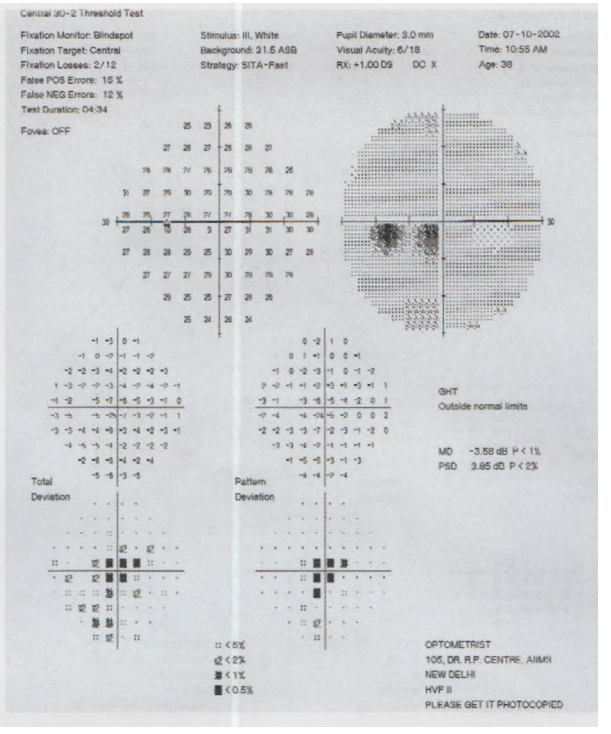


Fig. 22.1 Central scotoma documented by automated perimetry.

- the pattern of visual field loss and
- the appearance of the optic nerve head or optic disc.

Visual field defects are best detected by Goldmann kinetic perimetry (full field) and Humphrey automated threshold perimetry (30-2 programme for central field or neurological programmes). The field defects caused by various optic neuropathies are of different patterns but they can be broadly classified as either (i) central (Fig. 22.1) or centrocaecal scotomas (Fig. 22.2), or (ii) nerve fibre bundle defects (Table 22.1; *see also* Fig. 22.9).

The *appearance of the optic disc* may be normal, swollen or oedematous, hyperaemic or pale, in different disorders of the optic nerve. At a given point in time, any one of these appearances may be seen but the appearance may change with time and any optic neuropathy may eventually result in optic atrophy (Table 22.2).

PAPILLOEDEMA

Papilloedema is defined as oedema of the optic disc or nerve head due to raised intracranial pressure. Since the optic nerve is enclosed up to the lamina cribrosa within the meningeal sheaths common to the brain, and the subarachnoid and subdural spaces around the nerve are freely continuous with those around the brain, any rise in the intracranial pressure becomes equally evident around the nerve. When th is occurs the subarachnoid space sometimes becomes so distended that it is ampulliform

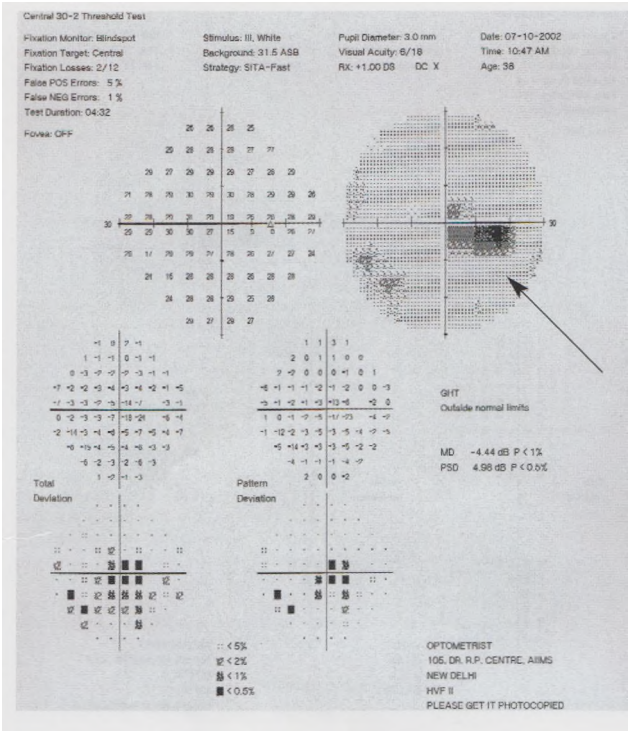


Fig. 22.2 Centrocaecal scotoma involving the centre of fixation and extending up to the normal physiological blind spot.

Table 22.1 Differential diagnosis of diseases of the optic nerve based on visual field defects

I. Central or centrocaecal scotomas (lesion involving the papillomacular bundle)

*A. Unilateral**

- Optic neuritis (sudden visual loss)
- Compressive lesion (slowly progressive visual loss)

B. Bilateral

- Poor nutrition, tobacco–alcohol neuropathy
- Drug-induced
- Toxin-induced
- Hereditary optic atrophy
- Infiltration of the optic nerves: sarcoidosis, leukaemias, etc.
- Bilateral compressive lesions such as pituitary adenoma with a post-fixed chiasma
- Bilateral optic neuritis

II. Nerve fibre bundle defects (lesion at the level of the optic disc sparing the papillomacular bundle)

- Glaucoma
- Optic nerve drusen
- Ischaemic optic neuropathy
- Retinal branch artery occlusion
- Some cases of optic neuritis
- Chronic papilloedema

*In the presence of a unilateral central scotoma, it is extremely important to assess the visual field in the fellow eye for the presence of a superotemporal field defect known as a junctional scotoma. This occurs due to compression of the posterior optic nerve and anterior chiasma from below, affecting the anterior crossing fibres (or von Willebrand knee) from the inferior nasal retina of the fellow eye.

just behind the globe. As a result, oedema develops at the optic disc; this is a purely hydrostatic, non-inflammatory phenomenon.

Pathogenesis

The genesis of papilloedema has been disputed and ascribed to several factors. It was considered to be due to compression of the central retinal vein as it crosses the subdural and subarachnoid spaces, causing its collapse, while the thicker-walled artery continued to transmit blood. The principal pathophysiology of optic disc swelling is now recognized to be blockage of axoplasmic transport. Elevated cerebrospinal fluid (CSF) pressure produces axoplasmic stasis in the optic nerve head leading to swelling of the optic disc and secondary vascular changes at the disc surface. The degree of papilloedema varies with the ease of access between the meningeal spaces within the cranium and around the optic nerve, and if the optic nerve sheath is opened surgically in patients with increased intracranial pressure, as in the operation of optic nerve sheath fenestration for pseudotumour cerebri, papilloedema is relieved.

Pathology

The pathology of papilloedema shows signs of passive oedema without evidence of inflammation; the oedematous changes are located in the optic nerve head in front of the lamina cribrosa. The small blood vessels are engorged and tortuous. The nerve fibres in the optic nerve head are swollen and axoplasmic stasis is noted in them. The physiological cup gets filled in and the internal limiting membrane is raised (Fig. 22.3). The nerve fibres become swollen and varicose, and ultimately degenerate. They show numerous cytoid bodies in front of but not behind the lamina cribrosa. Electron microscopy shows engorgement of axons in the laminar portion of the optic nerve. The swollen axons are filled with mitochondria primarily anterior to the choroidal lamina cribrosa. The mitochondria are structurally swollen and disrupted. The neuroglia proliferates and the mesoblastic tissue around the vessels becomes thickened. There is subpial oedema distal but not proximal to the site of entry of the central vessels, and the subarachnoid space is frequently distended. Pathological changes are also seen in the surrounding retina and macular region. Oedema in the nerve fibre layer raises the internal limiting membrane in folds. Retinal exudates distributed radially along the folds may be present in the macular region corresponding to the clinical appearance of a macular fan or macular star. The outer plexiform layer may be oedematous, but there are no large cystic spaces as seen in hypertensive retinopathy.

Table 22.2 Differential diagnosis of optic nerve disorders based on the ophthalmoscopic appearance of the disc

I. Swollen optic disc or disc oedema (true acquired disc oedema must be distinguished from pseudo swelling)
   A. *Unilateral*
      - Papillitis or optic neuritis involving the nerve head (sudden loss of vision with subsequent improvement)
      - Anterior ischaemic optic neuropathy (sudden loss of vision usually without improvement)
      - Orbital tumours (slowly progressive visual loss)
      - Papillophlebitis or optic disc vasculitis (rapid loss of vision without improvement)
      - Central retinal vein occlusion (may or may not be associated with profound visual impairment)
      - Infiltrative disorders (impaired vision)
      - Ocular hypotony (rapid loss of vision without improvement)
      - Foster–Kennedy syndrome (true papilloedema in one eye with optic atrophy in the fellow eye)
      - Pseudo Foster–Kennedy syndrome
   B. *Bilateral*
      - Increased intracranial pressure: papilloedema (optic nerve function is typically normal)
      - Hypertension (optic nerve function is typically normal)
      - Diabetic papillopathy (mild-to-moderate impairment of vision)
      - Advanced Graves disease or dysthyroid eye disease
      - Cavernous sinus thrombosis
      - Carotid–cavernous fistula
      - Leber hereditary optic neuropathy in the acute stage
      - Other systemic diseases such as anaemia and hypoxaemia
      - Any of the unilateral causes mentioned earlier can occasionally be bilateral

II. Normal optic disc
   A. *Unilateral*
      - Retrobulbar neuritis
      - Compressive lesion
      - Retrobulbar infiltration: granulomatous, carcinomatous, lymphomatous
   B. *Bilateral*
      - Tobacco- and alcohol-related neuropathy
      - Nutritional
      - Drugs
      - Toxins
      - Leber hereditary optic neuropathy
      - Any of the unilateral causes

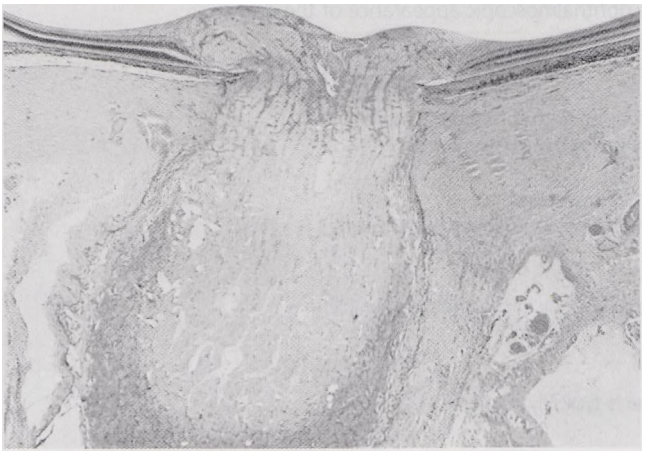
III. Atrophic optic disc*
   A. *Cupped disc*
      - Glaucoma
      - Giant cell arteritis (in the late or atrophic stage)
      - Compressive lesion (occasionally masquerades as 'normal tension' glaucoma)
      - Optic disc coloboma or pit
   B. *No significant cupping*
      - Any optic neuropathy

*Optic atrophy is also a consequence of lesions of the retina, optic chiasma and optic tract, all of which comprise axons arising from the retinal ganglion cells.

Aetiology

By definition, papilloedema is disc oedema due to *increased intracranial pressure.* An intracranial tumour in any position, may induce it, the highest percentage being found with tumours of the mid-brain, parieto-occipital region and cerebellum. Papilloedema due to tumours of the anterior fossa is relatively rare and occurs late in the course of the disease. In general, those tumours which tend to produce internal hydrocephalus are most likely to cause papilloedema. The site of the tumour is more important than its nature, size or rate of growth. Other intracranial causes include a brain abscess, thrombosis of the cavernous sinus or other intracranial veins, aneurysm, subarachnoid haemorrhage, pseudotumour cerebri and hydrocephalus. Malignant hypertension can also cause papilloedema, usually by raising the intracranial tension, but may produce signs of disc oedema in the absence of raised intracranial pressure as seen in grade IV hypertensive retinopathy.

Pseudotumour cerebri, previously often termed as benign intracranial hypertension, is a disorder associated



Fig, 22.3 Papilloedema in a cerebral tumour. Note the dilatation of the central vein. (By courtesy of Paton)

with raised intracranial pressure in the absence of an intracranial space-occupying lesion. It tends to occur in obese females in the second or third decades, producing headache with transient blurring of vision and occasional photopsia. Some loss of visual function occurs in 50% of patients, especially those with a high-grade or atrophic papilloedema or peripapillary subretinal haemorrhage. Transient obscurations (blurring) of vision and the presence of opticociliary shunts are bad prognostic factors for vision. Other risk factors, particularly in the older age group, are anaemia and high myopia. Neuroimaging of the brain may show small ventricles or may be completely normal, in which case the CSF pressure needs to be measured by a neurosurgeon to establish the diagnosis.

Clinical features

Symptoms are generally absent or vague and vision may be unimpaired for a long time. This applies particularly to the central vision which may be unaffected sometimes even in the presence of a macular fan. Episodes of transient attacks of blurred vision, or transient obscurations of vision, usually described as bilateral or monocular 'black-outs' lasting for a few seconds often precipitated by changes in posture, are not uncommon in the initial stages. As the condition progresses, however, two additional signs may be found—an enlargement of the blind spot owing to separation of the retina around the disc by the oedema and a progressive contraction of the visual field due to atrophy of the nerve. At this stage, relative scotomata, first to green and red, may be present. However, if the condition persists, the vision slowly diminishes. Severe loss of central visual acuity can occur with chronic papilloedema. As atrophy sets in, complete blindness ensues; the pupils, hitherto normal in size and reaction, are then large and immobile. Other symptoms include headache, which becomes worse in a recumbent position or is worst in the early morning when the patient wakes up, but may improve during the day. Patients may complain of nausea and vomiting and double vision due to non-specific paresis of the sixth nerve caused by raised intracranial pressure.

The first clinical sign of papilloedema is a blurring of the margins of the optic disc. The blurring starts at the upper and lower margins and extends around the nasal side, while the temporal margin is usually still visible and sharp. The disc becomes hyperaemic and gradually, progressive oedema extends over the surface of the disc reducing the size of the physiological cup, blurring the temporal margin and spreading into the surrounding retina (Fig. 22.4). As the disc swells the veins become

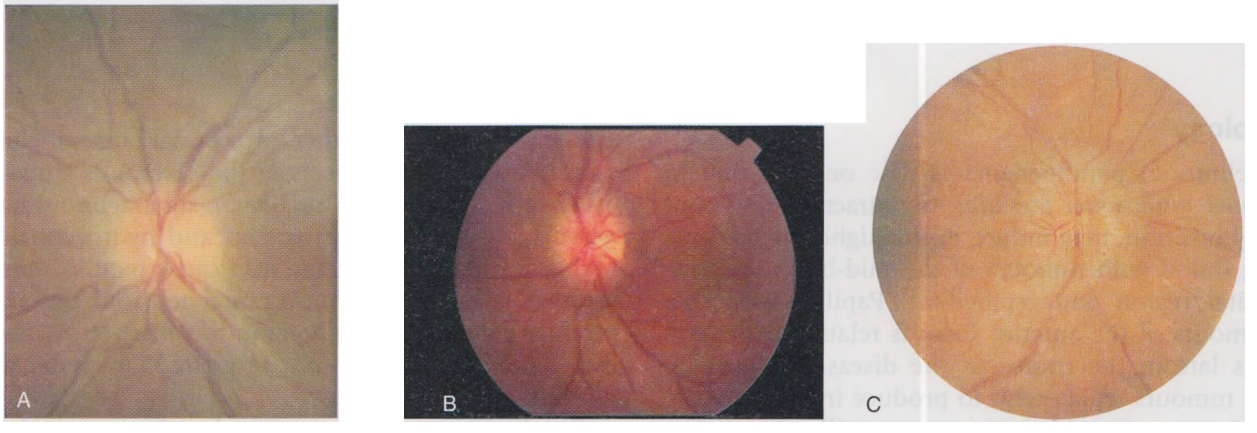


Fig. 22.4 Papilloedema. (A) Early (By courtesy of S Kedar); (B) Moderate; (C) Advanced.

congested and turgescent; their pulsations may be absent even on applying pressure on the globe. It is important to note that as venous pulsations are absent in 10-15% of the normal population, this sign in isolation cannot be taken as conclusive evidence of papilloedema. The small arterioles also become prominent, appearing as red streaks on the swollen disc, sometimes giving it a striated appearance. Eventually the disc becomes elevated into a mound higher than the surrounding retina and mushrooms out so that the vessels bend sharply over its margins. With the indirect method of ophthalmoscopy a definite parallax may be elicited between its summit and the retina beneath, and by the direct method a difference of 2-6 D may be found between the focus of the vessels at the surface of the disc and those on the retina a little way off.

Meanwhile, the vascular engorgement and stasis result in the appearance of numerous haemorrhages on the disc and in the neighbouring retina where they may be both flame-shaped and punctate. Oedema of the retina spreads so that this tissue is thrown into folds, and the veins, now tortuous and enormously dilated, may be buried for large tracts of their course in the swollen and oedematous retina (Fig. 22.4). The surface ofthe disc now loses its reddish hue and becomes opaque, and exudates begin to appear on its surface and in the retina itself. The radiating, oedematous folds around the macula take on the appearance of a macular star, usually incomplete and fan-shaped on the side towards the disc, while fluffy patches (cotton-wool spots due to retinal microinfarcts) appear scattered throughout the posterior half of the fundus. At this stage the ophthalmoscopic picture may be indistinguishable from that of malignant hypertension.

With increasing pressure in the tissue of the swollen disc, the vascular supply gets compromised leading to focal infarcts, ischaemia and direct pressure-induced axonal damage. Frequently, the swelling begins to subside before this final stage is reached, but in all cases subsidence eventually occurs, a process preceded by atrophic changes when the nerve fibres can no longer withstand the pressure and degenerate. When this process commences, the vascularity of the disc diminishes so that it appears pale grey in colour; and eventually, even though the increase in intracranial pressure may remain unrelieved, the disc becomes flat and atrophic. The ophthalmoscopic appearance of'post-papilloedema' optic atrophy (Fig. 22.5) resembles that of'post-neuritic' atrophy and is characteristically described as 'secondary optic atrophy' in both diseases. The appearance depends on the fact that the absorption of the exudates is accompanied by a certain amount of organization and the formation of a variable quantity of fibrous tissue on the disc. This tissue obscures the lamina cribrosa and fills in the atrophic cup. It extends over the edges, which are thus ill-defined, and along the vessels as a thickening

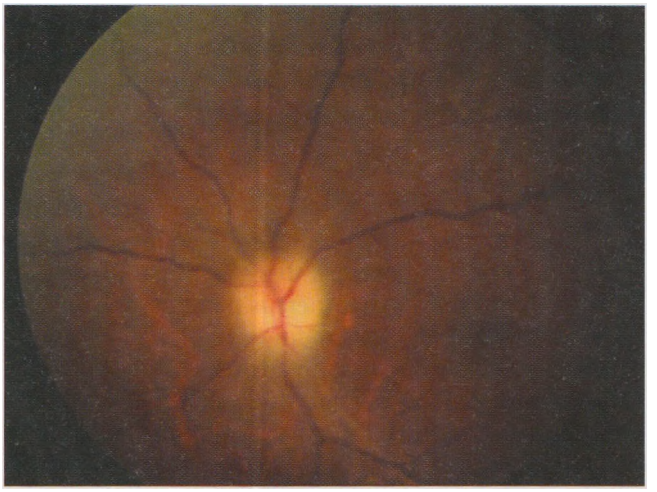


Fig. 22.5 Post-papilloedema optic atrophy.

of the perivascular sheaths. Further, it throttles the vessels, especially the arteries, so that they become markedly contracted. Meanwhile, owing to the widespread exudative deposits, the surrounding retina often shows permanent changes, chiefly manifested by pigmentary disturbances, which are most common at the macula. The amount of reactionary organization or gliosis varies greatly from case to case and, over time. The tissue laid down is gradually absorbed to some extent. When such changes are marked they suggest the previous occurrence of papilloedema, but their absence cannot justify the conclusion that there has been no papilloedema. Following considerable papilloedema the disc rarely regains its normal appearance, but after timely relief of the raised intracranial pressure, the changes may disappear leaving an apparently normal disc.

Papilloedema is usually bilateral, although not necessarily equal on the two sides. The relative amount of swelling may be of localizing significance in these cases but its value has been overestimated. In frontal tumours and middle ear disease, however, the swelling is usually greater on the side of the lesion. The time of onset is a more important indication than the amount of swelling, the localizing value being attached to the side first affected. Thus, the swelling may be actually less on the side first affected owing to subsidence associated with commencing atrophy. Unilateral papilloedema, with or without optic atrophy on the other side, suggests a tumour of the opposite olfactory groove or orbital surface of the frontal lobe or of the pituitary body (the *Foster- Kennedy syndrome).*

The diagnosis is easy in severe cases, but may be very difficult in mild cases as the colour of the disc is not a definite guide unless there is an undoubted difference between the two eyes, which is rare, as the condition is usually bilateral. *Fluorescein angiography,* however,

demonstrates dilatation of the surface capillaries and leakage of the dye, which accumulates 5-10 minutes after intravenous injection as a vertically oval pool surrounding the nerve head.

Differential diagnosis

If the edges of the disc appear clearly defined with any lens in the ophthalmoscope, there is no papilloedema, but it does not follow that there is papilloedema if they appear blurred. Astigmatism, for example, causes apparent blurring of the disc margin. Moreover, papilloedema maybe simulated in three conditions: (i) pseudoneuritis or pseudo disc swelling due to drusen of the nerve head; (ii) hypermetropia and (iii) a true optic neuritis involving the optic nerve head (papillitis). It may be necessary to keep the patient under careful observation for a period of time before a diagnosis can be made with certainty, while due attention should be paid to other signs and symptoms in the central nervous system.

Papilloedema must be distinguished from other causes of a swollen disc without raised intracranial pressure. The distinguishing features of some of these conditions is given below:

- *Ischaemic optic neuropathy:* This usually produces profound, sudden visual loss and could be (i) arteritic, associated with giant cell arteritis, or (ii) non-arteritic, associated with vasculopathy related to generalized atherosclerotic disease and diabetes mellitus. The swollen disc has a characteristically pallid appearance in both conditions and, in some patients, can be localized to one sector of the disc with a hyperaemia of the remaining portions. Giant cell or temporal arteritis is a self-limiting disease affecting people over the age of 55 years, particularly women. The coronary or the renal arteries may be involved.

  Non-arteritic ischaemic optic atrophy is seen in elderly vasculopathic individuals due to involvement of the short posterior ciliary branches of the ophthalmic artery leading, at first, to swelling of the optic nerve head and later to atrophy and sometimes cupping.
- *Drusen of the optic disc* occurs in families, is typically bilateral (70%), and inherited as an irregular dominant trait. The drusen bodies evolve slowly over many years showing increasing prominence with age. The appearance of the disc may mimic that of papilloedema associated with visual defects, which may not correspond to the position of the drusen. Drusen are often associated with rather small optic nerve heads, and are composed of calcified concentrically laminated globular aggregates. They may form as a result of altered axoplasmic transport at the optic disc secondary to local obstructing factors. Optic disc drusen may be associated with angioid streaks, subretinal neovascular membranes, vitreous haemorrhage and retinitis pigmentosa. Angiographically, the vessels of the optic nerve head are normal in pseudoneuritis and drusen.
- *Pseudoneuritis orpseudopapilloedema or pseudo disc oedema* is a condition occurring usually in hypermetropic eyes when the lamina cribrosa is small and the crowded nerve fibres are heaped up as they enter the nerve head from the surrounding retina. The ophthalmoscopic appearance of swelling and blurred margins is largely due to ophthalmoscopic reflexes. The swelling is never more than 2 D, there is no venous engorgement, oedema or exudates and the blind spot is not enlarged. A fluorescein angiogram reveals no leakage.
- In optic neuritis due to inflammation (*papillitis*) (Fig. 22.6A), the appearance of the disc (Fig. 22.6B)

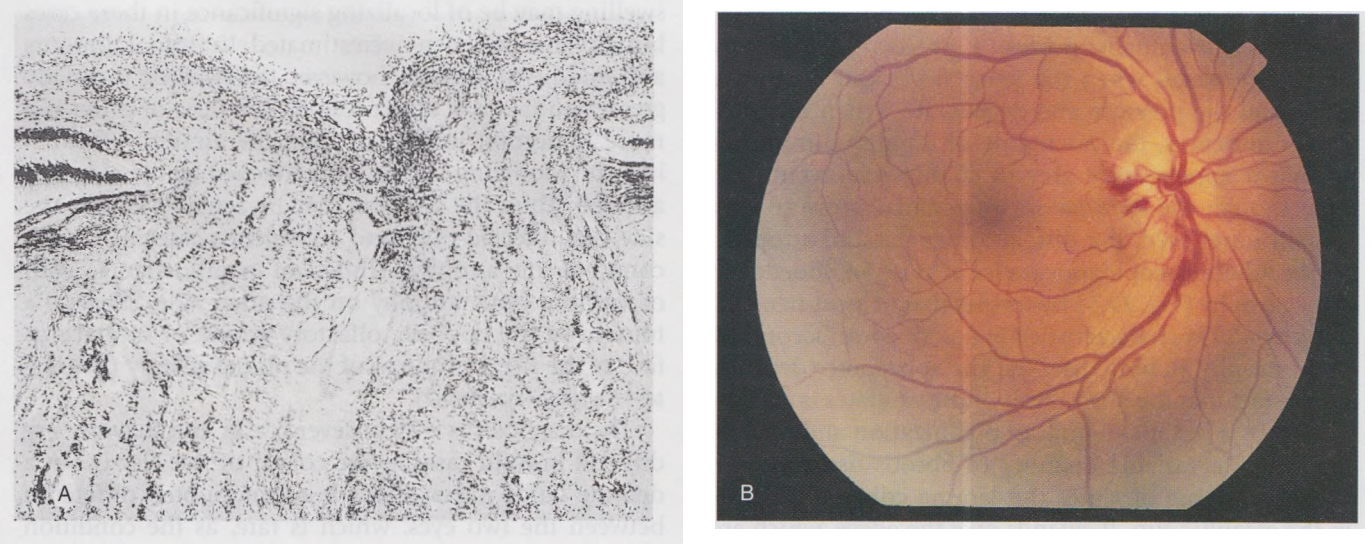


Fig. 22.6 (A) Papillitis in toxoplasmosis (By courtesy of Zimmerman). (B) Papillitis.

is often ophthalmoscopically indistinguishable from that in papilloedema. The swelling is usually moderate (2-3 D), shelving off gradually into the surrounding retina. Vitreous opacities are usual although they may be very fine. The visual symptoms are usually marked in papillitis. The acute depression of central vision, presence of a definite afferent pupillary defect or a relative afferent pupillary defect and the absence of signs of an intracranial space-occupying lesion form the most important differentiating features.

- Orbital *lesions and disc oedema:* Rarely, conditions causing stasis in the orbit may produce disc oedema—tumours of the optic nerve, a meningioma near the apex of the orbit, venous thrombosis, cellulitis or pseudotumour of the orbit, severe dysthyroid ophthalmopathy, or haemorrhage into the optic nerve sheath.

Other causes of disc oedema

See p. 343 (Table 22.2).

Treatment

For papilloedema, this is essentially the relief of the causal pressure; if this cannot be relieved, the prognosis is bad and blindness the normal outcome. If, however, timely decompression or removal of the tumour is successfully performed, the effect is remarkable. Along with relief of the general symptoms of raised intracranial pressure (headache, vomiting, stupor, etc.), vision improves rapidly (unless the nerves have been irretrievably damaged) and papilloedema subsides. The recovery of vision may be faster than the subsidence of the papilloedema. On the other hand, vision may deteriorate after operation, probably because of progressive sclerosis at the disc, especially if surgical intervention has been delayed. If signs of subsidence and commencing atrophy are present, further diminution of vision is to be anticipated. Subsidence of the papilloedema is usually rapid after operation and a marked change may be seen in a week to a fortnight, but this varies considerably from case to case.

In all cases, the visual fields should be carefully watched and decompression urged from the ophthalmological point of view before peripheral constriction becomes evident. This indicates that the optic nerve fibres have reached the stage when they are unable to withstand the effects of compression any further. Once atrophy becomes clinically visible at the disc, further visual deterioration will probably follow despite successful surgical relief. Surgical options for pseudotumour cerebri include a lumbar-peritoneal shunt by a neurosurgeon, or local decompression by making multiple slits or cutting a window in the optic nerve sheaths (dura and arachnoid) in the orbit, performed by an ophthalmologist or an otorhinolaryngologist.

DISTURBANCES OF THE CIRCULATION

Anterior ischaemic optic neuropathy

Aetiopathogenesis

Ischaemic optic neuropathy, producing an altitudinal field defect, has been recognized for many years as a complication of severe anaemia or after a massive haemorrhage. Patients suffering from a neglected acute attack of angle-closure glaucoma are also likely to develop ischaemic neuropathy with subsequent optic atrophy.

The condition, however, may arise spontaneously and the clinical entity comprises sudden loss of vision, initially associated with swelling of the optic disc (Fig. 22.7) which resolves to optic atrophy within a month or two leaving a permanent visual defect. It is due to interference with the blood supply of the posterior ciliary artery to the anterior part of the optic nerve, producing a post-laminar infarct, without necessarily involving the central retinal artery.

The underlying aetiology leading to anterior ischaemic optic neuropathy (AION) can be either inflammatory or non-inflammatory. Based on this, ischaemic optic neuropathy is broadly classified into two categories: (i) arteritic and (ii) non-arteritic. Table 22.3 summarizes the major differences between the two. In giant cell arteritis there is granulomatous inflammation of the small- and medium-sized arteries with infiltration of the full thickness of the vessel wall by lymphocytes, plasma cells and macrophages. Multinucleated giant cells are often conspicuous.



Fig. 22,7 Arteritic anterior ischaemic optic neuropathy showing typical 'pale' disc oedema with splinter haemorrhage.

Table 22.3 Clinical features distinguishing arteritic from non-arteritic anterior ischaemic optic neuropathy (AION)

	Features common to both	Arteritic AION	Non-arteritic AION
Sex ratio		Female > male	Female = male
Age	>40 years	Usually > 60 years (mean 70 years)	Usually 40–60 years (mean 60 years)
Vision loss	• Sudden	Usually severe	Usually moderate
	• Reduced colour vision	Up to 76%	Up to 61% >6/60 (20/200); non-progressive
	• Altitudinal or central field defect	<6/60 (20/200); occasionally progressive	
Ocular pain	Usually painless	May be present	Rare
Prior episodes of amaurosis	Uncommon	Occasional	Rare
Laterality	Initially unilateral but may become bilateral	Fellow eye affected in up to 95% within days to weeks	Fellow eye affected in <30% within months to years
Optic disc	Oedema and pallor of the disc; may be sectoral, flame-shaped haemorrhages	Pale >hyperemic oedema Cup normal	Hyperaemic >pale oedema Cup small
Other symptoms and signs		• Headache • Scalp tenderness; palpable, tender, non-pulsatile temporal artery • Proximal muscle and joint, aches 'polymyalgia rheumatica' • Anorexia, weight loss, fever • Jaw claudication • Cranial nerve palsies	• Associated hypertension in 40% of patients • Diabetes in up to 24% • Shock (acute systemic hypotension) • Nocturnal hypotension
Investigations			
ESR*		Usually >40 mm in first hour	Mean 20–40 mm in first hour
Temporal artery biopsy†		Giant cell granulomatous vasculitis involving all coats of the vessel wall	Not indicated if features do not suggest arteritis
Fluorescein angiogram		Disc and choroidal filling delay	Disc filling delay
Natural history		Improvement rare, fellow eye involvement in up to 95%	Improvement in up to 43%, fellow eye affected in <30%
Treatment		Corticosteroids	Not proved to be effective Levodopa–carbidopa combination for 3 weeks and then double dose for 1 month reported to be beneficial
Differential diagnosis	Idiopathic optic neuritis. Other types of optic nerve inflammation, e.g. syphilis, sarcoidosis, infiltrative optic neuropathy, compressive optic neuropathy, idiopathic disc oedema including diabetic papillopathy and optic disc vasculitis		

*'Occult' giant cell arteritis may be associated with a normal ESR.
◆Temporal artery biopsy may show a false-negative result due to 'skip areas' along the artery.

Clinical features

The typical features of giant cell arteritis are constant headaches, which may be unilateral or bilateral, in the temporal area with prominent vessels which are tender. Pulsation in the temporal artery, which is often palpably thickened, may be present or absent. There may be intermittent claudication of the jaw. The syndrome is self-limiting but may lead to blindness due to vascular occlusion, often heralded by intermittent attacks of loss of vision in one eye or an extraocular muscle palsy.

Non-arteritic cases may have no overt symptoms of systemic vasculopathy or may be known to have diabetes, hypertension or atherosclerotic disease. Ocular symptoms include sudden profound vision loss which is usually unilateral at presentation in both types. On examination

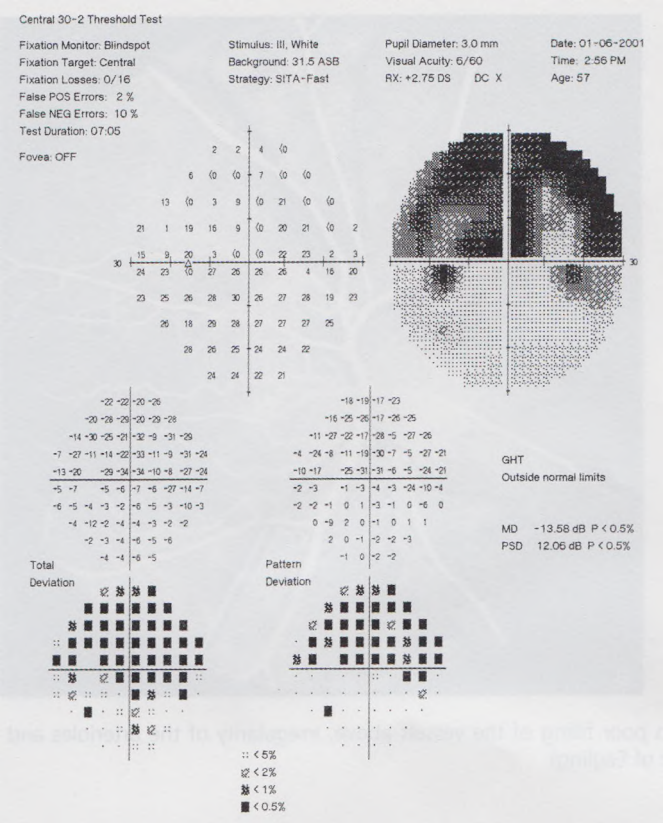


Fig. 22.8 Superior altitudinal field defect in the left eye of a patient with AION. The left fundus photograph of the same patient is shown in Fig. 22.9B. Generally an inferior attitudinal field defect is seen as the superior half of the disc is more often affected.

there may be decreased vision, an altitudinal field defect (Fig. 22.8), a relative afferent pupillary defect and disc oedema (Fig. 22.9).

Many patients with AION due to temporal arteritis show pallid swelling of the optic disc, often without haemorrhages, while others show pink oedema of the optic disc with flame-shaped haemorrhages. The latter is the common clinical picture in the absence of arteritis. The nature of the ophthalmoscopically visible pre-laminar swelling has been variably interpreted as an infarct of the disc or due to an accumulation of opaque axoplasmic debris in the optic nerve head.

Fluorescein angiography is helpful in demonstrating hypoperfusion of a sector of the underlying choroid and poor filling of a portion of the optic disc (Fig. 22.10).

The majority of optic discs with AION due to temporal arteritis develop cupping subsequently. If a cilioretinal or central retinal artery is compromised, there may be an associated infarction of a sector or of the entire retina, respectively.

Management

The triggering factor for an attack of acute ischaemic optic neuropathy, even in the presence of arteriosclerosis or other recognizable cardiovascular anomaly, is rarely identified. Management, therefore, presents complicated problems because ischaemic optic neuropathy is not a diagnosis but merely a recognition of local anoxia of the anterior region of the optic nerve and the causes are both multiple and complex.

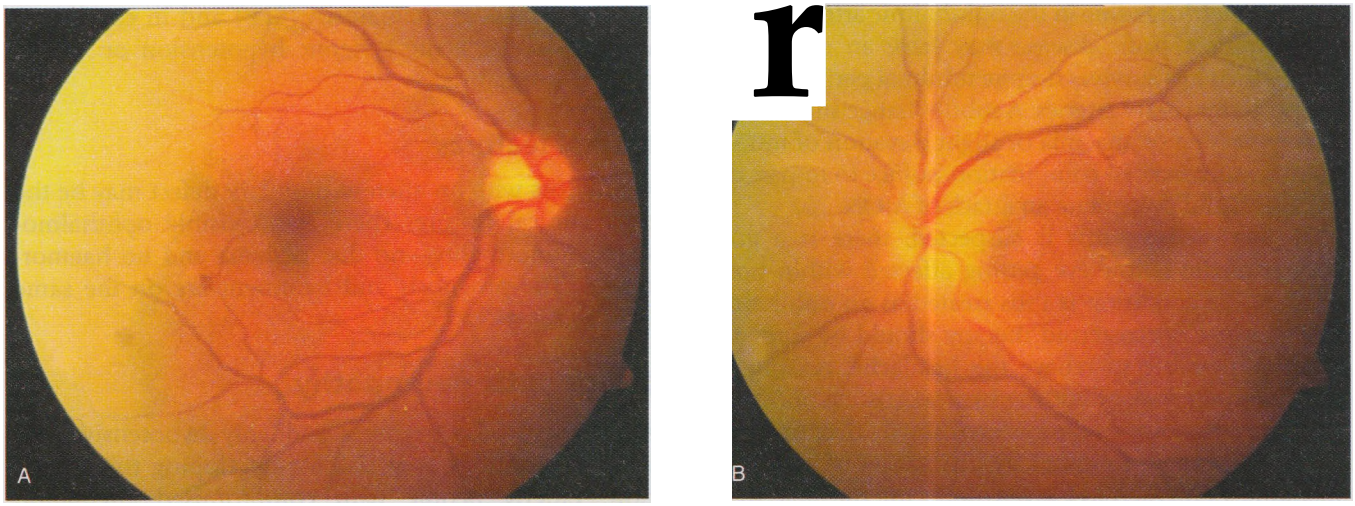


Fig. 22.9 Fundus photograph of both eyes of a 64-year-old woman with non-arteritic anterior ischaemic optic neuropathy. (A) Right eye: background diabetic retinopathy; (B) left eye: AION showing segmental pale disc oedema interiorly. Note hyperaemia of the other portions.

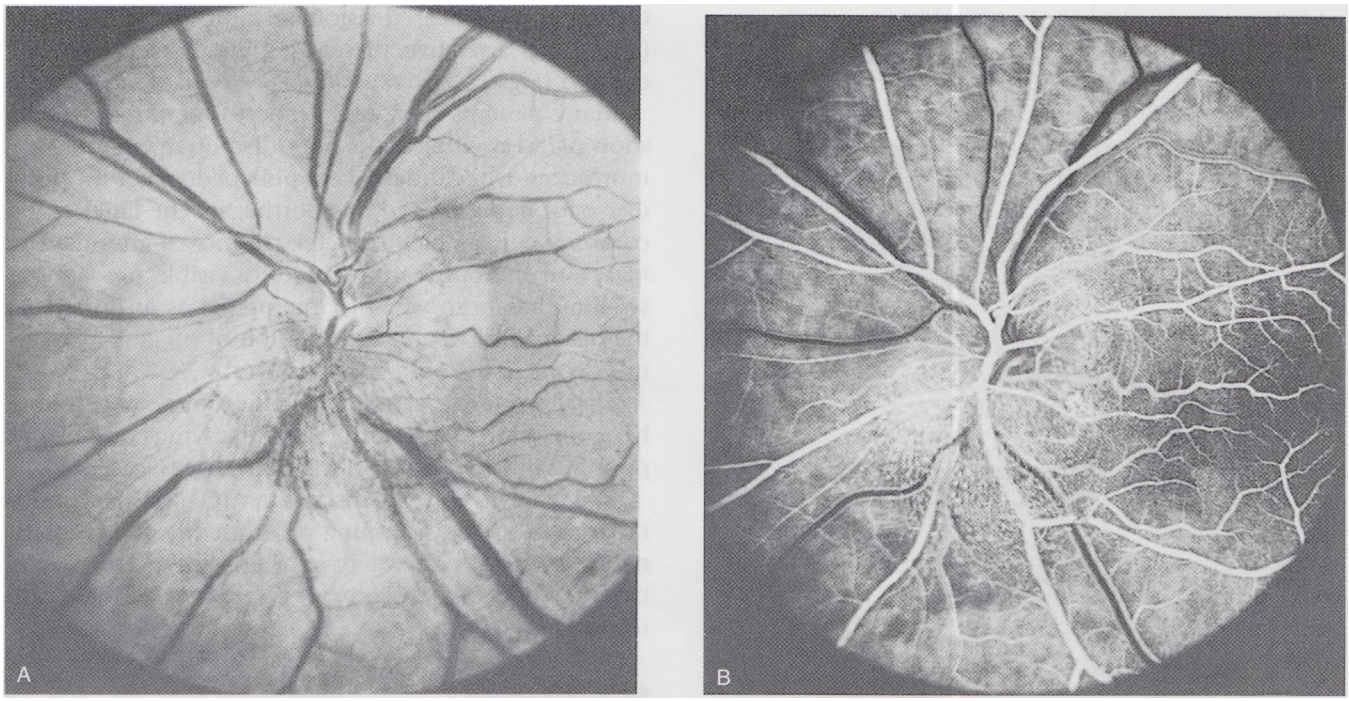


Fig. 22.10 (A) Anterior ischaemic optic neuropathy: swollen disc with poor filling of the vessels above, irregularity of the arterioles and dilated capillaries below; (B) fluorescein angiogram of (A). (By courtesy of Eagling)

Investigations should include assessment of the circulatory and microcirculatory systems, specific examination to exclude any form of arteritis [erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels], and further sophisticated immunological and haematological tests as and when indicated. In the presence of temporal arteritis, large doses of systemic steroids are mandatory and are gradually tapered off to a maintenance dose. The eye itself should be carefully assessed for raised intraocular pressure and for a low ophthalmodynamometric reading in the ophthalmic artery. Patients with arteriosclerotic disease may have an optic nerve head which just survives despite minimal perfusion from the posterior ciliary arteries. A subtle change such as mild polycythaemia or anaemia or slight elevation of intraocular pressure may, in combination, suffice to impair disc perfusion and precipitate an attack of AION.

If giant cell arteritis is suspected, there is a grave danger of the fellow eye getting affected within hours or days; the condition is thus treated as an ophthalmic emergency. Corticosteroid therapy should be started as soon as possible to relieve the headache. An intravenous loading dose of 200 mg hydrocortisone or 500 mg methylprednisolone administered slowly over one hour is recommended, followed by high doses of oral prednisolone (lmg/kg/day) given daily for the first week. The dose can be reduced as the ESR falls. A maintenance dose of 5-15 mg is continued for at least 6-12 months.

There is no specific treatment for non-arteritic AION.

Posterior ischaemic optic neuropathy

Aetiopathogenesis

This entity shares the features of AION except for the site of involvement. Posterior optic nerve ischaemia is believed to occur due to disorders affecting the small pial vessels which supply the intraorbital portion of the optic nerve away from the eyeball.

It has been reported to occur in various clinical disorders with vasculitis, including giant cell arteritis and systemic lupus erythematosus (SLE) and in conditions which produce acute systemic hypotension or 'shock' optic neuropathy.

Clinical features

Vision loss with an afferent pupillary defect may be the only clinical feature. There is no visible ophthalmoscopic abnormality—no disc oedema and no haemorrhages. The prognosis and treatment are on the same lines as AION.

Shock optic neuropathy

Any patient who becomes suddenly hypotensive due to systemic shock is at risk for developing this condition. Elderly people with compromised circulation may be more prone. It presents as blurred vision and a field defect and is usually noticed when the patient is recovering from the systemic illness. The disc may

appear oedematous, disc haemorrhage may also be seen and clinically it resembles ischaemic optic neuropathy. Visual field defects are generally nerve fibre bundle pattern defects or altitudinal loss. The visual loss is generally permanent. In later stages disc pallor or even cupping may occur, mimicking glaucoma.

INFLAMMATION OF THE OPTIC NERVE (OPTIC NEURITIS)

An inflammation of the optic nerve is known as optic neuritis. The optic nerve may be affected by inflammation in any part of its course, but for clinical convenience it is usual to divide inflammatory conditions into two categories:

- those affecting the part of the nerve ophthalmoscopically visible at the disc and therefore showing obvious signs of disease;
  - (i) papillitis or
  - (ii) neuroretinitis; and
- those which attack the nerve proximal to this region and therefore show no ophthalmoscopic changes, so that the diagnosis has to be made on the basis of symptoms alone;
  - (iii) retrobulbar neuritis.

Aetiopathogenesis

The aetiology of optic neuritis (Table 22.4) is composite and it is usually impossible to deduce the cause of the disease from local signs and symptoms. A systemic examination must be carried out and even then a definite aetiological diagnosis is frequently impossible. The disease can be idiopathic or associated with other local or systemic diseases. In most cases, whatever be the underlying aetiology, the pathogenesis of optic neuritis is presumed to be demyelination in varying degrees, which could be axial or peripheral. Histopathologically, in multiple sclerosis demyelinative plaques in the optic nerve show changes similar to those seen in the brain, with the inflammatory response marked by perivascular cuffing, T lymphocytes and plasma cells.

The commonest associated cause is a *demyelinating disorder* of the nerve as occurs in other tracts of the white matter of the central nervous system (*multiple sclerosis).* The occurrence of retrobulbar neuritis should always arouse suspicion of the presence of multiple sclerosis, of which it is frequently one of the first symptoms. In these cases, recurrences appear in either eye from time to time, occasionally at considerable intervals, but it may be many years before more widespread signs of the disease occur in the central nervous system.

Other diseases of the central nervous system in which optic neuritis occurs are neuromyelitis optica (of Devic),

Table **22.4** Aetiology of optic neuritis

Idiopathic

Demyelinating disorders
- Isolated
- Associated with multiple sclerosis
- Neuromyelitis optica

Associated with infections

Local
- Endophthalmitis
- Orbital cellulitis
- Sinusitis
- Contiguous spread from meninges, brain, base of skull

Systemic
- Viral*—Influenza, measles, mumps, chicken pox, herpes zoster, infectious mononucleosis, cytomegalovirus
- Bacterial—Tuberculosis, syphilis (perineuritis), cat-scratch disease (*Bartonella, Rochalimaea henselae* and *R. quintana),* Lyme disease (borreliosis)
- Fungal—Cryptococcosis, histoplasmosis (*Histoplasma capsu latum)*
- Protozoal—Toxocariasis (*Toxocara canis),* toxoplasmosis *(Toxoplasma gondii),* malaria (*Plasmodium*), pneumonia *(,Pneumocystis carinii)*
- Parasitic—Cysticercosis (*Cysticercus ceilulosae)*

Immune-mediated disorders

Local
- Uveitis
- Sympathetic ophthalmitis

Systemic
- Sarcoidosis
- Wegener granulomatosis
- Acute disseminated encephalomyelitis[1]

Metabolic disorders
- Diabetes
- Anaemia

*In children it is not unusual for bilateral neuritis with disc swelling to follow viral illnesses, e.g. measles, mumps and chicken pox. Most of these are parainfectious as opposed to direct tissue infiltration by microbiological agents.
■^Follows viral infections of childhood and may also rarely develop subsequent to vaccination for polio, measles, mumps, rubella, hepatitis, diphtheria-pertussis-tetanus and influenza.

acute disseminated encephalomyelitis, zoster, epidemic encephalitis and poliomyelitis. The more important of these are discussed in Chapter 31 but one condition in which the optic nerve is primarily affected without other obvious central nervous involvement is Leber disease.

The *local causes* of optic neuritis are intraocular inflammations and a contiguous spread of inflammation from the meninges, sinuses or orbit. Uveitis or retinitis may spread to the disc; among the former, sympathetic ophthalmitis is prominent. Meningitis may affect the nerve, primarily causing a perineuritis, as may be seen in both syphilis and tuberculosis. Sinusitis, particularly of the sphenoid and ethmoid, and orbital cellulitis may act similarly. Parasitic infestation by cysticercosis in the orbit or within the optic nerve is another cause.

Endogenous infections may also produce an optic neuritis; these include acute infective diseases such as

influenza, malaria, measles, mumps, chicken pox and infectious mononucleosis. Systemic granulomatous inflammations such as tuberculosis, syphilis, sarcoidosis, toxoplasmosis and fungal infections such as cryptococcosis have also been known to cause optic neuritis.

Autoimmune vasculitid.es such as SLE, polyarteritis nodosa and others may be associated with optic neuritis. The pathogenesis is related to ischaemia, which may produce demyelination alone, axonal necrosis, or a combination of the two. The clinical profile includes acute optic neuritis (both papillitis and retrobulbar neuritis), acute ischaemic optic neuropathy and chronic progressive visual loss.

Metabolic disorders (diabetes, anaemia, pregnancy, avitaminosis, starvation) may produce a similar clinical picture. The effect of exogenous toxins is discussed under the heading of toxic optic neuropathy. The importance of a careful history and thorough systemic and ophthalmic examination cannot be overemphasized in evaluating a patient with optic neuritis. This will help in arriving at a clinical diagnosis and avoid unnecessary, elaborate and expensive investigations in most cases.

Clinical course: In the majority of cases, especially those with demyelinating disease, vision starts to improve in the second or third week and by the fourth to fifth week visual acuity returns to normal or near normal (6/18 to 6/12; 20/60 to 20/40). Subsequently, vision slowly and steadily improves over several months and is ultimately usually restored to 6/6(20/20). Colour vision, contrast sensitivity and visual fields take longer to recover (6-12 months orso) and may never return completely to normal. However, in a small percentage of cases, vision does not improve to functional levels and, rarely, does not improve at all, suggesting an atypical neuritis. Clinical features suggestive of atypical optic neuritis such as a patient out of the typical age range, no pain on eye movements, poor vision persisting beyond 2 weeks from onset, or progressive diminution of vision beyond the first week are indications for specific further investigations.

Clinical features

Optic neuritis due to local or systemic infections or other disorders will have similar visual symptoms but will differ in their clinical course and have other associated symptoms and signs in accordance with the underlying disease. Unless specified otherwise, the term optic neuritis implies an idiopathic or demyelinative syndrome associated with multiple sclerosis. The clinical features of 'typical' optic neuritis are described below.

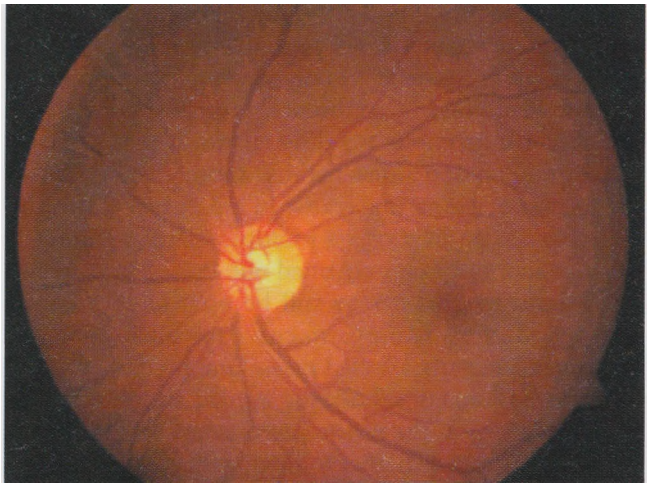
The predominant symptom in a patient suffering from optic neuritis is loss of vision which typically deteriorates over hours to days and reaches a trough about 1 week after the onset. In retrobulbar inflammations, this rapid deterioration of vision in the presence of a normal fundus may suggest hysteria. In these cases the diagnosis depends on the presence of local tenderness, the pupillary reactions and abnormalities in the visual fields. Often, the vision gradually improves spontaneously but sometimes remains static for a while before improving.

The visual loss can be subtle or profound (there may even be complete blindness in a few patients); it is usually unilateral but may be bilateral, typically affecting those between 18 and 45 years of age. It is accompanied by deep orbital, retroocular or brow pain usually aggravated by eye movement and is increased by pressure upon the globe. Neuralgia and headache may be present. The tenderness of the eyeball on digital pressure is limited to a small area corresponding roughly with the site of attachment of the superior rectus tendon. This is present only in the early stages of the disease and disappears in a few days.

The visual impairment is accompanied by disturbance of other visual functions such as loss of colour vision (typically red desaturation) and reduced perception of light intensity. There may be other associated symptoms such as a history of an antecedent influenza-like viral illness or focal neurological symptoms such as weakness, numbness and tingling in the extremities. Occasionally, patients may observe an altered perception of moving objects (Pulfrich phenomenon) or a worsening of symptoms with exercise or an increase in body temperature (Uhthoff sign).

Clinical signs include a variable degree of decreased visual acuity, decreased colour vision, abnormal contrast sensitivity, decreased stereoacuity, and visual field defects which could be central, centrocaecal, arcuate, sectorial, altitudinal focal pattern defects or a generalized non-specific depression in retinal sensitivity. Perimetry shows visual function depression over the entire field but is more marked in the central 20 ° with varied patterns of field defects. At first glance, in some patients the pupillary reactions may be apparently normal, both directly and consensually, to light as well as to convergence. More detailed inspection, however, will show that although the pupil of the affected eye reacts to light, the contraction is not maintained under bright illumination so that instead of remaining contracted the pupil slowly dilates while the light is still focused on the eye. Lack of sustained constriction of the pupil to light, if it can be proved beyond dispute, is of great diagnostic significance. Presence of a relative afferent pupillary defect or Marcus Gunn pupil is of greater diagnostic significance, indicating a defect in the afferent limb of the pupillary light reflex due to a pathological lesion in the optic nerve.

The field defects may be relative or absolute for colours. There is usually some peripheral loss of the visual field and there may even be complete blindness. Prolonged latency is seen on testing the visual evoked potentials (VEP).



Fig, 22.11 Normal appearance of the fundus in a 27-year-old girl with acute retrobulbar neuritis and 6/24 vision.

Ophthalmoscopically, the disc could be normal in retrobulbar neuritis (Fig. 22.11), which is more common in adults. It may be hyperaemic and swollen with or without peripapillary flame-shaped haemorrhages in papillitis (Fig. 22.6B), which is most commonly seen in children and young adults. It may be inflamed with involvement of the neighbouring retina showing a stellate pattern of retinal exudates in neuroretinitis (Fig. 22.12), which is commonly due to an infectious aetiology, secondary or atypical optic neuritis or in children and is not seen in multiple sclerosis.

Papillitis may be ophthalmoscopically indistinguishable from early papilloedema (*see* pp. 344-347). The disc is at first hyperaemic; later the margins become blurred, swelling and oedema ensue which spread onto the retina, the retinal veins become tortuous and extensively distorted, exudates may accumulate upon the disc and there are fine vitreous opacities. Even in the most severe cases, however, the swelling of the disc rarely exceeds 2-3 D. Clinically, the visual loss is profound with a disturbance of colour vision, decrease in contrast sensitivity, diminished stereoacuity and abnormal visual fields unlike papilloedema, where central vision is relatively unaffected. Pupillary reactions demonstrate a prominent relative afferent pupillary defect.

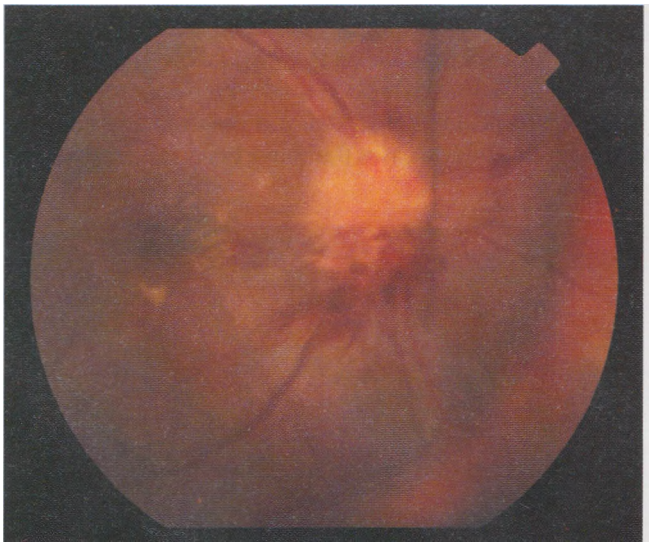


Fig. 22.12 Fundus photograph of neuroretinitis showing a hyperaemic disc (papillitis) with inflammation in the surrounding retina (retinitis). This later proved to be syphilitic.

If the inflammation is mild, the optic disc may appear normal once the inflammation subsides, but if it has been sufficiently serious to destroy the nerve fibres, the picture of *post-neuritic atrophy* results. Here again, the ophthalmoscopic picture is indistinguishable from that following papilloedema—the disc margins are blurred, the floor has a dirty grey colour and is filled in with organized tissue which extends onto the constricted arteries as perivascular sheaths.

Neuroretinitis is simply papillitis with retinal exudates which are in the retinal nerve fibre layer and usually radially oriented forming a macular fan or star.

Acute *retrobulbar neuritis* produces no ophthalmoscopically visible changes, unless the lesion is near the lamina cribrosa when some signs of papillitis may be seen with distension of the veins and attenuation of the arteries. If atrophic changes follow, the degeneration extends not only towards the brain but also towards the eye. In milder cases, pallor of the disc may be limited to the temporal side.

Differential diagnosis

The differential diagnosis includes ischaemic optic neuropathy, which affects the elderly, as opposed to optic neuritis, which affects a younger age group. One should hesitate to make a diagnosis of optic neuritis in patients above 50 years of age and look for evidence of ischaemic optic neuritis or other disorders. Ophthalmoscopically, AION mimics papillitis while posterior ischaemic optic neuritis resembles retrobulbar neuritis. Papilloedema, grade IV hypertensive retinopathy, Leber hereditary optic neuropathy, toxic and metabolic optic neuropathy and a compressive space-occupying lesion in the orbit or intracranially in the chiasmal region are other conditions which can be mistaken for optic neuritis.

The clinical work-up of a case presenting with the constellation of symptoms outlined above includes careful history-taking: noting the age of the patient, the rapidity of onset, occurrence of any previous episodes and the presence of pain on eye movements; complete ophthalmic examination including recording the visual acuity, colour vision, assessing pupillary reactions, retinal examination with dilatation of the pupil to assess

the optic nerve and evaluate the vitreous for cells. The visual fields should be tested and VEPs recorded for both eyes, as asymptomatic fellow eye abnormalities are common and can be detected with these techniques. Additional tests should be performed for 'atypical' optic neuritis. These include a complete blood count, estimation of rapid plasma reagin, CRP and ESR, fluorescent treponemal antibody absorption (FTA-ABS) test, and antinuclear antibody (ANA) test. For the first episode and in every atypical case, magnetic resonance imaging (MRI) of the brain and orbits with gadolinium enhancement is recommended. The scan helps in predicting the likelihood of multiple sclerosis and ruling out a space-occupying lesion masquerading as optic neuritis. Patients with demyelination of the central nervous system on MRI or an abnormal neurological examination should be referred to a neurologist for evaluation and management of possible multiple sclerosis.

Treatment

Treatment is guided by the degree of the patient's visual impairment, visual needs, presence of previous episodes, results of MRI and specific aetiology, if identified. The primary disease (e.g. syphilis or toxoplasmosis) needs appropriate treatment. Typical cases which are idiopathic or proven to be due to demyelination are known to recover spontaneously, slowly over time, with restoration of normal vision, including the visual field, though some residual deficit in contrast sensitivity may remain in some cases.

General guidelines for treatment are based on a major multicentre trial (the Optic Neuritis Treatment Trial [ONTT]).

1. If a patient with profound visual loss but no previous history of optic neuritis or multiple sclerosis is seen early and if MRI shows at least one area of demyelination, treatment with intravenous methylprednisolone is recommended in a dose of 250 mg intravenously slowly over 30-60 minutes repeated 6 hourly for 3 days, followed by oral prednisolone 1 mg/kg/day for 11 days. Prednisolone is rapidly tapered off over the next 3 days. This treatment hastens visual recovery and decreases the likelihood of recurrence, though the long-term visual outcome is no different from that achieved by observation alone, because spontaneous recovery occurs in the natural course in most cases. If the MRI is normal, a diagnosis of multiple sclerosis is unlikely but cannot be entirely ruled out. Pulsed intravenous steroid treatment may still be used to shorten the period of visual impairment, particularly in severe and bilater ally affected cases. Oral prednisolone, in conventional doses of 1 mg/kg/day, should never be used alone as the recurrence rate has been found to be significantly higher following this regime.
2. If a patient has already been diagnosed to have multiple sclerosis or has suffered from prior episodes of optic neuritis, observation is the rule, unless faster visual recovery is specifically required.

Parasitic infestations of the optic nerve

Cysticercus cellulosae within the optic nerve is rare. However, there is profound visual loss and the condition may mimic optic neuritis, papillitis, neuroretinitis or unilateral severe disc oedema (Fig. 22.13A). As the condition is often mistaken for an optic nerve tumour on neuroimaging, the diagnosis is often delayed or missed. The cyst has a highly reflective pinhead lesion within it representing the scolex which may be detected by ultrasonography or careful examination of CT or MRI scans performed with 1 mm sections (Fig. 22.13B).

Treatment includes the use of high doses of steroids to reduce inflammation as the toxins released by the dying parasite are believed to be responsible for the visual loss. Medical treatment with oral albendazole and surgical removal of the cyst have been tried with poor results. This, however, could be due to delayed presentation and late diagnosis in the few cases that have been reported so far.

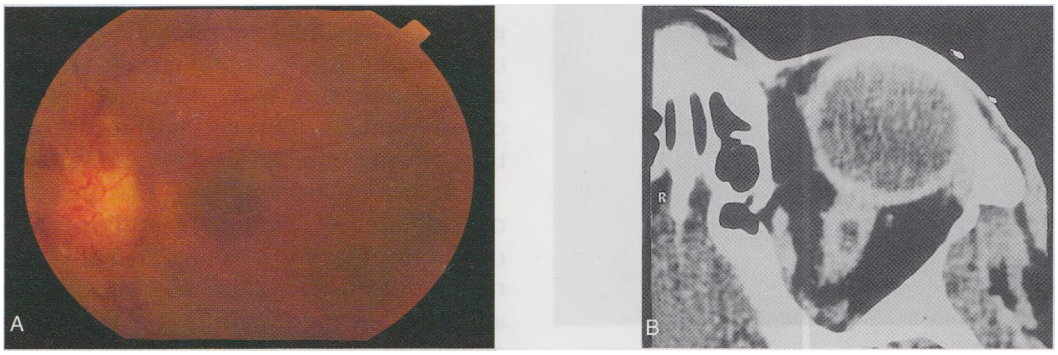


Fig. 22.13 (A) Fundus photograph showing severe disc oedema with inflammation; (B) CT scan of the same patient shows a cystic lesion within the optic nerve with an internal, hyperdense lesion suggestive of a scolex.

Sarcoid optic neuropathy

In patients with sarcoidosis, granulomatous infiltrations of the optic nerve can occur. Here, the appearance of the fundus may be typical with a white lumpy swelling of the optic nerve head and the loss of vision may vary from no loss to severe loss. Treatment with corticosteroids is usually effective. Optic nerve involvement could either be isolated or combined with ocular or central nervous system involvement.

OPTIC ATROPHY

This term is usually applied to the condition of the disc following degeneration of the optic nerve. It has been pointed out that injury to the nerve fibres in any part of their course from the retina to the lateral geniculate body leads to degeneration not only on the proximal (cerebral) side—as might be anticipated for afferent fibres—but also on the distal (ocular) side. Optic atrophy therefore follows extensive disease of the retina from destruction of the ganglion cells, as in pigmentary retinal dystrophy or occlusion of the central artery; these cases are sometimes called *consecutive optic atrophy.* The break in continuity of the fibres may be at the disc itself, such as results from the strangulation occurring in papillitis, neuroretinitis or papilloedema. These cases are characterized as secondary or *post-neuritic atrophy.* It also follows destruction of the nerve in the orbit, as in fracture of the base of the skull or severe retrobulbar neuritis. In addition, there are some conditions in which optic atrophy occurs without local disturbances but associated with general disease usually of the central nervous system, toxic neuropathy or without any discoverable cause. Such cases have a similar clinical appearance of a chalky white optic nerve head with well-defined margins and are described as *primary atrophy.* The fourth type of atrophy is accompanied by enlargement and excavation of the optic disc cup, i.e. *glaucomatous atrophy,* which has already been discussed.

Aetiology

When the atrophy is due to disease or poisoning of the second visual neurone proximal to the disc, so that there are no ophthalmoscopic evidences of previous local inflammation, it is called *primary atrophy.*

The most common cause is multiple sclerosis, in which recurrent attacks of transient demyelination cause an increasing degree of atrophy, but in this disease it is rarely complete (Fig. 22.14). Other causes are the various diseases already mentioned in the aetiology of optic neuritis (*see* p. 351), Leber disease, compressive space-occupying lesions in the orbit or cranium that compress the optic nerve or chiasma and the many exogenous poisons which give rise to toxic neuropathy.

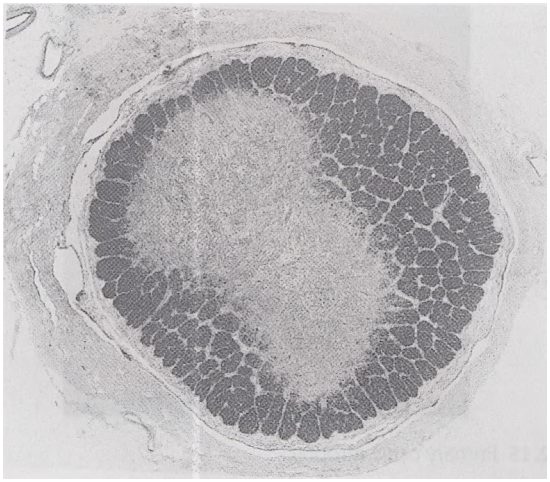


Fig. 22.14 Optic atrophy showing demyelination of the fibres from the papillomacular bundle.

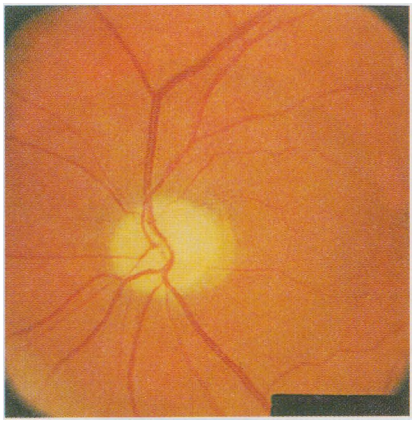
The classical cause of primary atrophy used to be tabes. In this condition, degeneration was due to a chronic inflammation of the pia which caused a secondary degeneration of the nerve fibres commencing in the optic nerve near the chiasma. Tabetic optic atrophy is slowly progressive and the prognosis is bad, but with the availability of effective antisyphilitic treatment, the disease has now become relatively rare. The same applies to the atrophy of general paralysis.

Clinical features

The essential ophthalmoscopic features of optic atrophy in general are an alteration in the colour of the disc and changes in the blood vessels. The disc is always pale, but may show a variety of tints, especially associated with different types of atrophy. The pallor affects the whole disc and must be carefully distinguished from the white centre, often encroaching upon the temporal side, due to physiological cupping. The pallor is not due to atrophy of the nerve fibres, but to loss of vascularity, secondary to obliteration of the vessels; it is thus an uncertain guide to visual capacity.

In primary atrophy the disc is grey or white, sometimes with a greenish or bluish tint (Fig. 22.15). Stippling of the lamina cribrosa is seen; the edges are sharply defined and the surrounding retina looks normal. Owing to the degeneration of the nerve fibres there is slight cupping (atrophic cupping) which must be carefully distinguished from glaucomatous cupping. Cupping in optic atrophy is shallow and saucer-shaped, as shown by the slight bending of the vessels, but is scarcely measurable with the ophthalmoscope. There is no retraction of the lamina cribrosa and the vessels are only slightly contracted.

Secondary atrophy, also called post-neuritic atrophy, has a slightly different ophthalmoscopic picture as



Fig, 22.15 Primary optic atrophy.

compared to the primary variety, and follows an injury or direct pressure affecting the visual nerve fibres in any part of their course from the lamina cribrosa to the geniculate body. A brain tumour will produce primary atrophy if it presses upon the chiasma or optic nerve, and a secondary optic atrophy (Fig. 22.16) if it causes papilloedema due to increased intracranial pressure. The differentiation does not indicate the nature or site of the pressure; it merely differentiates whether the atrophy has affected a normal disc or one which has been choked. The characteristic ophthalmoscopic picture of *post-neuritic atrophy* has already been described.

In the *consecutive atrophy* of retinal and choroidal disease, the disc has a yellowish waxy appearance, the edges are less sharply defined, and the vessels are very markedly contracted, sometimes almost to the point of disappearance.

In total optic atrophy the pupils are dilated and do not respond to light, and the patient is blind; when unilateral, the consensual reaction to light is exaggerated. In partial optic atrophy, central vision is depressed and there is concentric contraction of the field, with or without scotomata, relative or absolute, depending upon the cause. It is important to note that no deduction as to the amount of vision can be made from the ophthalmoscopic appearances, for the presence of all the signs of atrophy is not inconsistent with a certain, sometimes a considerable, amount of vision.

No *treatment* is effective for optic atrophy; the prognosis depends on the possibility of early control of the causal factor.

COMPRESSIVE NEUROPATHY AND TUMOURS OF THE OPTIC NERVE

Aetiopathogenesis

Direct pressure on the optic nerve or chiasma by orbital masses, pituitary tumours, craniopharyngiomas, meningiomas and optic nerve tumours (gliomas or meningiomas) are likely to cause optic atrophy. Aneurysms arising from the internal carotid artery or the ophthalmic artery can also affect the optic nerve.

Clinical features

Slowly progressive unilateral visual loss is the rule but occasionally the loss is acute or is noticed acutely. Bilateral involvement occurs if the posterior optic nerve or chiasma is affected. The critical signs include visual loss, field deficits and a relative afferent pupillary defect. The optic disc is usually pale but can be normal initially or swollen and oedematous. Other signs may include proptosis and opticociliary shunt vessels (Fig. 22.17). These are small vessels around the disc that shunt blood from

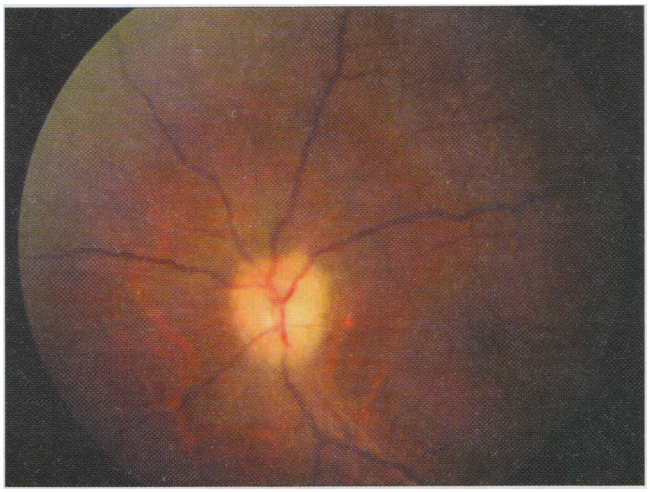


Fig. 22,16 Secondary optic atrophy.

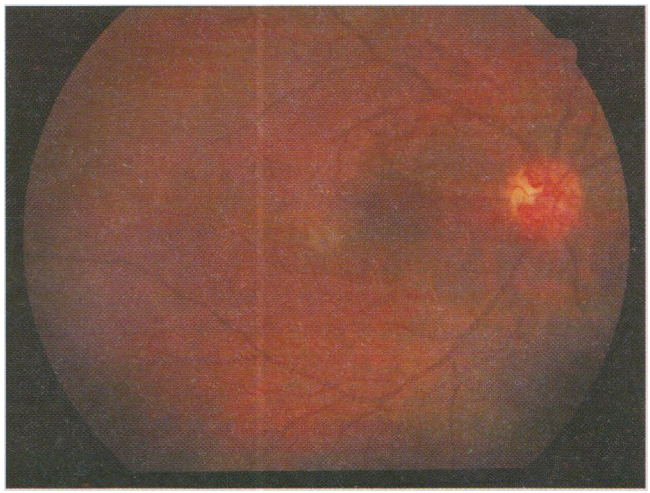


Fig. 22.17 Opticociliary shunt vessels in a patient with optic nerve sheath meningioma.

the retinal to the choroidal venous circulation. They are present normally but enlarge and become visible only when there is a compressive obstruction to venous drainage by a tumour compressing the optic nerve.

Tumours of the optic nerve

See Chapter 30.

TOXIC, NUTRITIONAL AND HEREDITARY OPTIC NEUROPATHY

Aetiopathogenesis

Many nutritional deficiencies, toxic and hereditary optic neuropathies produce a very similar clinical picture because there are common pathways by which these vitamins work and by which many of these toxins interact. Vitamin deficiencies associated with poor diet may be compounded by the ingestion of cassava and elevated levels of cyanide. Within the mitochondria, oxidative phosphorylation involves the process of electron transfer to oxygen at one end and the production of adenosine triphosphate (ATP) at the other end. Vitamins such as $B_{12}$and folic acid are crucial to this process. Agents such as cyanide or formate (a metabolic product of methanol) block this electron transport. The net result of these deficiencies and toxins is the decreased production of ATP by mitochondria within all the cells of the body, most of which have compensatory mechanisms to cope with this metabolic stress, such as muscle cells, which can produce more mitochondria. Neurones with very low, very thin or unmyelinated axons, such as the papillomacular bundle, are at a great disadvantage and more prone to be damaged by these disorders.

Clinical features

Usually, there is a sudden or rapid painless bilateral vision loss. Simultaneous involvement of both eyes is more common with nutritional deficiency, toxic and some hereditary disorders, but monocular onset and fellow eye involvement occurring later (days, weeks or months) is more common with Leber hereditary optic neuropathy.

Visual loss occurs, ranging from mild [6/7.5 (20/25)] to severe (finger-counting). Other clinical signs include disturbed colour perception and field defects typically characterized by a centrocaecal scotoma (Fig. 22.2). Later, a temporal pallor of the disc becomes evident. Associated neurological features such as paraesthesiae, ataxia and impaired hearing may be seen.

Differential diagnosis

- Leber hereditary optic neuropathy
- Kjer autosomal dominant optic neuropathy
- Compressive optic neuropathy (pituitary adeno ma or craniopharyngioma compressing the optic chiasma)
- Bilateral optic neuritis

Treatment

Avoidance of smoking, improvement of diet, nutritional supplementation and administration of vitamins ($B_{1(}$ B_6, B_{12}) may show good results if the diagnosis is made early and treatment instituted. Vision can return to normal or near normal over several months. However, visual loss is permanent in chronic, long-standing nutritional or toxic optic neuropathy.

The toxic optic neuropathies: These include a number of conditions in which the optic nerve fibres are damaged by exogenous poisons. Previously, these were called the toxic amblyopias, which is a misnomer going by the modern definition of amblyopia. The most common of these poisons are tobacco, ethyl alcohol, methyl alcohol, arsenic, lead, thallium, quinine, ergot, carbon disulphide, stramonium and *Cannabis indica.* In some of them (tobacco, methyl alcohol), the disease is primarily retinal and follows poisoning of the ganglion cells of the retina which results in degeneration of the nerve fibres. Others are due to a direct effect on the nerve fibres themselves.

The neuropathy produced by *diabetes, carbon disulphide* (seen in the rayon industry), and *iodoform* resembles that of tobacco.

Methyl alcohol, lead, nitro- and *dinitrobenzol* produce more serious optic atrophy than the agents mentioned earlier. There is probably always a stage at which a central scotoma is present, but it is often missed.

Tobacco-induced optic neuropathy: This results from the excessive use of tobacco, either pipe smoking or chewing, and occasionally from the absorption of dust in tobacco factories. Smokers of shag and strong tobacco mixtures or cigars suffer the most; cigarette smokers are rarely affected. In many cases there is also an over-indulgence of alcohol but this is not invariable. Patients, usually 35-50 years of age, may have smoked excessively for years with impunity, the attack coinciding with some intercurrent cause of debility or digestive disturbance. Various substances have been regarded as the toxic agent, but a potent factor may be poisoning with the cyanide in tobacco smoke associated with a deficiency of vitamin B_{12}.

Pathologically, the condition is due to degeneration of the ganglion cells of the retina, particularly of the macular area where the cells show vacuolation and Nissl degeneration. In the nerve, the papillomacular bundle is degenerated.

Clinically, the patient complains of increasing fogginess of vision, usually least marked in the evening and in dull light. Central vision is greatly diminished, so that

reading and near work become difficult. Although the condition is bilateral, one eye is usually more affected.

The fundus is normal or a slight temporal pallor may be seen in the disc, but the diagnosis is made from the characteristic defects in the central fields. These primarily involve the centrocaecal area between the fixation point and the blind spot. Here, occupying a horizontally oval area, there is a relative scotoma to white and colours, particularly red, and in it, on the horizontal meridian, there are one or more islands of complete visual loss. The scotoma gradually extends to involve the fixation area itself so that central vision may be lost but the peripheral field remains unaffected.

Treatment consists of abstaining from or severely curtailing the use of tobacco and alcohol. If this is done the prognosis is eventually good although visual improvement may not be evident for a period of some months; thereafter it may be slow. Improvement may be hastened by intramuscular injections of 1000 |xg hydroxycobalamine. This dose should be repeated five times at intervals of 4 days and then at 2-weekly intervals for a few months. Recovery may be monitored by the VEPs. Recurrences are very rarely seen even if tobacco is resumed in strict moderation.

Ethyl alcohol: Although alcohol is usually an adjuvant in tobacco-induced optic neuropathy, it may cause a similar neuropathy in the absence of the latter. Such patients frequently suffer from alcoholic peripheral neuritis. The disease, characterized by a central scotoma, may be due essentially to avitaminosis owing to chronic lack of nourishment.

No specific therapy is available. General measures such as stopping alcohol intake, improved diet and injections of hydroxycobalamine as outlined above can be tried. Steroid therapy has not been found to be of any benefit.

Methyl alcohol: Poisoning from drinking wood alcohol has always been common in countries during prohibition, and occurs sporadically from drinking methylated spirit. Individual susceptibility is marked. It may occur in an acute or chronic form. In the acute form there may be severe metabolic acidosis with nausea, headache and giddiness followed by coma. If the patient survives, vision fails very rapidly, passing through the stages of contracted fields and absolute central scotomata to blindness. The vision may improve, but usually relapses, becoming gradually abolished by progressive optic atrophy. Restoration of sight is rarely complete.

Ophthalmoscopically, there may be blurring of the edges of the discs and diminution in the size of the vessels in the early stages. Later there are signs of optic atrophy, usually of the primary type. Pathologically there is widespread degeneration of the ganglion cells of the retina probably caused by histotoxic anoxia and relative axonal preservation in the retrolaminar portion of the optic nerve.

Treatment in the acute stage includes intra-venous bicarbonate and ethyl alcohol. In the chronic form there is a gradual, progressive loss of vision with the development of optic atrophy.

Arsenic: This is especially liable to cause optic atrophy, usually total, when administered in the form of pentavalent compounds such as atoxyl or soamin. These were used for attacking the trypanosome of sleeping sickness, but have now been abandoned.

Manifestations of acute toxicity include burning in the throat, difficulty in swallowing, nausea, vomiting, diarrhoea and abdominal pain, with cyanosis, hypotension, delirium, seizures and haemolysis. Manifestations of chronic poisoning include erythroderma, hyperkeratosis, hyperpigmentation, exfoliative dermatitis, skin carcinoma, bronchitis and polyneuritis.

The condition is diagnosed by the detection of arsenic in the hair and nails and the measurement of arsenic levels in the blood (normal <3 |JLg/dl) and urine (normal <100|xg/L). Acute ingestion is treated as a medical emergency with gastric lavage and dimercaprol. D-penicillamine is useful in the treatment of chronic poisoning.

Lead: Lead poisoning is rarely seen nowadays since precautions have been taken to eliminate salts of this metal from pottery glazes, children's paints, painted toys, etc. However, it may still be a major problem due to vehicular pollution in some areas of the world and in countries where indigenous systems of medicine may include therapy with heavy metals for prolonged periods.

Adults develop abdominal pain, anaemia, renal disease, headache, peripheral neuropathy with demyelination, ataxia and memory loss. Childhood poisoning is manifested by anaemia, abdominal pain, lethargy, anorexia, ataxia, slurred speech and convulsions. This syndrome is almost always associated with a high dose exposure to lead, pica and malnutrition, with iron, calcium and zinc deficiency.

The subclinical form of childhood plumbism includes selective defects in language, cognitive functions and behaviour.

The ocular signs are optic neuritis or optic atrophy, which may be primary or post-neuritic. Some patients develop a retinopathy which may be due directly to lead or of the renal type, secondary to lead nephritis.

Laboratory tests to establish the diagnosis include a haemogram, measurement of the blood lead levels (normal <10fxg/dl or <0.5|xmol/L) and 24-hour urinary excretion of lead (normal <80 (xg/dl).

Treatment includes removal of the source of exposure and the use of chelating agents such as the calcium salt of EDTA, dimercaprol and D-penicillamine.

Quinine neuropathy: Total blindness may follow the use of the drug, even in doses as small as 60 mg in susceptible persons; 150 mg is the maximum amount of quinine sulphate which should be given within 24 hours. The largest doses were usually taken for malaria, but quinine was also used as an abortifacient. The pupils are dilated, and there is associated deafness and tinnitus. Ophthalmoscopically, the retinal vessels are extremely contracted and the disc is very pale; oedema of the retina has been described in the early stage. Occasionally blindness is permanent and optic atrophy ensues. In less marked cases or at a later stage, the visual field is severely contracted but central vision may be completely restored so that tube vision results. The discs may remain pale for years or become normal.

Ethambutol: This is an oral chemotherapeutic agent used in the treatment of tuberculosis and may produce an optic neuritis resulting in reduced visual acuity and colour vision, and eventually, a central scotoma. The neuritis is reversible when the drug is discontinued but patients should be examined monthly during the early stages of therapy. A dose of 15 mg/kg/day is the upper limit of safety with regard to eye complications.

Optic atrophy has also been reported following the use of other antitubercular drugs such as streptomycin and isonicotinic hydrazide (INH).

No specific treatment is useful, apart from discontinuation of the drug. Gradual recovery to a variable extent has been known to occur.

Chloroquine: This is an antimalarial drug also used in the treatment of SLE, discoid lupus and rheumatoid arthritis. Prolonged administration may give rise to a keratopathy, myopathy, retinopathy and optic neuropathy. Optic nerve involvement is rarely directly related, but is more commonly a consecutive response consequential to the retinopathy. The retinopathy is a serious pigmentary degeneration of the retina which may lead to loss of vision. A mild pigmentary disturbance in the macular area leads to visual field defects, most commonly a central scotoma and a characteristic 'bull's-eye' retinal lesion, well demonstrated by fluorescein angiography. Eventually there is a widespread retinal atrophy with pigment clumping and attenuated retinal vessels. A few cases of retinopathy have been reported in patients receiving a total dose of less than 100 g.

Patients with lupus erythematosus are more susceptible to chloroquine toxicity. In the past, the fears of toxicity were based on the total accumulated dosage the patient had ingested over his lifetime. It now appears that this is not a problem if the actual effective doses are adhered to, and the daily dosage is considered the most critical factor in preventing eye damage.

Hydroxychloroquine, which has a lower risk of ocular toxicity than chloroquine, is perceived to be a safer drug but it has a weaker anti-inflammatory effect than chloroquine. The maximum dose allowed for chloroquine is 6 mg/kg in 24 hours while for hydroxychloroquine it is 4.5 mg/kg. The latter is more commonly used nowadays (300-400 mg/day). Blurring of vision and diplopia produced by short-term therapy are reversible on stopping the drug. Keratopathy produced by long-term use and seen in up to 90% cases, is sometimes used as an index of effective dose, and is completely reversible on discontinuing treatment. Pigmentary retinopathy and optic atrophy following large doses for prolonged periods may be irreversible if detected late.

Careful perimetry, preferably static, with determination of threshold sensitivities within 5 ° of the fixation point with red stimuli is a reliable method of detecting the early signs of chloroquine retinal toxicity. Monitoring of vision at home with an Amsler grid *(see* p. 92) and periodic testing of colour vision are also useful.

Amiodarone: Amiodarone, a drug used to treat cardiac arrhythmias, is known to produce keratopathy (in 70-100% of patients), anterior subcapsular cataract, optic neuropathy, pigmentary retinopathy and pseudotumour cerebri. The optic nerve involvement can be a slowly progressive atrophy or it can present a picture similar to non-arteritic ischaemic optic neuropathy, when it may be difficult to distinguish if the ischaemic optic neuropathy is due to the amiodarone or the underlying vasculopathy. Amiodarone-induced optic neuropathy has no correlation with duration, dose or levels and can develop after weeks to months of starting therapy.

About 0-11% of patients are symptomatic and may complain of blue-green rings around lights, blurred vision, glare, dryness and eyelid retraction. These symptoms are all related to the corneal deposits, but fundus examination and an evaluation of optic nerve function are indicated. If toxicity is detected, the drug should be discontinued and another therapeutic alternative substituted if available. However, in life-threatening situations, which respond only to amiodarone, the drug may have to be continued; fortunately, complete blindness is rare.

Other drugs: To complete the list, antibiotics such as chloramphenicol, sulphonamides, digitalis, oral hypoglycaemic agents (chlorpropamide and tolbutamide), disulphiram and D-penicillamine have also been known to cause optic neuropathy in some cases. Oral contraceptives, which are a combination of progestogens and oestrogens, may play a part in the production of occlusive vascular disease, particularly in women who suffer from vascular hypertension, migraine or other vascular syndromes. Infarction of the brain or of the optic nerve head occurs more commonly in women using contraceptive therapy. In such cases the drug must be discontinued.

Nutritional deficiency

A deficiency of vitamins in the diet, particularly thiamine, may be responsible for the development of an optic neuritis, usually of the axial type, resulting in the loss of central vision. Similar lesions in the mid-brain cause various types of ophthalmoplegia (acute haemorrhagic anterior encephalitis of Wernicke).

Such an involvement is seen in extreme degrees of pellagra. An optic atrophy, usually partial but occasionally apparently complete, may eventually develop and, in severe cases, the prognosis is bad. An appropriate diet, if resumed before atrophy develops, is curative; after atrophy has set in the visual defect is permanent.

Hereditary optic neuropathy

This is a group of disorders all of which ultimately lead to optic atrophy. There are several forms which follow a Mendelian (dominant or recessive) or non-Mendelian (Leber) inheritance pattern.

Dominant optic neuropathy (Kjer autosomal dominant optic atrophy): This is the commonest inherited optic nerve disorder. Insidious visual loss begins between the ages of 5 and 10 years. Visual impairment varies from mild to moderate. Visual acuity may remain 6/6(20/20) or be as low as 6/60 (20/200); very rarely is it worse. Though bilateral, involvement of the two eyes may be asymmetrical.

There is loss of colour perception and a central scotoma. Visual loss may progress for a few years but generally stabilizes after the teens. There are generally no associated neurological abnormalities.

The ***differential diagnosis*** is from: (i) a compressive lesion; (ii) vitamin deficiency; (iii) drug effect and
(iv) toxin-induced neuropathy. A detailed family history should be taken. In case other family members are unaffected or unavailable for examination, a CL or MRI scan should be performed to rule out the possibility of a compressive lesion.

Recessive optic neuropathy

Simple: Isolated optic atrophy of recessive inheritance represents a rare entity described in the older literature where, in most instances, detailed investigations were not done and not well documented clinically. Cases reported were of optic atrophy with consanguineous parentage.

Complicated hereditary optic neuropathy: This is a group of disorders with recessive inheritance with several other associated systemic features. These include bilateral optic atrophy with polyneuropathy (e.g. Charcot-Marie-Tooth disease), or inborn errors of metabolism, or spinocerebellar degenerations with mild mental deficiency (Friedrich and Marie ataxia and Behr syndrome). Also included in this category is Wolfram syndrome, which is characterized by the association of early childhood-onset optic atrophy with diminished vision (usually in the 6/60(20/200) range) and juvenile diabetes. It is recalled by the mnemonic DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy and deafness).

Leber hereditary optic neuropathy

Aetiopathogenesis: This form of retrobulbar neuropathy usually commences at about the 20th year of life. Initially, cyanide intoxication was believed to play a part but a genetic aetiology has now been established. Transmission of the disease is generally through an unaffected female to all offspring, but the disease manifests mostly in males although females are also affected. Hereditary transmission is by mitochondrial DNA, which resembles the X-chromosomal inheritance pattern in some ways, in that all daughters are carriers and it is transmitted by women to all offspring, but while 50-70% of sons and 10-15% of daughters manifest the disease, none of the sons can transmit it. It differs from sex-linked (X-linked) transmission in that affected males do not pass on the trait or carrier state to any of their offspring—sons or daughters.

Clinical features: Although it is an inherited disorder, in some cases a positive family history is not elicited. Members of the same family often show identical peculiarities in the progress of the disease.

Males are affected 5-10 times more commonly than females and the ratio varies from country to country. It usually occurs in young males 15-30 years of age and sometimes manifests in females in the second or third decade of life. Vision generally fails rapidly at first, the loss is gradual thereafter but remains stationary or slowly improves after 6 months. Visual loss is painless and both the eyes are always involved, although one may precede the other by a period varying from a few days to 18 months.

In two-thirds of the cases there is a central or centrocaecal scotoma, either partial for colours or also for white. The peripheral field is usually normal, but concentric contraction or sector-shaped defects may occur. Total and permanent colour blindness has been known to follow. The central scotoma generally persists, but progressive constriction of the field to complete blindness is rare.

The fundus is at first normal or there is slight swelling with blurring of the edges of the disc. Small, telangiectatic blood vessels are seen near the disc which do not leak on fluorescein angiography. In the later stages, after several months, optic atrophy ensues, with pallor confined to the temporal side or involving the whole disc. Apart from headache, the general health is good. Several

Leber-specific gene mutations have been identified and if facilities for testing are available, blood samples can be sent for analysis. No specific treatment is effective and genetic counselling should be offered.

MISCELLANEOUS CONDITIONS

Diabetic papillopathy

This is an uncommon condition seen in young patients in their teens or twenties who are suffering from juvenile insulin-dependent diabetes. They present with unilateral or bilateral blurred vision of insidious onset, or may be asymptomatic and the condition detected incidentally in these patients. The disc is swollen with telangiectatic vessels lying over its surface. Visual field defects could be central scotomas or arcuate pattern defects, but vision is not severely affected. The presence of telangiectatic vessels overlying the swollen disc is characteristic and useful in diagnosis. If bilateral, neuroimaging is mandatory to rule out an intra-cranial space-occupying lesion; pseudotumour cerebri is another important differential diagnosis. Neurosurgical consultation and documentation of the CSF pressure may be needed. Though visual field defects tend to be irreversible, disc oedema usually resolves over several months.

Two clinical features differentiate it from ischaemic optic neuropathy: (i) diabetic papillopathy is often simultaneously *bilateral*; and (ii) optic nerve function is often not impaired in diabetic papillopathy.

No treatment is specifically recommended. The cause is not established, and there does not appear to be any relationship with the degree of glycaemic control or the presence of diabetic retinopathy.

Thyroid-related optic neuropathy

In Graves disease, optic neuropathy is caused by compression of the nerve at the apex of the orbit by enlarged extraocular muscles. Though visual loss is usually gradual, a rapid deterioration has also been seen to occur. The severity of optic neuropathy and the amount of proptosis are not directly interrelated and, in some patients, optic neuropathy occurs in the absence of any apparent proptosis. In fact, proptosis is often a natural mechanism to decompress the orbit and those patients with tight orbits and no proptosis are more likely to develop features of optic nerve dysfunction. When examined at presentation, the optic nerve head may be normal, swollen or even pale.

Clinical work-up for evidence of neuropathy includes recording the visual acuity, colour vision and visual fields. Additional tests include measuring the degree of proptosis and lagophthalmos, slit-lamp examination for exposure keratopathy, recording of intraocular pressure and testing of ocular motility.

Treatment depends upon the extent of nerve involvement and is tailored to the individual. The options include systemic steroids, orbital decompressive surgery, or orbital radiation. If visual loss is mild with a minimal field defect, oral steroids with careful monitoring is the norm. Additional measures such as sleeping propped up, avoiding smoking and eye protection are advised.

If visual loss is not controlled by these measures or is severe from the outset, high-dose intravenous methylprednisolone 1 g per day is administered. If vision does not improve within 24-48 hours, orbital decompression is required.

Surgery remains an option for patients who cannot be given systemic steroids for any reason. In those not considered fit for surgery, or in whom other measures are only partially effective, orbital radiation (2000 rad in 10 divided doses over a fortnight) is an alternative.

Radiation optic neuropathy

This delayed effect, which may manifest 1-5 years after radiation therapy, is more likely to occur following radiation therapy to the eyes, orbit, paranasal sinuses, nasopharynx and occasionally the brain. Visual loss, which is often severe, can be acute or gradual. Disc swelling and retinopathy may or may not be evident or present. There is no specific or effective treatment. Corticosteroids may be helpful in some cases.

Thermal burns

A rare, delayed type of optic neuropathy has been reported following thermal bums of the body. A 'burn neurotoxin' was proposed as a pathogenetic factor, as neither septicaemia nor circulatory failure were found to play a role. Bilateral involvement and a delayed onset 2-3 weeks after the initial burn injury were noted. In other burn victims an early visual loss attributed to diffuse cerebral oedema and hypoxia with other signs and symptoms of encephalopathy have also been known to occur.

Traumatic optic neuropathy

When a rotational or shearing force is transmitted to the frontal areas in closed head injuries, damage to the optic nerve can occur. The blow is typically ipsilateral to the frontal area and usually severe enough to produce a loss of consciousness. The nerve damage is produced by shearing forces that may be induced in the relatively immobile canalicular portion of the nerve by the movement of the brain due to frontal impact. There may be direct damage by disruption of the nerve fibres or indirect damage by disruption of the blood supply. Oedema

or haemorrhage can also induce nerve damage by compressing the nerve within the optic canal. In addition, in a fracture of the wall of the optic canal, bone fragments can directly exert pressure on the optic nerve. Rarely, blunt trauma can lead to optic nerve damage in the orbit, producing an optic nerve head avulsion.

Though optic nerve injuries are usually unilateral, bilateral visual loss can occur less commonly due to optic chiasmal damage in blunt head injuries.

Apart from decreased vision, signs include a field defect and a relative afferent pupillary defect. An avulsed optic nerve head is visible ophthalmoscopically as a defect in the pupillary region and may be accompanied by haemorrhage. Sometimes a picture resembling a central retinal artery occlusion may be seen if there is damage to the intraorbital part of the nerve. However, in most cases, traumatic optic neuropathy affects the canalicular part of the nerve and the fundus usually appears normal, with the disc pallor typical of optic atrophy developing after 3-4 weeks. Early onset of pallor implies a substantial disruption of the blood supply to the optic nerve head.

In most cases, the visual loss is maximum from the time of impact but can also be delayed by a few hours and progress over the next few days. Computed tomography helps diagnose a fracture of the canal with a bone fragment pressing on the nerve and the presence of a haemorrhage in the nerve sheath. If either of these conditions is present, surgical intervention is required. High-dose intravenous corticosteroids (dexamethasone 3-5 mg/kg/day or methylprednisolone 20-30 mg/kg/day) have been reported to be effective in some cases. Visual evolved potentials help in monitoring the response to therapy, particularly when the visual acuity is very poor.

Treatment should be instituted within 24-48 hours and if improvement occurs, oral steroid therapy can be started and the drug tapered off over the next 2 weeks. If there is no visual improvement within 1-2 days of this high dose of steroids and particularly if there is worsening, presumably from oedema or haemorrhage within the nerve or canal, optic canal decompression through either a transethmoidal or transfrontal approach should be performed. Another indication for optic canal decompression in such cases is if vision worsens as the steroids are tapered off.

CONGENITAL ABNORMALITIES OF THE OPTIC DISC

Coloboma of the optic disc

This occurs in two forms, one of which is common and the other rare (Fig. 22.18). The common form is due to incomplete closure of the embryonic fissure, and manifests itself as an *inferior crescent*, resembling the myopic crescent but situated at the lower edge of the disc. It occurs most commonly in hypermetropic and astigmatic eyes, which often have slightly defective vision in spite of the correction of any error of refraction. It is often slightly ectatic *(conus)*.

In *coloboma of the disc* (or nerve sheath), there is greater failure of the embryonic fissure to close. The disc looks large and the vessels have an abnormal distribution, appearing only above or irregularly round the edges. The apparent disc is really the sclera and the inner surface of the sheath of the nerve, the nerve itself being usually spread out as a pink, horizontal, linear band at the upper part. The floor of the coloboma is white and measurably depressed, and often ectatic. The eye usually has defective vision.

Rarer anomalies related to coloboma are round cavities *(holes)* on the disc known as optic disc pits, generally situated in the temporal portion.

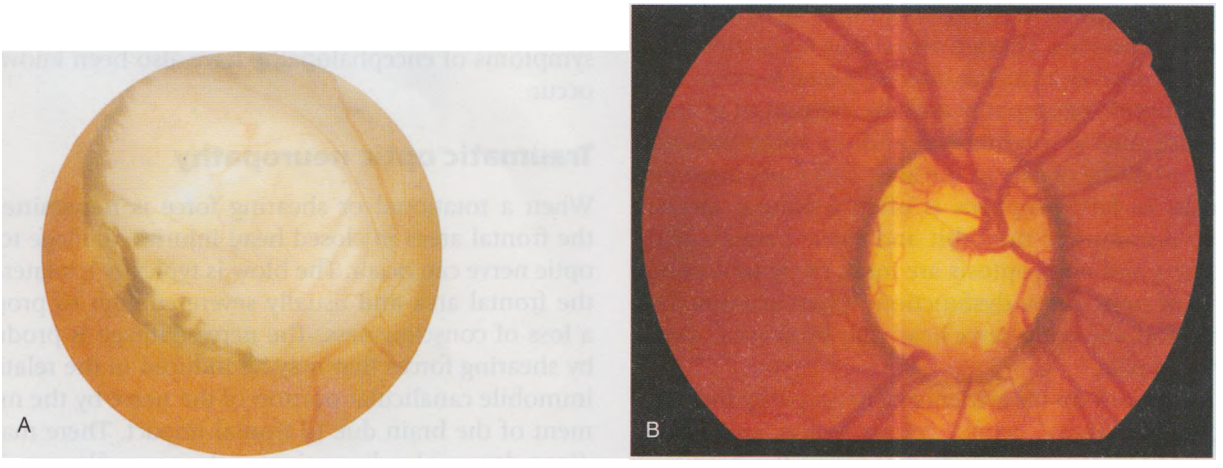


Fig. 22.18 Coloboma of the optic disc. (A) Extensive involvement of the disc and peripapillary retina; (B) inferior involvement.

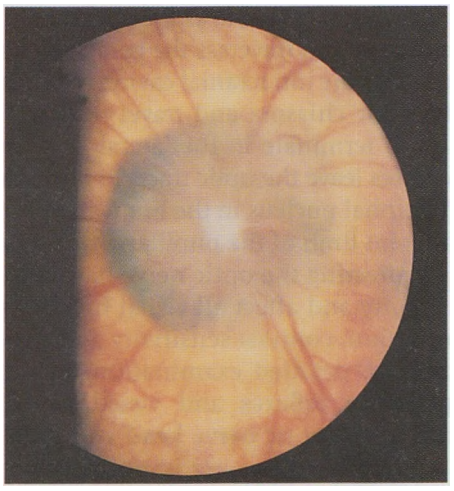


Fig. 22.19 Morning glory disc anomaly. (By courtesy of JF Talbot)

Another variant is the *morning glory* disc which resembles the morning glory flower. It has a central excavation surrounded by an elevated rim of pink neuroglial tissue with the vessels emerging radially from the disc as spokes in all directions (Fig. 22.19).

Sometimes remnants of the sheaths of the hyaloids vessels form an excess of fibrous-like tissue on the disc which extends a short distance along the vessels. Occasionally the fibrous tissue takes the form of a delicate semi-transparent membrane that covers the disc and appears to be slung from the vessels. This is sometimes referred to as *Bergmeister papilla.*

Hypoplasia of the optic nerve head

The diagnosis of hypoplasia presents little difficulty in the extreme case. The disc is small (Fig. 22.20) with slightly tortuous and occasionally small vessels and is surrounded by a yellowish, mottled, peripapillary halo with a pigmented rim approximately corresponding to the size of a normal disc, also referred to as a *double ring sign.* The vessels on the disc may show anomalous branching (Fig. 22.20A and B). The retinal nerve fibre layer is thin. The condition is often bilateral but may be asymmetrical and central vision is usually impaired.

There is an important association between a hypoplastic disc and cerebral malformations, which may include absence of the septum pellucidum, con-genital hypopituitarism and agenesis of the corpus callosum. This condition has been described following the maternal ingestion of the anticonvulsant phenytoin, which has known teratogenic properties.

Optic disc pit

This congenital anomaly appears as a round or oval, grey, sometimes black, greyish-white or yellowish crater-like excavation, most commonly located temporally in the optic disc (Fig. 22.21). Adjacent peripapillary retinal pigment epithelial changes are often seen, and the involved disc is usually slightly larger than the normal disc in unilateral cases.

Its exact pathogenesis is unknown but histologically a herniation of rudimentary neuroectodermal tissue in a pocket-like depression within the nerve substance has been demonstrated.

The pit usually looks grey or black owing to shadowing of light and patches of pigment from the inclusion of retinal pigmentary epithelium. It may be associated with oedema of the macula or a serous macular detachment due to accumulation of subretinal fluid, believed to be either CSF trickling in from the pit or fluid vitreous gaining access to the subretinal space through a defect near the edge of the disc.

Pits can be asymptomatic or associated with poor vision and variable visual field defects, the most common

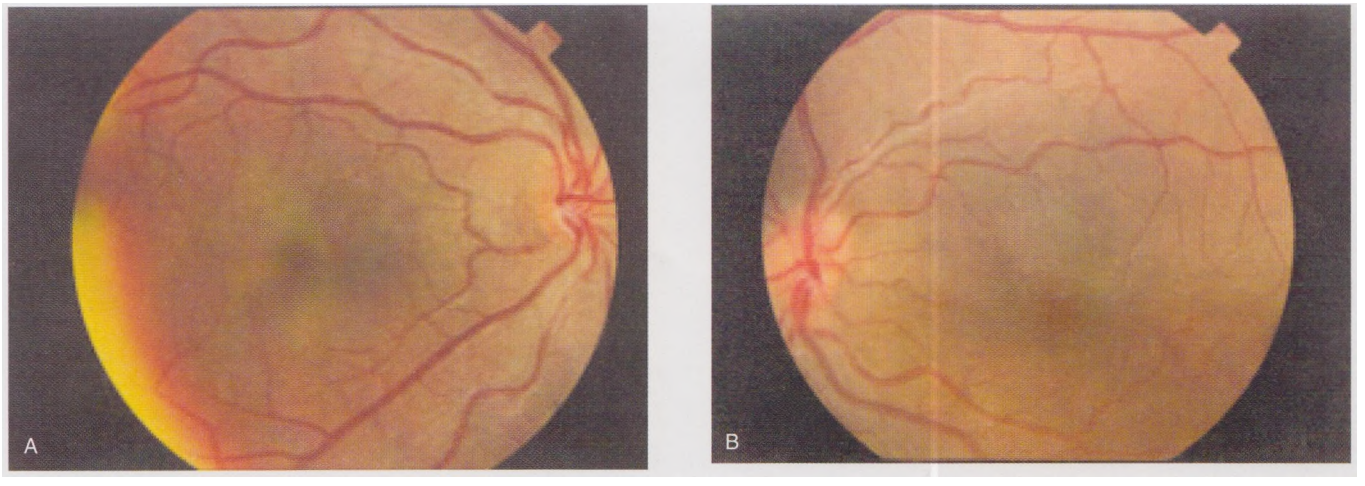


Fig. 22.20 (A and B) Hypoplasia of the optic nerve head in both eyes of a 12-year-old girl with hypermetropia.

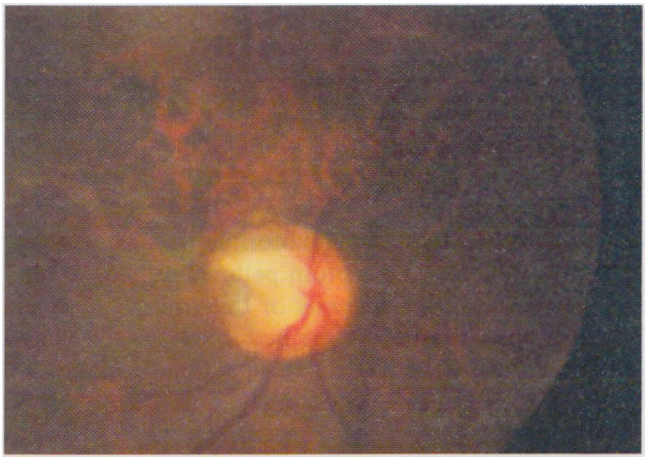


Fig. 22.21 An optic disc pit.

being a paracentral arcuate scotoma connected to an enlarged blind spot. Approximately 45-50% of eyes with optic pits develop serous retinal detachments involving the macula, some of which resolve spontaneously, but the overall visual prognosis is often poor in such cases. If retinal detachment occurs, treatment by internal gas tamponade is preferred over the previously recommended practice of photocoagulation at the disc margin.

SUMMARY

The optic nerve essentially consists of the axons of the retinal ganglion cells, leaves the eye by piercing the sclera at the lamina cribrosa visible as the optic nerve head on ophthalmoscopy and traverses the orbit, the bony optic canal and enters the intracranial cavity. The fibres decussate at the optic chiasma and travel further along the optic tracts to terminate in the lateral geniculate bodies. Some fibres leave the optic tracts to terminate in the Edinger-Westphal nucleus in the brain stem to form the sensory afferent limb of the pupillary light reflex.

Diseases affecting the optic nerve have great impact on visual acuity and affect all visual functions including colour vision, contrast sensitivity and visual fields. Careful history, detailed examination including testing of pupillary reflexes and visual fields, fundus appearance of the optic nerve head and judicious use of ancillary investigations are important. The pattern of presentation, clinical picture and course of the disease, and type of visual field defect help to localize the site of involvement and establish the aetiological diagnosis.

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23

Intraocular Tumours

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Intraocular tumours are rare, but of great importance, since they are usually malignant and endanger the life of the patient.

The *clinical course* of intraocular tumours is commonly divided into four stages: (i) the quiescent stage; (ii) the glaucomatous stage; (iii) the stage of extraocular extension and (iv) the stage of metastasis. This is probably the typical chronological order of events, but secondary glaucoma may arise sometimes acutely at an early stage, or be delayed until after extraocular extension has taken place, and metastasis may occur at any stage.

TUMOURS OF THE UVEAL TRACT

The common primary malignant tumours of the uveal tract are *malignant melanomata.*

Tumours of the iris

It is not uncommon to see irides with dark brown spots (melanomata), due to congenital aggregations of pigment cells. As a rule these are benign *naevi,* but occasionally they take on malignant proliferation. Any increase of size must be watched with suspicion.

Hamartomatous lesions (*Lisch nodules)* are found on the iris of prepubertal children who suffer from neurofibromatosis. Their presence is correlated with age but not with the number of *cafe-au-lait* spots, the number of neurofibromata or the severity of the disease. They are bilateral, multiple, well defined, dome-shaped gelatinous elevations protruding above the iris surface and ranging from clear to yellow or brown in colour. They are pathognomonic of neurofibromatosis.

Malignant melanoma is the only neoplasm of importance met with in the iris but is rare. Composed of pigmented or unpigmented spindle shaped or round cells, it occurs as an isolated nodule which grows rapidly (Fig. 23.1) and, if

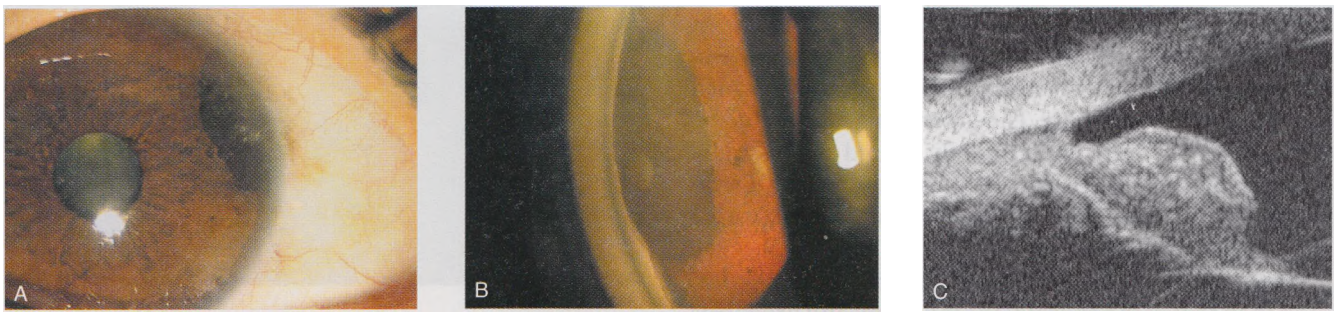


Fig. 23.1 Malignant melanoma of the iris. (A) Note the deformation of the pupil; (B) gonioscopic view of the tumour; (C) ultrasound biomicroscopic picture of the mass infiltrating the iris stroma.

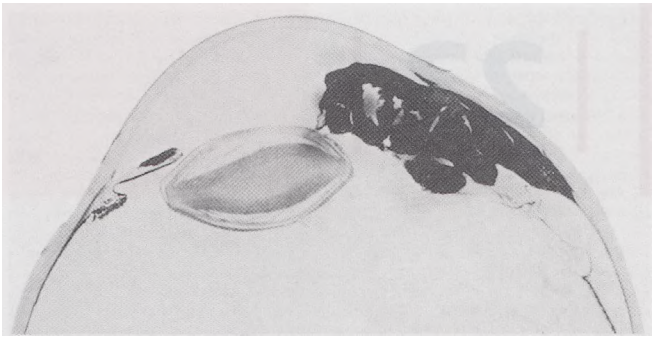


Fig. 23.2 Malignant melanoma involving the iris, ciliary body and choroid, with a metastatic tumour the iris on the other side of the pupil in the same eye. (By courtesy of Doherty)

untreated it may penetrate the comeosclera and perforate the globe. Differentiation from a granulomatous lesion depends on the absence of inflammation and the density of pigmentation. The occasional absence of pigmentation *(amelanotic melanoma*) may give rise to difficulties.

Treatment: The growth should be observed for a short time, preferably by repeated photography and, if found to increase in size, should be removed by iridectomy if this is feasible. If the tumour involves the root of the iris and the ciliary body (Fig. 23.2), it should be removed by iridocyclectomy. If completely removed the prognosis is excellent.

Malignant melanoma of the ciliary body

A *ciliary body melanoma* may attain a considerable size (Fig. 23.3) before it causes symptoms, which are usually related to displacement or distortion of the lens and interference with the ciliary muscle. The ciliary circulation is impeded, and conspicuous dilatation of one or two anterior perforating ciliary vessels (sentinel vessels) (Fig. 23.4) should always arouse suspicion. The growth may invade the angle of the anterior chamber when it has the appearance of an iridodialysis, a dark crescent showing at the root of the iris; that it is not an iridodialysis is shown by the fact that no red reflex can be obtained through it on illuminating with the ophthalmoscope and from the absence of a history of a blow. In an unpigmented tumour the crescent may be yellowish, but vessels will usually be visible upon the surface which render the diagnosis easy. The growth may be visible by oblique illumination with a widely dilated pupil and by gonioscopy, and is opaque to transillumination. Occasionally it takes on a *ring* or *annular* distribution, extensively infiltrating the ciliary region.

Malignant melanoma of the ciliary body is less common than that of the choroid; the treatment and prognosis are similar, but surgical excision is an option for smaller tumours.

Epithelial hyperplasia of the ciliary processes is not uncommon in old eyes. Rarely, *malignant epitheliomata* occur; also growths resembling the embryonic retina *(diktyoma).* They cause the same clinical signs as malignant melanoma.

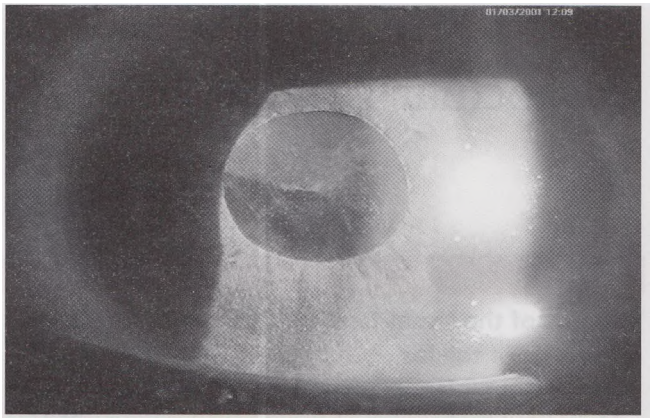
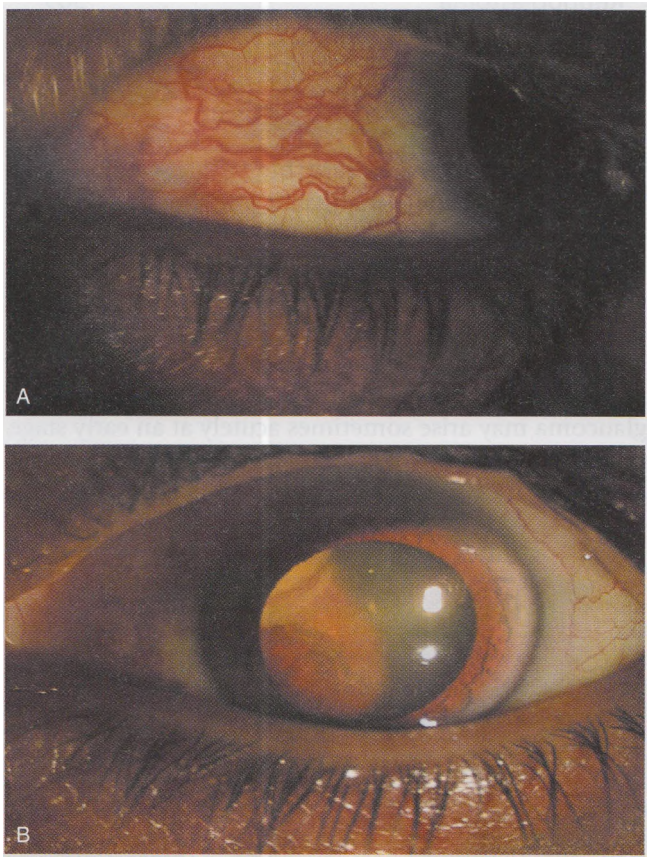


Fig. 23.3 Malignant melanoma of the ciliary body extending from 4 to 9.30 o'clock and pushing the iris forward.



Fig, 23.4 Ciliary body tumour. (A) Sentinel vessels seen; (B) a non-pigmented tumour extending from behind the iris into the choroid.

Malignant melanoma of the choroid

Pathology

This arises from the outer layers of the choroid. It forms at first a lens-shaped mass, raising the retina over it. As it grows, it stretches the elastic membrane of Bruch, which finally ruptures; the tumour then proliferates through the opening and the retinal pigment epithelium to form a globular mass in the subretinal space, separated from the part in the choroid by a narrow 'neck'. The neurosensory retina remains in contact with the tumour at the summit, but is detached from the choroid at the sides, the intervening space being filled with exudative fluid. The growth may be in any location, and the fluid may sink down to the lowest part of the eye, forming a detachment isolated from that over the tumour, but with continuing growth the retina becomes more and more detached, until no part remains *in situ*. The nutrition of the lens then suffers, so that it becomes opaque. The tumour may fill the globe before perforating the sclera, or this may occur relatively early along the perivascular spaces of the vortex veins or ciliary vessels. The orbital tissues then become infiltrated. The lymph nodes are not commonly affected, but metastases occur abundantly in the liver and elsewhere.

Flat malignant melanoma of the choroid: In rare cases the choroid becomes widely infiltrated so that a uniform thickening results, with a shallow 'detachment' of the retina.

The cells are usually spindle shaped; they may also be cylindrical or palisade-like, arranged in columns or around blood vessels, or even resemble endothelial cells in appearance; most tumours are mixed-celled. Malignant melanomas can be classified by cell type as

1. *Spindle* A—predominance of slender spindles with flattened nucleus and no nucleolus;
2. *Spindle B*—predominance of larger spindles with round/oval nucleus and prominent nucleolus;
3. *Epithelioid*—large cells with nuclei that are round and eccentric. There is a high mitotic figure count; and
4. *Mixed type.*

Silver staining reveals a variable amount of argyrophil 'reticulin' fibres, generally more numerous in spindle-celled sarcomata. There is evidence that those with the most reticulin are the least malignant. Epithelioid tumours are the most malignant.

Clinical features

In adults, *choroidal melanoma* is the commonest intraocular malignant tumour. The tumour usually occurs in adults of between 40 and 60 years of age. It is less common in those of African or Asian origin as compared to Caucasians. It is always primary, single and unilateral. The earliest patients to seek advice are those in whom the tumour is located centrally, near the macula, since vision is then most strikingly affected. The growth is usually pigmented but is occasionally unpigmented, a distinction which is relatively unimportant. Metastases from melanotic growths are often unpigmented. The pigment is chiefly melanin, but haematogenous pigmentation occurs after haemorrhages. The surface may have a mottled orange and black appearance (Fig. 23.5).

Peripherally located tumours usually attain a considerable size, and cause a retinal detachment before the patient becomes symptomatic. The patient may also seek relief from the pain of glaucoma. It is of the utmost importance that the cause of a detachment of the retina should be identified in all cases. If a retinal detachment is accompanied by raised intraocular pressure, a growth may be diagnosed almost with certainty. A simple detachment

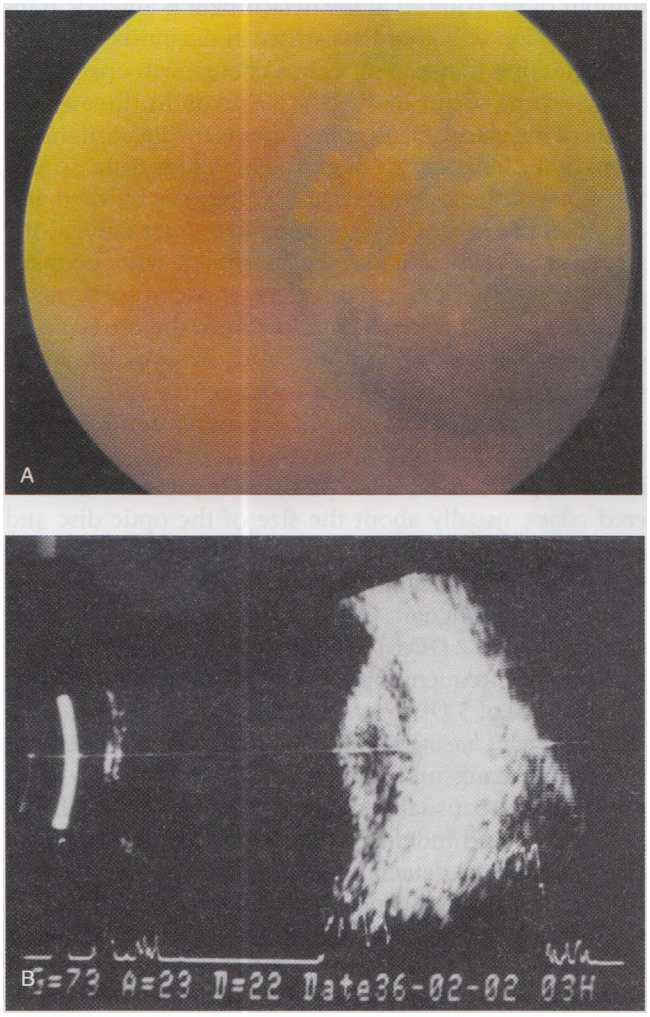


Fig. 23.5 Malignant melanoma of the choroid. (A) A yellowish-grey elevated lesion is seen inferonasal to the disc; (B) ultrasound of a choroidal mass showing an elevated solid tumour with medium-to-high internal reflectivity, suggestive of a choroidal haemangioma.

shows numerous folds and undulations can be seen to travel over the surface when the eye moves. On the other hand, a detachment at the summit of a tumour is usually rounded and fixed, though in the surrounding parts it may show all the signs of a 'simple' detachment. Patches of pigment upon the rounded part support the diagnosis of a tumour, but pigmentary disturbance, more particularly at the periphery, is not uncommon in a simple detachment. Commonly an orange pigment, lipofuscin, is deposited on the surface of the tumour. A simple detachment of the non-exudative type always has a hole or tear in the retina somewhere; if it can be found it is the most positive evidence that a growth is probably not present. Rarely a dual circulation develops and a system of blood vessels having an entirely different mode of distribution from the retinal vessels can be made out between the latter; this is the most positive evidence of a growth, but it is only occasionally seen. Avery small, round detachment in the macular region or upper part of the globe is almost certain to be due to a tumour of the choroid. If the detachment is anterior, transillumination will afford assistance in diagnosis; a simple detachment is transparent, a choroidal growth opaque.

Glaucoma occurs in the later stages of the disease. The cause of the glaucoma in some cases is the forward movement of the lens and iris due to posterior pressure, so that the angle of the anterior chamber becomes blocked and a sudden rise in tension is precipitated. Alternatively, the trabecular meshwork may be infiltrated with neoplastic cells. In other cases, particularly those of early onset, obstruction to the venous outflow from the eye is a possible explanation, the tumour being, in some instances, so situated as to press upon a vortex vein.

In the differential diagnosis, two other tumours must be kept in mind, particularly in the early stages. A *choroidal naevus* appears as a bluish patch with some-what feathered edges, usually about the size of the optic disc and situated near the posterior pole of the eye. It is congenital and symptomless but like naevi elsewhere, may occasionally assume malignant characteristics. Naevi are usually small, less than 2 DD (disc diameter) with indistinct margins and are frequently associated with drusen. A lesion over the size of 5 DD may be considered malignant.

A *cavernous haemangioma* of the choroid, another rare tumour of congenital origin and of exceedingly slow growth, is also usually situated near the disc. It has a greyish hue and indefinite margins and often causes an exudative retinal detachment.

The differential diagnosis also includes *posterior scleritis* which may be difficult to distinguish from a malignant melanoma of the choroid if localized posteriorly.

Diagnosis

Investigations for the diagnosis of choroidal melanoma include B-scan ultrasonography, radio-isotope uptake studies, especially when the media are opaque, and fluorescein angiography.

Ultrasonography permits the delineation of the overlying retinal detachment and provides details of any underlying tumour mass. The classic mushroom shape of the melanoma extending through Bruch's membrane can be seen, with acoustic hollowing within the mass, choroidal excavation at its base and orbital shadowing behind. An A-scan through the mass will show rapid attenuation and a large angle κ. Ultrasonographic measurements of the dimensions of the tumour, particularly the height or thickness and maximum horizontal diameter, are helpful in planning treatment.

Radioactive tracers: Neoplastic tissue has an increased rate of phosphate uptake and retains the isotope longer than non-neoplastic tissue. ^{32}P emits p-rays and is relatively safe because 20% of the dose administered is excreted in the first 24 hours. The range of (3-rays is small, about 2-3 mm on an average with a maximum of 7-8 mm, and this restriction makes the technique of the measurement of ^{32}P uptake difficult. A solid-state detector is capable of distinguishing clearly between the majority of benign and malignant intraocular lesions. Most malignant tumours show uptakes in excess of 80% of controlled values, a level which is not reached by benign tumours. The ^{32}P uptake should be read 48 hours after the administration of the isotope. Gallium-67 (^{67}Ga) is another radio-active material that is injected into the bloodstream and picked up by rapidly dividing cells, and is more sensitive in the diagnosis of these tumours.

Fluorescein angiography in choroidal malignant melanomata in conjunction with the clinical examination may provide sufficient evidence for a correct diagnosis. A double circulation, with an increased fluorescence in the mass, is characteristic of malignant melanoma. Initially one can see the filling of abnormal vessels in the tumour during the choroidal phase followed by a diffuse leak. Overlying this, the retinal vasculature can be visualized. The abnormal circulation is better delineated by indocyanine green angiography. The fluorescein angiographic findings of lesions in the differential diagnosis may have certain distinguishing features. Naevi of the choroid are hypofluorescent. They obscure choroidal fluorescence and are associated with drusen and the absence of late staining. The vascular channels within choroidal haemangiomata fluoresce before the surrounding choriocapillaris. Metastatic tumours tend to produce poor fluorescence in the early phase but are probably indistinguishable from malignant melanomata in the late phase.

Treatment

A pigmented lesion with a diameter larger than 5 DD (7.5 mm) should be considered a malignant melanoma

until proven otherwise. The tumour is generally very slow growing and conservative management is advocated especially if the tumour is small or if no alteration in size can be demonstrated. However, if changes such as an increase in size or occurrence of a retinal detachment ensue, or if sight is threatened, therapy should be instituted. Treatment is directed primarily at eradication of the tumour, with the goal of maintaining vision and ultimately, if all else fails, a cosmetically acceptable globe.

A tumour less than 10 mm across and up to 2 mm thick may be treated by *brachytherapy* using radioactive discs of gold, cobalt-60 (^{60}Co) or iodine-125 (^{125}I). The plaques are surgically placed externally on the sclera over the tumour and removed 3-7 days later, causing tumour regression over 6-12 months. External beam radiation, cryotherapy or laser ablation and even transpupillary thermotherapy are other modalities of treatment for 'small' tumours. Medium-sized tumours 10-15 mm in diameter and 3-5 mm in height can also be treated by plaque or external proton beam radiation. *Enucleation* is an option that is not frequently used today, but must be considered in larger tumours. Orbital spread of the malignant melanoma necessitates *exenteration* but metastasis elsewhere can be treated by enucleation and radiation. Clinical trials are assessing these treatment modalities.

Evidence is accumulating to suggest that the surgical trauma of enucleation leads to vascular spread of the tumour by embolization. Thus, deaths from secondaries are rare before surgery and their incidence rises dramatically in the period immediately following surgery. If the patient can see well with the affected eye and there is no evidence of scleral involvement, conservative management is recommended.

The disease is invariably fatal, usually within 5 years, if not eradicated by operation, but metastasis may be delayed for 10 years or more. Prognosis is fair if the tumour is small (under 10 mm in size) and entirely intraocular, especially if it contains much reticulin. However, death usually occurs within a year of the detection of metastasis.

Secondary carcinoma of the choroid

Metastasis to the choroid occurs primarily in cases of carcinomas, particularly of the breast and alimentary tract. The patient may complain of a diminution of vision, and ophthalmoscopic examination reveals a widespread shallow elevation of the retina, usually at the posterior pole. The disease is nearly always bilateral, and as it is frequently only one of many metastatic deposits and the patient is usually in the stage of general carcinomatosis, excision of the eye is not generally indicated. These metastases, however, are radiosensitive and treatment by radiation often provides sufficient improvement to maintain some vision and prevent the occurrence of pain while the patient survives. They may be hormone-dependent and respond to ovariectomy or cytotoxic drugs.

Reticulum cell sarcoma

The malignant cell of reticulum cell sarcoma resembles a histiocyte. It originates usually within the reticuloendothelial system, but less commonly in the central nervous system, where the neoplasm is referred to as a microglioma. When a reticulum cell sarcoma affects the eye, it may do so as a primary ocular lesion or, if associated with a similar lesion elsewhere, the site is usually the central nervous system.

Patients are typically in their sixth or seventh decade at the time of presentation. They complain of decreased visual acuity with floaters or photopsiae. The principal finding is vitreous involvement with 'inflammatory' cells, which are refractory to topical steroid therapy. There may be a mild anterior segment reaction resembling a non-granulomatous iritis with or without keratic precipitates.

In some cases, lesions of the fundus resemble retinal or subretinal infiltrates. They are patchy with yellow-white fluffy outlines, which quickly become confluent. If the macula is affected, diminished visual acuity rapidly results. The vitreous may be so involved that details of the retina are obscured.

Vitrectomy may provide the only available source for tissue diagnosis in ocular reticulum cell sarcoma. The tumour cells are large and pleomorphic with scanty cytoplasm and prominent nuclear membranes. Nuclei are round or oval, occasionally multiple with frequent mitoses, clumped chromatin and prominent nucleoli.

The differential diagnosis is from leukaemic infiltrates, retinitis secondary to bacterial or fungal sepsis, toxoplasmosis and cytomegalovirus infection.

The diagnosis is of some importance because radiation therapy is effective and can lead to permanent improvement in visual acuity.

TUMOURS OF THE RETINA

Retinoblastoma

Retinoblastoma is a proliferation of neural cells which have failed to evolve normally. It used to be commonly known as 'glioma' retinae, but malignant proliferations of neuroglia, such as those that occur in the brain and optic nerve, are very rare in the retina and it is better termed retinoblastoma.

Aetiology

The tumour is confined to infants and very young children and is frequently congenital, although it may remain quiescent or pass unnoticed until the fifth or

sixth year of life or sometimes even later. The disease is rare. The fellow eye is affected independently, not by metastasis, in about one-fourth of the cases. However, frequently the growth cannot be recognized, even on careful examination, until months or even years later. In 10% of cases a relative may also have had a retinoblastoma, and in such cases the disease is usually, but not always, bilateral. Several children of the same family are sometimes affected as the inheritance is dominant with variable gene penetrance. Retinoblastoma was the first cancer to be directly associated with a genetic abnormality—deletions or mutation of the ql4 band of chromosome 13 *(see* Chapter 33). This chromosome is responsible for controlling retinal cell division, and in children with retinoblastoma, retinal cell division continues unchecked, causing the retinal tumour(s).

Pathology

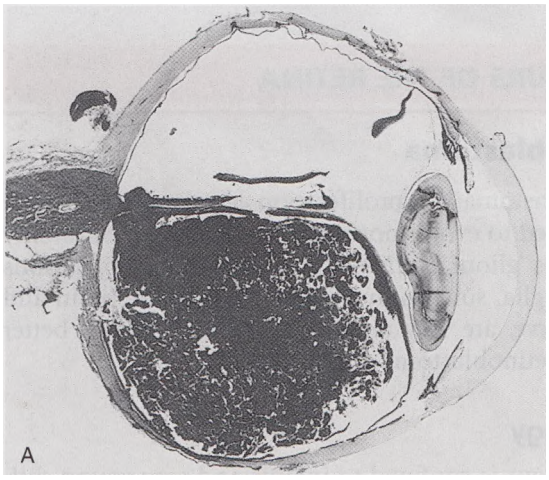
The growth consists chiefly of small round cells with large nuclei resembling the cells of the nuclear layers of the retina. Many of these stain poorly, showing that they are undergoing necrosis (Fig. 23.6A). Rosette-like formations of cells resembling the rods and cones may be found (Fig. 23.6B).

Retinoblastoma is invariably multiple. When noticed very early, as may occur in the fellow eye, a larger mass is seen surrounded by numerous punctuate satellites. Microscopically, minute deposits are seen scattered in various areas throughout the globe. It may grow mainly outwards, separating the retina from the choroid *(glioma exophytum),* or inwards towards the vitreous *(glioma endophytum);* there is no fundamental distinction between the two, but the ophthalmoscopic appearances differ. In the former, the condition resembles a detachment of the retina; in the latter polypoid masses, sometimes with haemorrhages on the surface, may be seen spreading into the vitreous.

Clinical course

The child is usually brought to the surgeon on account of a peculiar yellow reflex from the pupil, sometimes called leucocoria or 'amaurotic cat's eye' *(see* Fig. 23.8). Other modes of presentation include a convergent or divergent squint, cataract, buphthalmos, a hypopyon or proptosis. If left untreated retinoblastoma runs through the same stages as melanoma of the choroid: (i) the quiescent stage, lasting from 6 months to a year; (ii) the glaucomatous stage; (iii) the stage of extraocular extension and (iv) the stage of metastasis. The second stage results in enlargement of the globe, with apparent or real proptosis. Pain is severe during this stage, but is relieved when the tumour bursts through the sclera, an event that usually occurs at the limbus and is followed by rapid fungation. Metastasis first occurs in the preauricular and neighbouring lymph nodes, later in the cranial and other bones. Direct extension by continuity to the optic nerve (which is affected early) and brain is more common, while metastases in other organs, usually the liver, are relatively rare. Clinically a cauliflower-like mass arising from the retina is seen extending into the vitreous (exophytic type, Fig. 23.7). There is neovascularization on the surface with white areas of calcification. Vitreous or anterior chamber seedings are seen as fluffy whitish-grey deposits. The endophytic type of retinoblastoma presents as an exudative retinal detachment, the summit of which is immobile. Secondary glaucoma is common, hypopyon with esotropia is sometimes the presenting clinical picture.

Reese and Ellsworth developed a classification for intraocular retinoblastoma which was of prognostic significance for the control of local disease. At that time, most patients were treated by either enucleation (removal of the eye) or local therapies such as external beam radiation therapy and cryotherapy. This classification was used



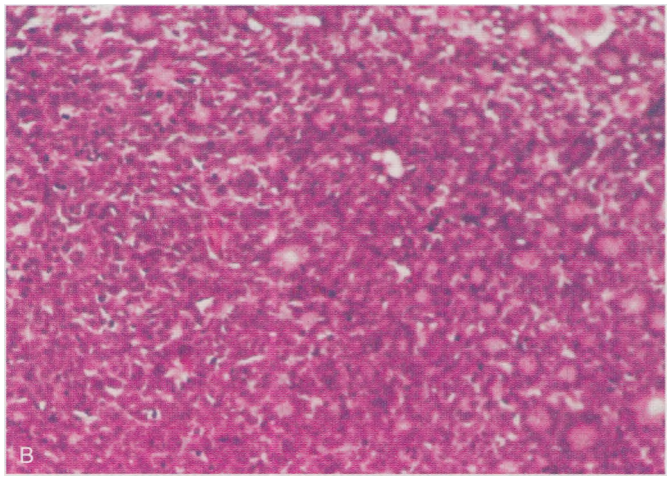


Fig. 23.6 (A) Exophytic retinoblastoma. The neoplasm is entirely external to the detached retina (By courtesy of Wolter). (B) Histopathological section of a well-differentiated retinoblastoma, showing Flexner–Wintersteiner rosettes (By courtesy of S Kashyap).

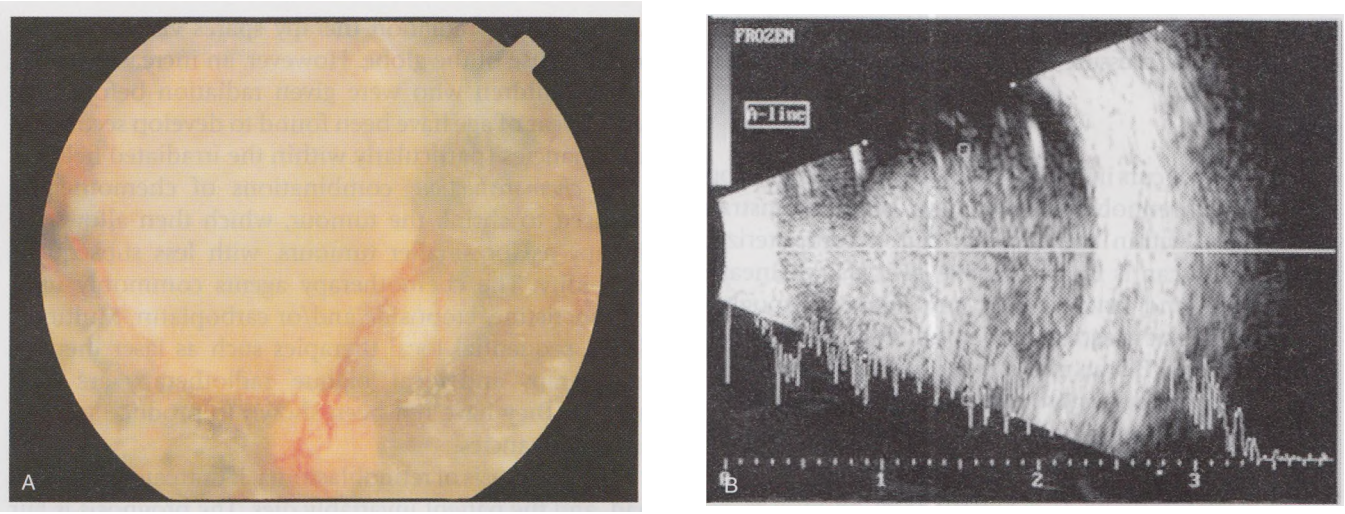


Fig. 23,7 Exophytic retinoblastoma. (A) Colour photograph showing areas of calcification; (B) ultrasound of a large retinoblastoma showing a V–Y pattern of internal reflectivity.

to predict which eyes were likely to survive local therapy and keep useful vision.

Group I. Very favourable for maintenance of sight:

- solitary tumour, smaller than 4 DD in size, at or behind the equator;
- multiple tumours, none larger than 4 DD in size, all at or behind the equator.

Group II. Favourable for maintenance of sight:

- solitary tumour, 4-10 DD in size, at or behind the equator;
- multiple tumours, 4-10 DD in size, behind the equator.

Group III. Possible to maintain sight:

- any lesion anterior to the equator;
- solitary tumour, larger than 10 DD in size, behind the equator.

Group IV. Unfavourable for maintenance of sight:

- multiple tumours, some larger than 10 DD in size;
- any lesion extending anteriorly to the ora serrata.

Group V. Highly unfavourable for maintenance of sight:

- massive tumours involving more than one half the retina;
- vitreous seeding.

Improved diagnostic techniques, including the indirect ophthalmoscope and new treatment options, underline the need for a revision of the Reese-Ellsworth classification. For example, anterior lesions, now easily recognized and treated, were categorized as a more advanced stage. Any vitreous seeding places the eye in group Vb, suggesting the worst possible prognosis. However, local vitreous seeding is now frequently treated successfully with brachytherapy.

Retinoblastoma can also be classified into intraocular and extraocular disease, in the tumour-node-others (TNO) system. The prognosis for 5-year disease-free survival in intraocular retinoblastoma is more than 90%. However, in extraocular extensions the 5-year disease-free survival is less than 10%.

Differential diagnosis

Several conditions occurring in children may give rise to similar signs, and cause great difficulty in diagnosis (Fig. 23.8). These have been grouped together under the term *pseudoglioma.* The chief ones are: (i) inflammatory deposits in the vitreous, with or without detachment of the retina following a plastic cyclitis or choroiditis; (ii) *Toxocara* infestation; (iii) congenital defects such as Norrie disease and persistent hyper-plastic vitreous at the back of the lens and (iv) retro-lental fibroplasia. In all cases both eyes should be well dilated and thoroughly examined ophthalmoscopically, under general anaesthesia if necessary. The intraocular pressure should be recorded, as it is

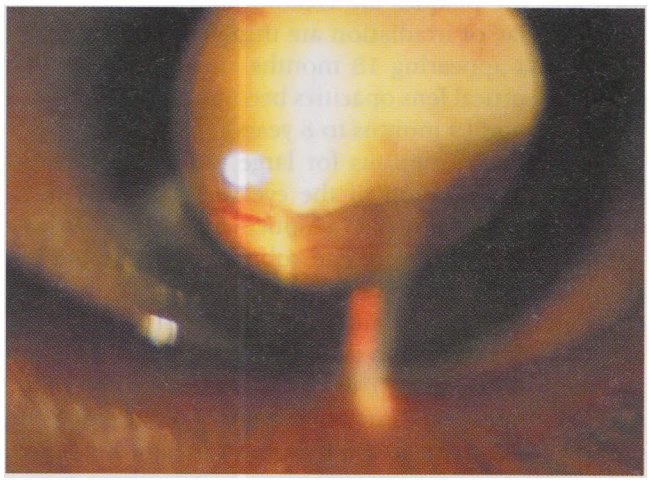


Fig. 23.8 Leucocoria.

raised more often seen in retinoblastoma, whereas lowered intraocular pressure is common in pseudoglioma.

Diagnosis

Calcification occurs in 75% of cases and is almost pathognomonic of retinoblastoma. X-rays can demonstrate calcification within the tumour, but a computerized tomography scan is more sensitive, as it also delineates the tumour and extension, if any, more thoroughly. Ultrasonography is extremely helpful in the diagnosis of retinoblastoma. B-scan ultrasonography displays a cauliflower-like mass arising from the retina, with or without a retinal detachment, or vitreous seedings. Extraocular spread can also be visualized. A scan through the mass shows a characteristic V-Y pattern (Fig. 23.7B), as the tumour tissue is echo dense giving rise to high spikes and areas of necrosis within the mass return spikes of lower amplitude. Supranormal spikes due to calcification can also be appreciated. The pseudogliomas have a very different ultrasonographic picture. Biochemical tests are rarely helpful. If the lactic dehydrogenase activity is raised in the aqueous relative to the serum level, it is suggestive of retinoblastoma.

Even when every precaution is taken, in some cases it is impossible to be certain of the diagnosis. Considering that the life of the patient is at stake, if the eye is rendered useless as an organ of sight, these should be treated as malignant.

Treatment

The treatment of small tumours is by local modalities such as cryotherapy for anterior lesions, photocoagulation for posterior ones, brachytherapy with ^{60}Co or 1251 can also be used. Radioactive cobalt discs sutured to the sclera over the site of the nodule are employed to deliver a dose of 4000 rad (~40 Gy) to the summit of the tumour in 1 week. The isotope^{125} I is increasingly being used and the plaques are custom-built for each child. Late sequelae of irradiation are thin greyish exudates at the macula appearing 18 months after treatment, and posterior cortical lens opacities becoming evident after a varying period (9 months to 8 years).

The treatment options for large tumours have now increased. Enucleation of the eye was the usual treatment for large tumours. The optic nerve was cut at least 10 mm long, and the cut end submitted to microscopic examination. Extension of the disease to the conjunctiva or orbital tissues warranted exenteration of the orbit. External beam radiation therapy is now one of the alternatives to enucleation. This confines the radiation to the affected sectors of the posterior segment of the globe and thus avoids damage to the lens and surrounding retina.

External beam radiation therapy spares vision and the cosmetic use of the globe. However, an increasing number of children who were given radiation before they were 1 year of age have been found to develop secondary malignancies (particularly within the irradiated field).

In *chemoreduction,* combinations of chemotherapy are used to shrink the tumour, which then allows for therapy as for smaller tumours, with less subsequent morbidity. The chemotherapy agents commonly used are vincristine, etoposide and/or carboplatin. Multimodality, sequential local therapies such as laser therapy, cryotherapy and local 'plaque' radiotherapy are then used, as they have not been shown to produce secondary malignancies.

The prognosis of retinoblastoma, if untreated, is always bad, and the patient invariably dies. The prognosis is fair if extraocular extension is avoided. In the absence of disease of the fellow eye the patient may be regarded as out of danger, if there is no recurrence in the orbit within 3 years, but the remaining eye should be carefully examined under dilatation at frequent intervals for a much longer period. Owing to its familial tendency the eyes of subsequent siblings or descendants should be carefully watched during infancy and childhood.

SUMMARY

Several different types of tumours affect the eye. Intraocular tumours arise from the uveal tract or retina. Retinoblastoma is the commonest intraocular malignancy in children and malignant melanoma of the choroid in adults. A large variety of therapeutic options are now available and sight saving procedures are getting wider acceptance in modern times.

Metastatic deposits from tumours in other parts of the body are usually from primary malignancies of the breast, lung, gastrointestinal tract, kidneys, prostate, thyroid and testes and are most commonly located in the choroid, but can also be seen in the iris. The metastatic tumours are, however, radiosensitive so they do respond to local radiotherapy. Some are also hormone dependent.

SUGGESTED READING

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Chapter 24

Injuries to the Eye

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The eye is protected from direct injury by the lids, eyelashes and the projecting margins of the orbit. Nevertheless, it can be injured in a variety of ways; by chemicals, heat, radiation and mechanical trauma.

CHEMICAL INJURIES

Alkalis

Injuries by caustics such as lime usually occur from fresh mortar or whitewash entering the eye or from laboratory alkalis. These may cause considerable damage to the eye because they penetrate and cause necrosis of the surface epithelium in a few seconds with occlusion of the limbal vasculature. This leads to a diminished vascularity of the anterior segment, corneal opacification and melting, cataract and symblepharon. Ammonia and sodium hydroxide are particularly harmful, as they cause necrosis of the cornea.

Immediately after the accident there is intense conjunctivitis and chemosis, but the cornea often looks clear, and it is therefore difficult to ascertain the severity of the injury. A drop of fluorescein solution will reveal the extent of the denuded area of epithelium. Circumferential limbal ischaemia and the degree of corneal clarity provide some indication of the final visual status of the patient (Fig. 24.1 and Table 24.1).

Prognosis should therefore be guarded, care being taken to impress upon the patient the gravity of the injury and the necessity for supervision. In the worst cases, the cornea is dull or opaque. In the succeeding days an eschar forms and is thrown off, followed by granulation of the injured conjunctiva and frequently

Table 24.1 Grading of ocular chemical injuries

Grade I	(mild) no limbal ischaemia
Grade II	(moderate) 180° limbal ischaemia with epithelial defect and clear cornea
Grade III	(severe) 180° limbal ischaemia with epithelial defect and hazy cornea
Grade IV	(severe) 270° limbal ischaemia with epithelial defect and hazy cornea

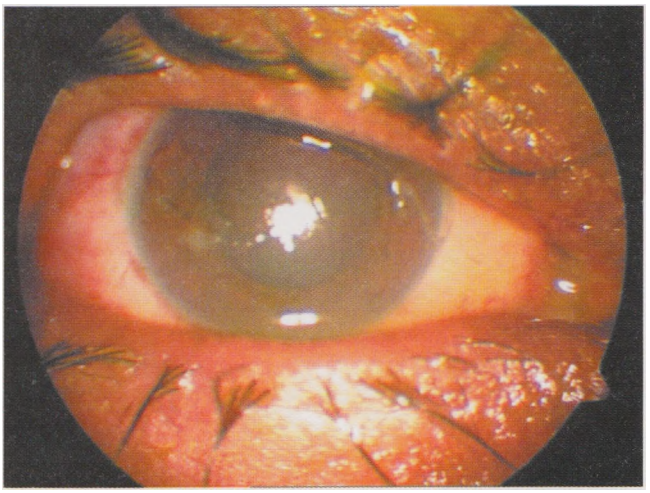


Fig. 24.1 Alkali burn. Ischaemia can be seen in the inferior 180° of the limbus and the cornea appears hazy.

by ulceration of the cornea. The corneal changes should be treated as an ulcer. In severe lime burns the entire cornea may be destroyed, perforation takes place and the eye shrinks. In less severe cases a porcelain-like, dense, vascularized leucoma forms and sight is lost. The chief danger resulting from the condition of the conjunctiva is damage to the ocular surface, with severe dry eye and adhesion of the lid to the globe. It is most likely to occur in the lower lid where the lower fornix is obliterated by organization of the granulation tissue. The symblepharon thus produced impedes the movements of the globe and may even interfere with its nutrition. Every precaution must be taken to prevent its occurrence. Limbal ischaemia leads to severe damage of the limbal stem cells. This causes persistent corneal epithelial defects and conjunctivization of the corneal epithelium.

Treatment

In injury caused by caustics the excess of deleterious material must be removed at the earliest by a copious and immediate irrigation with normal saline. An intravenous infusion line is useful in directing a steady, controlled flow of saline onto the ocular surface. All fornices should be washed and irrigation continued till the pH returns to normal or for a minimum of 30 minutes. There should be no delay in instituting therapy and, if saline is not immediately available, the eye should be copiously irrigated at once with water. Particles of lime must be perseveringly picked out with forceps after instillation of a local anaesthetic. An antibiotic ointment or drops and cycloplegics should be instilled.

Corticosteroids are potent agents in reducing the inflammatory reaction and prevent the formation of excessive granulation tissue, which determines the development of symblepharon. They can be used topically as drops or ointment for the first 10 days, together with acetazolamide tablets to lower the intraocular pressure. Thereafter, steroids are stopped as they impair healing and may precipitate corneal melting. Ascorbic acid and tetracyclines are given topically and systemically to enhance collagen formation. To inhibit collagenolysis and stromal damage, 10% sodium citrate, 5% N-acetylcysteine or 1% medroxyprogesterone eye drops are useful adjuncts.

Symblepharon may be prevented by sweeping a glass rod well coated with a lubricant round the upper and lower fornices, so that they are well packed with ointment. This procedure should be repeated several times a day, depending upon the severity of the case. The fitting of a contact lens separates the two mucosal surfaces and prevents their adhesion.

Revascularization of the limbus and re-epithelialization of the ocular surface can be stimulated by a limbal cell transplant or amniotic membrane graft.

Acids

Acids (hydrochloric, sulphuric) coagulate the surface layers and do not penetrate the eye. They should also be treated by copious irrigation with normal saline or any clean fluid at hand. Acids can also produce limbal ischaemia. Symblepharon and shortening of the fornices occur as the raw surfaces heal, and this needs to be taken care of assiduously, as described above.

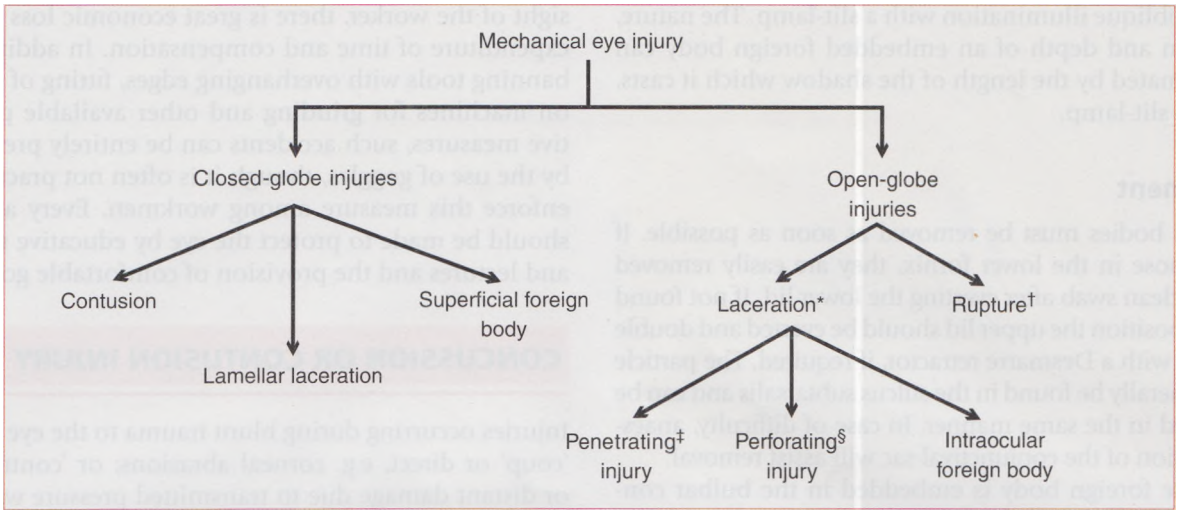
MECHANICAL INJURIES

Mechanical injury to the globe can occur in a variety of ways and produce myriad clinical sequelae. The Ocular Trauma Classification Group has attempted to develop a uniform classification system for mechanical injuries to the eye, based on primary evaluation. Injuries are broadly divided into two categories:

1. open -globe—ful 1-thickness defects in the corneoscleral coat of the eye; and
2. closed-globe—ocular injury without a full-thickness defect of the coats.

A number of types of injury are included in each category, which may occur alone or in various combinations *(see* Flowchart 24.1). Three zones are described in both these categories, from the anterior segment backwards, and the injury is further graded with regard to visual acuity and the presence or absence of an afferent pupillary defect.

Open-globe injuries can be secondary to blunt trauma, when they are known as *ruptures* of the globe, with an inside-to-outside break in the ocular coats. Open-globe injuries may also be caused by sharp objects. The term *laceration* is used to denote a full-thickness



Flowchart 24.1 Classification of ocular trauma.*Outside-in injury; †inside-out injury; ^single break in eye wall; §through-and-through injury of globe, dual breaks or double perforation. (Adapted from Kuhn and associates, *Ophthalmology* 1996; 103:240-3.)

outside-to-inside break in the ocular coats. This can be further sub-divided into a *penetrating injury* if the object traverses the coats only once, or a *perforating injury* (earlier known as a 'double perforation'), if both an entry and exit wound are present, as in missiles.

Closed-globe injuries generally follow blunt trauma and are then known as contusion or concussional injuries.

Superficial foreign bodies are frequently found on the cornea and conjunctiva.

Lamellar laceration, as the name implies, refers to a partial-thickness injury of the coats.

Superficial foreign bodies

Foreign bodies, which are usually small particles of dust, emery, steel, etc. may impinge upon the conjunctiva or cornea. In the former case they cause sudden discomfort and reflex blinking. The foreign body sticks to the palpebral conjunctiva and is liable to be dragged across the cornea, which it excoriates. It may be washed by tears towards the inner canthus, and then into the nasal duct; more frequently, it becomes lodged at about the middle of the upper sulcus subtarsalis where it is most likely to irritate the cornea, or in the upper fornix, or it may occasionally become embedded in the bulbar conjunctiva. Fairly large foreign bodies, e.g. a grain of corn, may be retained for a long time in the upper fornix and give rise to severe irritation and some discharge. They may be overlooked unless the upper lid is double everted. They are generally embedded in a mass of granulation tissue, which may simulate the cockscomb type of tuberculosis. The wing cases of insects and husks of seeds may adhere to the cornea by their concave surfaces, usually at the limbus, for several weeks.

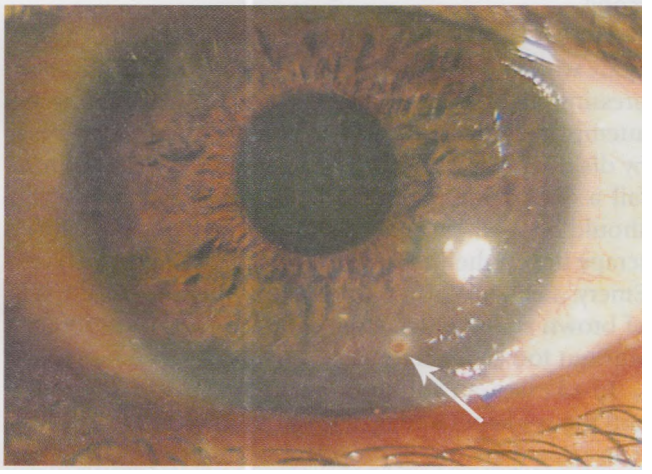


Fig. 24.2 Metallic foreign body on the cornea, with a deposition of rust.

Particles of steel and emery are very liable to fly straight onto the cornea (Fig. 24.2) and penetrate into the epithelium or substantia propria. Larger particles of steel or, less commonly, stone, glass, etc. may perforate the globe. When situated in the cornea they cause immense pain and irritation. The pupil is often constricted. If not removed they expose the cornea to the dangers of infection by organisms in the conjunctival sac with resultant ulceration, which may lead to the extrusion of the foreign body in the slough. The ulcer thus formed may heal, but if virulent organisms are present a spreading ulcer, with or without hypopyon, may develop.

It is not easy to discover a foreign body on the cornea. The use of fluorescein will nearly always reveal the position of a foreign body. In case of doubt, the eye should be anaesthetized and the cornea thoroughly examined

under oblique illumination with a slit-lamp. The nature, position and depth of an embedded foreign body can be estimated by the length of the shadow which it casts, using a slit-lamp.

Treatment

Foreign bodies must be removed as soon as possible. If lying loose in the lower fornix, they are easily removed with a clean swab after everting the lower lid. If not found in this position the upper lid should be everted and double everted with a Desmarre retractor, if required. The particle will generally be found in the sulcus subtarsalis and can be removed in the same manner. In case of difficulty, anaesthetization of the conjunctival sac will assist removal.

If the foreign body is embedded in the bulbar conjunctiva, it should be removed by a foreign body spud or fine forceps under topical anaesthesia. A disposable sterile hypodermic needle may also be used.

Foreign bodies from the cornea are removed under magnification using the slit-lamp or operating microscope.

The eye is anaesthetized and the surgeon holds the lids apart with the first and second fingers of his left hand, pressing slightly backwards so as to steady the globe. An attempt may first be made to remove the foreign body by dislodging it with a sterilized spud. If repeated efforts fail a disposable hypodermic (26 or 27 gauge) needle should be used. The greatest care should be taken not to scrape the epithelium more than is absolutely necessary. Emery, steel and iron particles leave behind a little ring of brown stain, which should be scraped off if possible without too much trauma.

In all cases, an antibiotic ointment should be applied and the eye kept bandaged for a day. If ulceration occurs, it is treated in the appropriate manner. Special attention should be paid to particles of stone, which show a greater tendency than metal to cause infective ulceration, probably because metallic particles are often hot and therefore sterile when they enter the eye.

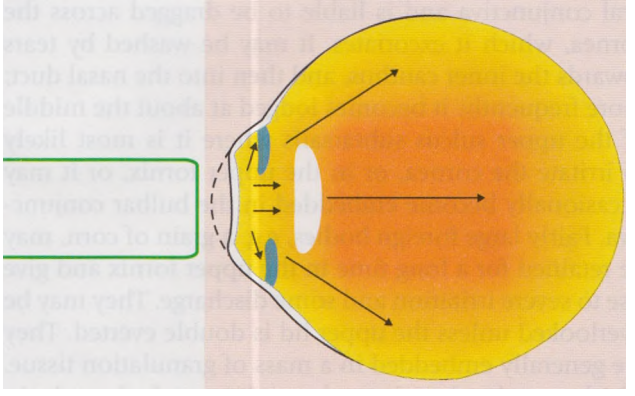
Occasionally, sharp steel and other particles penetrate deep into the cornea without perforating it. The efforts made to remove them may push them in still deeper or even into the anterior chamber. When such an accident is feared, special precautions must be adopted. If the particle is magnetizable, magnetic removal should be tried, but it is usually necessary to incise the cornea overlying the foreign body. However, this method may fail, particularly if the particle is small. If the foreign body escapes into the anterior chamber it must be removed by other methods.

Prophylactic measures: Foreign bodies in the eye are extremely common in industrial workers, especially in those working with grinding tools, lathe work or hammering on a chisel. Apart from endangering the sight of the worker, there is great economic loss due to expenditure of time and compensation. In addition to banning tools with overhanging edges, fitting of guards on machines for grinding and other available preventive measures, such accidents can be entirely prevented by the use of goggles, though it is often not practical to enforce this measure among workmen. Every attempt should be made to protect the eye by educative notices and lectures and the provision of comfortable goggles.

CONCUSSION OR CONTUSION INJURY

Injuries occurring during blunt trauma to the eye can be 'coup' or direct, e.g. corneal abrasions; or 'contrecoup' or distant damage due to transmitted pressure waves as in commotio retinae. Injuries by blunt objects vary in severity from a simple corneal abrasion to rupture of the globe. Numerous lesions may result; indeed, every part of the eye may be so injured by a contusion as to seriously diminish vision. Moreover, in some cases, the changes are delayed or progressive so that *in all cases a guarded prognosis should be given and the patient kept under review for months to years.*

As a general rule, either the anterior segment of the eye in front of the iris-lens diaphragm, or the posterior half, is preferentially affected. The mechanism is as follows. When a force impinges upon the cornea this tissue is thrust inwards and may even be forced against the lens and iris; the wave of aqueous pushes these structures backwards and as the compression wave rebounds from the back of the eye, they are thrust forwards again (Fig. 24.3). They may thus be severely traumatized. At the same time, there is a horizontal wave of pressure striking the retina and choroid as well as the angle of the anterior chamber, which may do considerable damage.



Fig, 24.3 Diagrammatic representation of the effect of a concussion injury and the consequent deformations of the eyeball.

Table 24.2 Ophthalmic effects of contusion or concussion injury

Ocular tissue involved	Clinical manifestations
Orbit	Blow-out fracture of medial wall or floor
	Orbital haematoma
	Carotid–cavernous fistula
Eyelids	Haematoma
	Avulsion of the lower lid
Conjunctiva	Subconjunctival haemorrhage
Anterior uvea	Hyphaema
	Tears of the iris sphincter and iridodialysis
	Angle recession and cyclodialysis
Lens	Rosette cataract
	Subluxation of the lens
	Rupture of the anterior or posterior capsule
Sclera	Rupture, commonly at the limbus or behind the insertion of the recti
Vitreous	Haemorrhage
Choroid	Choroidal rupture
	Suprachoroidal haemorrhage
Retina	Retinal or subretinal haemorrhage
	Retinal oedema, commotio retinae
	Retinal dialysis
	Macular oedema or hole
Optic nerve	Optic nerve avulsion
	Haemorrhage of the optic nerve sheath

Delayed complications such as secondary glaucoma, cataract, vitreous haemorrhage, retinal detachment or traumatic iridocyclitis may follow.

The various conditions resulting from contusion or concussional injury are given in Table 24.2 and briefly described below.

Cornea

The cornea may suffer an abrasion, deep opacities may develop, or partial or complete rupture may occur.

A simple *abrasion* may be caused, which is recognized by distortion of the corneal reflex and by the use of fluorescein.

Recurrent erosion (recurrent traumatic keratalgia): This may occur spontaneously but is particularly liable to happen after scratches especially with babies' fingernails. The abrasion, however produced, usually heals quickly, but is followed some days, weeks, or even months later by acute pain and lacrimation, generally on first opening the eyes in the morning. If the cornea is then stained with fluorescein an abrasion will be found, usually at the original site but sometimes elsewhere, or there may be one or a group of vesicles. The attack rapidly passes off with appropriate treatment, but often recurs repeatedly, particularly on waking up in the morning. There is no doubt that in these cases the epithelium is abnormally loosely attached to Bowman's membrane, and is liable to be torn off by the lid on waking. Early attacks should be treated in the same manner as a simple abrasion, but if the attacks are repeated, debridement is indicated, whereby the loose epithelium is removed and the eye padded for 48 hours so that firm healing takes place. An alternative is the use of a bandage soft contact lens.

A *deep opacity* in the substance of the cornea may result from a contusion. Delicate grey striae may be seen interlacing in different directions, due to oedema of the corneal stroma or occasionally to wrinkling of Descemet's membrane. It generally clears up without leaving a permanent opacity. There may be ruptures in Descemet's membrane as in a forceps delivery (Fig. 24.4), followed by acute oedema of the stroma.

Blood staining of the cornea: This occasionally results from a contusion, which has caused a hyphaema usually accompanied by a rise of intraocular pressure and endothelial damage. The entire cornea is at first stained, the colour varying according to the duration of the condition. It may be reddish-brown or greenish; in the latter case the condition simulates dislocation of the clear lens into the anterior chamber. The cornea gradually and very slowly clears from the periphery towards the centre, the complete process taking 2 years or more. Microscopically, there are myriads of minute, highly refractile rods packed in the lamellae of the stroma, and sometimes round granules of pigment in the corneal corpuscles. These are derivatives of haemoglobin, which may or may not contain iron and are removed slowly by phagocytic action. In the absence of other causes of defective vision, sight may eventually be completely restored but is usually permanently impaired.

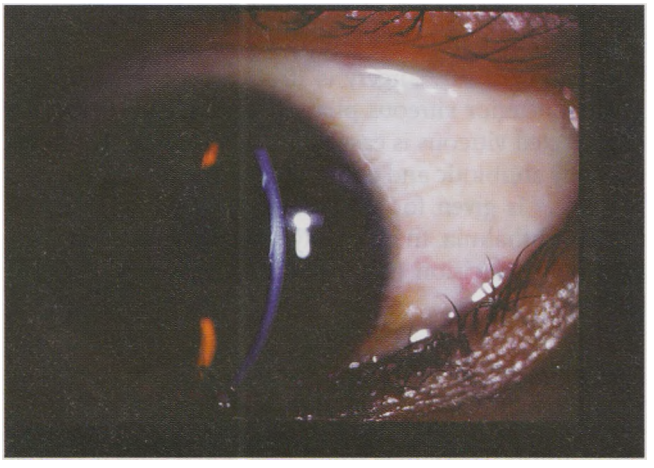


Fig. 24.4 Vertical Descemet's membrane tears caused by ocular pressure of forceps during a difficult obstetric delivery.

Sclera

Rupture of the globe: Rupture of the sclera is an open-globe injury occurring from inside outwards. This is generally due to its being suddenly and violently forced against the orbital walls. It is often caused by a fall upon some projecting object, such as a knob or a key in a door. The force usually comes from the inferotemporal direction, where the eyeball is least protected by the orbital margin and the globe is pushed against the pulley of the superior oblique muscle. The sclera gives way upwards and at its weakest part, in the neighbourhood of the canal of Schlemm or just posterior to the insertion of the recti. The wound runs obliquely outwards and backwards from the canal through the sclera to appear more or less concentric with the corneal margin and about 3 mm behind it. The conjunctiva is often intact, but there are always severe injuries to other parts of the eye. The iris is generally prolapsed or tom away (iridodialysis) or retroflexed. The lens may be expelled from the eye, escape under the conjunctiva (subconjunctival dislocation of the lens) or be forced back into the vitteous, in which case the anterior chamber becomes deep. Intraocular bleeding may be profuse, filling the anterior chamber and vitreous, and the condition may be complicated by a detachment of the retina with or without subretinal or suprachoroidal haemorrhage.

Treatment

The eye must be carefully examined using lid retractors, under anaesthesia if necessary. The full extent of the rupture is identified and prolapsed uvea, if previously covered by conjunctiva, is reposited or other-wise excised. The edges of the sclera are identified and interrupted mattress 8-0 nylon or polypropylene sutures applied to reappose the tissues, starting at definite landmarks such as the limbus. If the rupture extends posterior to the ciliary body, gentle cryotherapy may be applied to prevent a future retinal detachment. If the rupture extends posteriorly, vitreous haemorrhage and a late retinal detachment are common. A vitreoretinal surgery may also be required. The best timing of this surgery is 10-14 days after the injury as the posterior vitreous phase detaches and removal of the affected vitreous is easy and less traumatic. Local and systemic antibiotic and corticosteroid therapy is essential. The latter is given for a few months to prevent sympathetic ophthalmia. In extremely severe cases with no light perception, excision of the collapsed globe is the only option.

Iris and ciliary body

A violent and intractable *post-traumatic iridocyclitis* is not uncommon. These may suffer functional defects or may be actually torn. A *traumatic miosis* due to irritation of the nerves occurs initially in every severe contusion.

In *traumatic mydriasis* following a contusion, the pupil is large and immobile and usually remains moderately dilated permanently.

The substance of the iris is often torn. The most common lesions are minute *ruptures in the pupillary margin* which are of little significance, while *radiating lacerations* of the iris, sometimes extending to the ciliary margin, are rare. *Iridodialysis,* in which the iris is torn away from its ciliary attachment for a variable distance, occurs more frequently (Fig. 24.5). A black biconvex area is seen at the periphery, and the pupillary edge bulges slightly inwards forming a 'D'-shaped pupil. With the ophthalmoscopic mirror a red reflex can be obtained through the peripheral gap, and the fibres of the suspensory ligament (lens zonules) and the edge of the lens may be visible. Uniocular diplopia may be produced by this injury. In extensive iridodialysis, the detached portion of the iris may be completely rotated so that the pigmented back of the iris faces forwards (*anteflexion of the iris).* The iris becomes re-attached only in exceptional cases but, apart from other injury, the lesion rarely causes serious consequences.

In *traumatic aniridia* or *irideremia* the iris is completely torn away from its ciliary attachment, contracts into a minute ball, and sinks to the bottom of the anterior chamber, where it may be invisible. Rarely, the same appearance is caused by *total inversion* or *retroflexion* of the iris, the whole iris being doubled back into the ciliary region out of sight. More commonly, inversion is partial so that the appearance of a coloboma *(see* pp. 253-254) is obtained, but the fibres of the suspensory ligament cannot be seen. The ciliary body may also be torn or ruptured near its anterior attachment *(angle recession,* Fig. 24.6) resulting in its subsequent retraction with a deepened anterior chamber and a tendency to glaucoma.

Histologically, there are longitudinal tears in the face of the ciliary body, which split the circular from the radial fibres and result in angle recession. Any injury to the iris, especially angle recession, leads to a haemorrhage

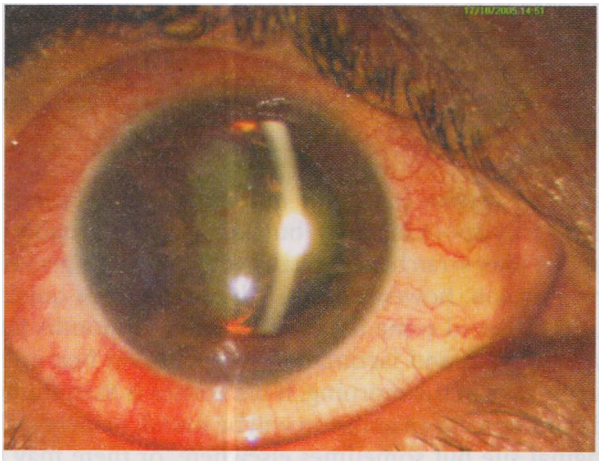


Fig. 24.5 Iridodialysis.

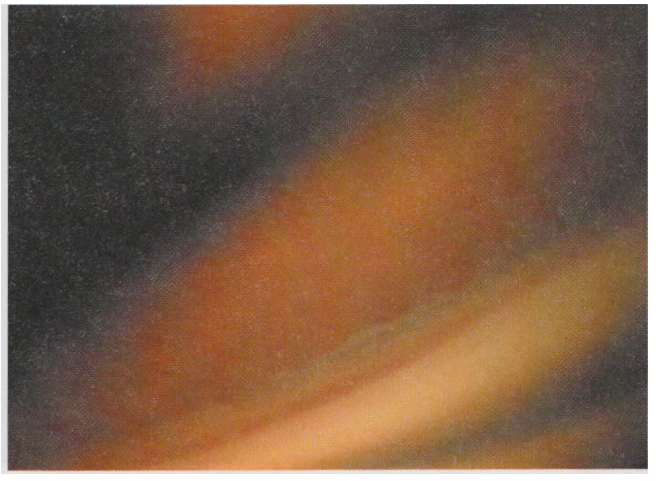


Fig. 24.6 Angle recession. There is a tear between the circular and longitudinal muscles of the ciliary body to the right of the picture resulting in a widening of the grey ciliary body band. Blood can be seen in the canal of Schlemm.

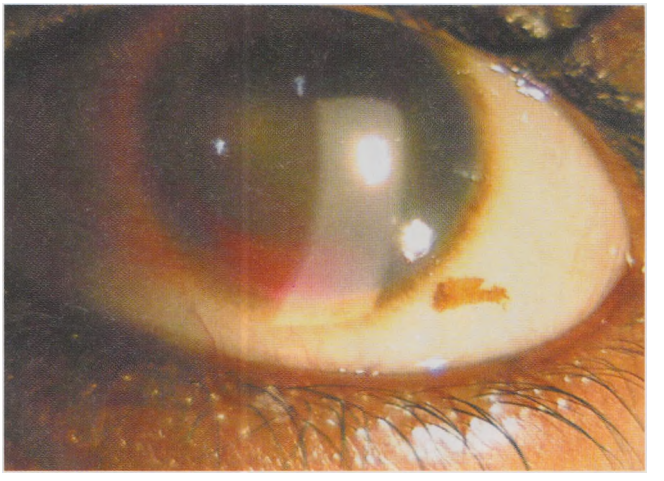


Fig. 24.7 Traumatic hyphaema.

in the anterior chamber (hyphaema). This commonly reabsorbs rapidly if it fills less than half the anterior chamber. If it is more extensive, it clots, leading to pupillary block or a trabecular block. In all these cases there is usually a hyphaema, secondary rise of intraocular pressure in the long term as well as other injuries.

Traumatic hyphaema (Fig. 24.7) may be trivial or serious. Admission to hospital is advisable if the hyphaema occupies more than half the anterior chamber, and the patient observed for 72-96 hours because of the danger of secondary haemorrhage. The affected eye is patched and the patient made to rest with the head elevated. Atropine and steroids have no part in the management. Topical and systemic antiglaucoma therapy is used if the intraocular pressure is raised. Aspirin is to be avoided and treatment with sodium edetate may be used to prevent rebleeding in severe cases. If pain is unrelieved or there is a threat of blood staining the cornea, evacuation of the central clot is carried out using a two-way aspiration cannula, which preserves the anterior chamber. This may be accompanied by a glaucoma-filtering surgery, if the intraocular pressure cannot be controlled medically.

The *treatment* consists of anti-inflammatory medications given locally. Atropine should be instilled in iridodialysis, but avoided in ruptures of the iris or if the lens is subluxated. When the eye has settled, if the iridodialysis is gross and causes symptoms such as diplopia, the tom peripheral edge of the iris may be anchored with a 9-0 or 10-0 prolene suture into a scleral incision just behind the limbus.

Lens

The lens may show cataractous changes or be dislocated. In some cases a circular ring of faint or stippled opacity is seen on the anterior surface of the lens due to

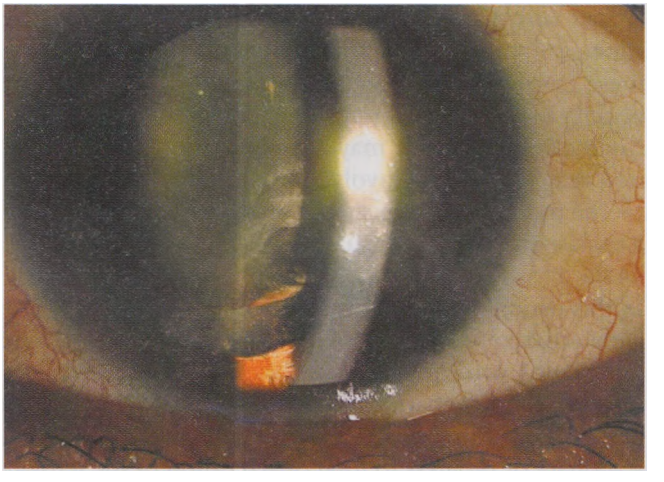


Fig. 24.8 Traumatic mydriasis. A Vossius ring and inferior subluxation of the lens seen as a deepening of the anterior chamber.

multitudes of brown amorphous granules of pigment lying on the capsule (*Vossius ring,* Fig. 24.8). It usually has about the same diameter as the contracted pupil, and is due to the impression of the iris on the lens, produced by the force of the blow driving the cornea and iris backwards. Minute, discrete sub-capsular opacities may be seen after resorption of the pigment.

Concussion cataract: This may assume many varied forms. It is due partly to the mechanical effects of the injury on the lens fibres and largely to the entrance of aqueous due to damage to the capsule, either secondary to impairment of its semipermeability or often the result of actual tears. The tears, particularly if they are small and peripheral, may not be clinically visible. They frequently occur at the thinnest portion of the capsule covering the posterior pole of the lens. Sometimes, especially if

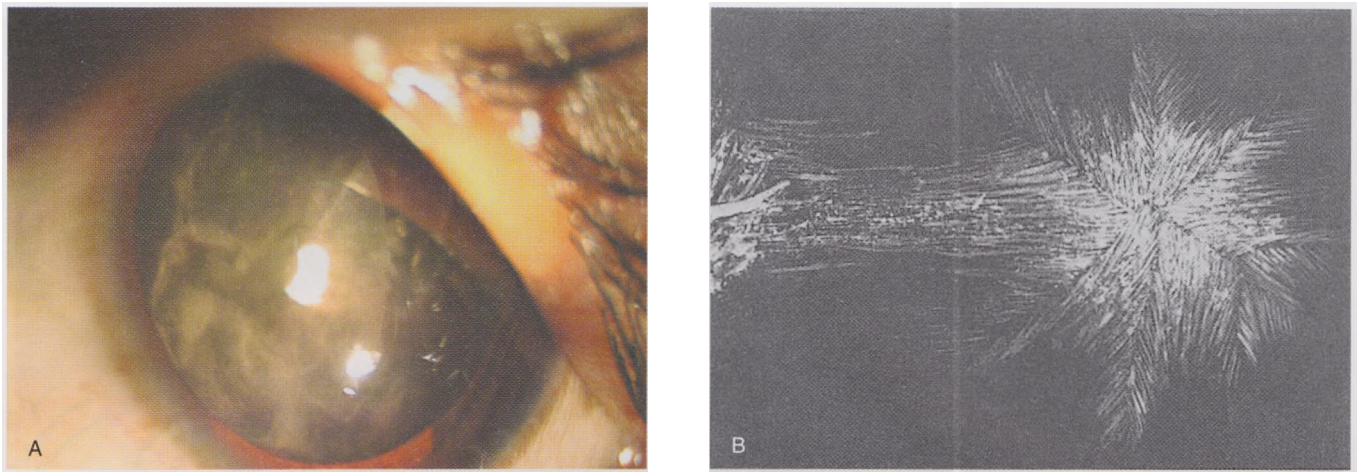


Fig. 24.9 (A) Traumatic cataract following a concussional injury, showing a posterior rosette and zonular dialysis to the left. (B) Rosette-shaped cataract at the posterior pole following perforation of the lens by a foreign body. A disturbance in the lens along the track of the foreign body is seen.

they are covered by the iris, such tears are rapidly sealed, at first with fibrin and later by the proliferation of the subcapsular epithelium which secretes a new capsule. In these cases the entrance of aqueous is stopped and the opacity in the lens may remain stationary or even regress. Alternatively, the tear may remain open and opacification may progress to involve the entire lens.

The most typical appearance after concussion is that of a *rosette-shaped cataract,* usually in the posterior cortex (Fig. 24.9A and B), sometimes in the anterior cortex or both. In this condition an accumulation of fluid marks out the architectural arrangement of the lens (*see* Chapter 1). The star-shaped cortical sutures are therefore delineated and feathery lines of opacities outlining the lens fibres radiate from them. The rosette may occasionally disappear, remain stationary or progress to total opacification of the lens—a complication which may appear rapidly within a few hours after the injury, or may be delayed for many months.

A *late rosette-shaped cataract* may develop in the posterior cortex 1 or 2 years after a concussion. It is smaller and more compact than the early type and its sutural extensions are short.

The treatment of such cataracts is on general lines *(see* p. 271) unless the rapid intumescence of the lens leads to a secondary glaucoma which may then require immediate treatment. Any surgical interference should be delayed for some months until the final outcome is apparent. If possible, the eye should be left until all signs of inflammation have subsided, following which it should be treated as indicated for unilateral cataract. Posterior capsular integrity should be assessed by ultrasonography so that the type of cataract surgery employed and the intraocular lens to be inserted can be tailored to the eye.

Dislocation of the lens: This may occur when the relatively fragile suspensory ligament or zonules are torn by the to-and-fro wave of pressure set up by the contusion. If the tear is partial, the lens may be *subluxated* so that it is displaced laterally and sometimes slightly rotated. This leads to a variation in the depth of the anterior chamber, which is deeper in the part unsupported by the lens. With the pupil dilated, the edge of the lens may be seen as a grey convex line by oblique illumination, but is more readily and unmistakably identified as a black line with the ophthalmoscope. The lack of support to the iris causes tremulousness when the eye is moved *(iridodonesis).*

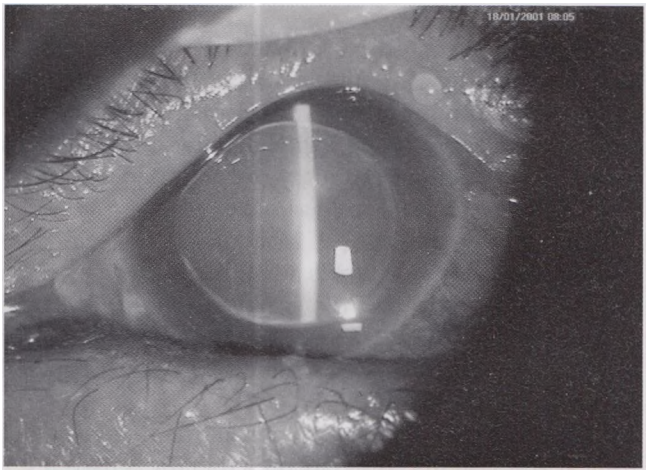


Fig. 24.10 Anteriorly dislocated lens.

If the rupture to the suspensory ligament is complete the lens is *dislocated,* usually into the vitreous. Sometimes it remains clear and can be seen only with difficulty, at other times it turns opaque and appears as a yellow mass. Alternatively, particularly if the blow has been slanting, the lens is dislocated into the anterior chamber (Fig. 24.10), an accident which may follow a trivial injury if the lens is shrunken. A clear lens in the anterior chamber is not always easily recognized, but it

does not remain dear for long and the diagnosis is then easy. It is more globular than normal owing to its freedom from the restraint of the suspensory ligament, and when still clear, looks like a globule of oil in the anterior chamber. With oblique illumination it has a golden rim, due to total reflection of the light. This is the exact opposite of the total reflection when the edge of the lens is seen with the ophthalmoscope, the light being then totally reflected away from the observer's eye. The lens in the anterior chamber causes spasm of the sphincter pupillae, which may occur at the point where it is passing through the pupil. An iridocyclitis or an intractable secondary glaucoma is then set up so that vision is usually completely lost if the anteriorly dislocated lens is allowed to remain in that position.

Dislocation of the lens always causes a considerable disturbance of vision. In subluxation there is astigmatism, which is greatly increased by tilting of the lens. The slackening of the suspensory ligament causes increased curvature and lenticular myopia which, however, may be more than compensated by its backward displacement.

If the lens is displaced so much laterally that the edge crosses the pupil, uniocular diplopia is present. Through the aphakic area of the pupil the eye is highly hypermetropic, through the phakic portion it may be myopic, in addition to which the periphery of the lens acts as a prism. Ophthalmoscopic examination by the indirect method in these conditions shows two images of the disc differing considerably in size, and by the direct method the fundus may be observed through the phakic or aphakic portion of the pupil. In total dislocation into the vitreous (Fig. 24.11), the effect is similar to that of the old cataract operation of couching; the pupillary area is aphakic and the refraction is highly hypermetropic, requiring cataract spectacles for its correction. In these cases the vision may be retained for many years.

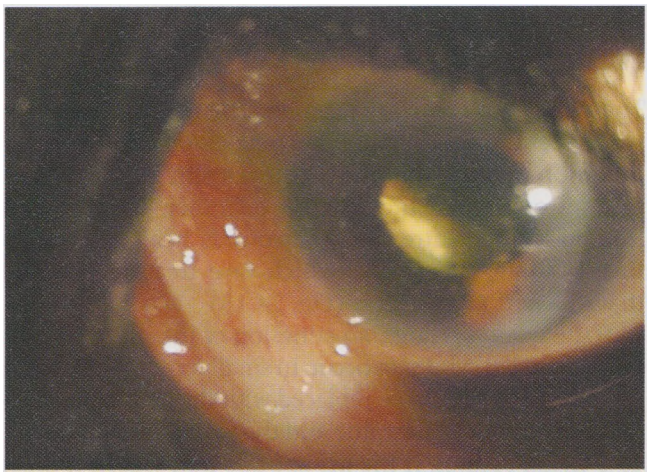


Fig. 24.11 Posteriorly dislocated lens.

Treatment

In forward dislocation the lens should be extracted by a cryoprobe or vectis combined with anterior vitrectomy as early as possible. Vision may be improved by suitable glasses in cases of total luxation into the vitreous and subluxation. In the latter case, it is usually impossible to correct the astigmatism and a correction for the aphakic part of the pupil may give better visual results. A lens dislocated into the vitreous should be left there, but if uveitis or glaucoma supervene, extraction of the lens is necessary, together with a vitrectomy.

Vitreous

The vitreous is usually disorganized to some extent by either *anterior or posterior detachment* or by a combination of both. The most common occurrence is the appearance of clouds of fine *pigmentary opacities.* The vitreous framework, when examined with the slit-lamp, is bespangled with innumerable golden-brown dots derived from the uvea.

Haemorrhage into the vitreous is also common. The whole vitreous chamber may be filled with blood so that no reflex is obtained with the ophthalmoscope, but with oblique illumination a dull red hue may be seen, especially if the pupil is dilated.

Choroid

The choroid may be torn or haemorrhages may occur.

Rupture of the choroids: This follows a severe contusion by a blunt body striking the front of the eye. Immediately after the injury, the view is obscured by extravasation of blood. When it has been absorbed, the rupture, usually not far from the disc, concentric with it and on its temporal side, is seen as a curved white streak over which the retinal vessels pass and which rapidly becomes pigmented along its edge (Fig. 24.12); the white appearance is due to the sclera

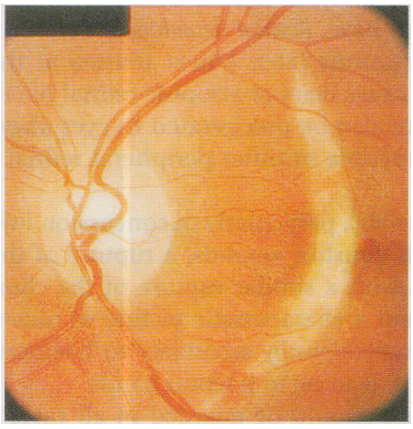


Fig. 24.12 Choroidal rupture.

shining through. Sometimes multiple ruptures occur, more or less concentric with each other. If the choroid is ruptured near the macula, loss of central vision results, but simple ruptures in which the macula is not involved cause little impairment of vision. These are treated conservatively with steroids to decrease inflammatory changes and the extent of later chorioretinal scarring. A late complication could be choroidal neovascularization.

A contusion may also cause a *choroidal or supra-choroidal haemorrhage.*

Retina

The retina may suffer oedematous or degenerative changes, be torn, or haemorrhages may occur in it.

Commotio retinae (Berlin oedema): This is a common result of a blow on the eye. A milky white cloudiness due to oedema appears over a considerable area at the posterior pole which may sometimes disappear after a few days when vision is usually restored. In other cases, although vision may be good at first, central vision gradually diminishes, the loss of function being associated with the development of pigmentary deposits at the macula. The presence of *intraretinal haemorrhage* signals a more severe involvement.

Traumatic macular degeneration: This may often appear slight and the fine pigmentary changes are easily overlooked immediately after the accident. The pigmentation, however, which mainly aggregates at the fovea, has a tendency to increase progressively and has a serious and permanent effect on central vision. Alternatively, oedema may lead to cystic changes at the macula and, on the rupture of a cyst, a *macular hole* may be formed. This appears clinically as a round or oval, deeply red patch, as if a hole has been punched out. In the stage of cyst formation some central vision may remain, but if a hole is formed centrally, vision is lost.

Retinal breaks can be induced and are commonly superonasal dialyses caused by differential traction at the vitreous base. *Retinal detachment* may occur slowly, weeks to months later. Direct trauma at the equator can rarely cause tears or atrophic retinal breaks. Retinal breaks may also be precipitated in eyes already suffering from myopia or other peripheral retinal degenerations.

Occasionally, particularly in concussion injuries associated with gunshot wounds, a rupture of the retina is associated with a similar rupture of the choroid. Such cases present a characteristic picture of *traumatic proliferative chorioretinopathy* secondary to haemorrhage into the vitreous, leading to traction bands.

Prognosis should be guarded in all cases of serious blows upon the eye.

Optic nerve

The optic nerve may be injured in fractures of the base of the skull by fragments of the optic canal. Injuries by sticks, knives or other penetrating instruments are rare. Avulsion of the optic nerve is very rare in civilian life but occurs in gunshot wounds of the orbit. Haemorrhages of the optic nerve sheath and contusion injuries of the nerve are common in road traffic accidents.

Intraocular pressure

This may be seriously disturbed following concussion injuries, particularly if they are severe. A condition of *hypotony* or, alternatively, of *traumatic glaucoma* may supervene. Angle recession is associated with traumatic effects on the outflow channels leading to an insidious glaucoma. *Ghost cell* obstruction of the trabeculae in long-standing vitreous haemorrhages may also induce a secondary glaucoma. Such glaucoma may be controlled by medication, but is sometimes intractable even to operative treatment.

PENETRATING INJURIES

Penetrating injuries caused by sharp instruments or foreign bodies are all potentially serious and should be treated as emergencies. The patient should immediately have an eye shield applied and be thoroughly examined under general anaesthesia. Evaluation for repair should be done at the same time. The gravity of such injuries is due to the immediate damage to the eye, *post-traumatic iridocyclitis* (a common sequel to a perforating wound), the introduction of *infection* and *sympathetic ophthalmitis,* one of the most dreaded complications of perforating wounds *(see* p. 387).

Wounds of the conjunctiva

Wounds of the conjunctiva are common and should be sutured with absorbable sutures.

Wounds of the cornea and sclera

These may be linear or lacerated. The margins swell up soon after the accident and become cloudy due to accumulation of fluid, thus facilitating closure of the wound and restoration of the anterior chamber. If small and limited to the centre, corneal wounds heal well unless they become infected, in which case treatment is like that of a perforating ulcer (Fig. 24.13).

If the wound is large, an adhesion of the iris or its prolapse is almost certain to occur. In small recent injuries, the prolapsed iris should be replaced with the help of intraocular miochol or pilocarpine and the wound repaired with 10-0 nylon sutures. If the iris appears non-viable, it must be abscised and the edges of the wound sutured directly

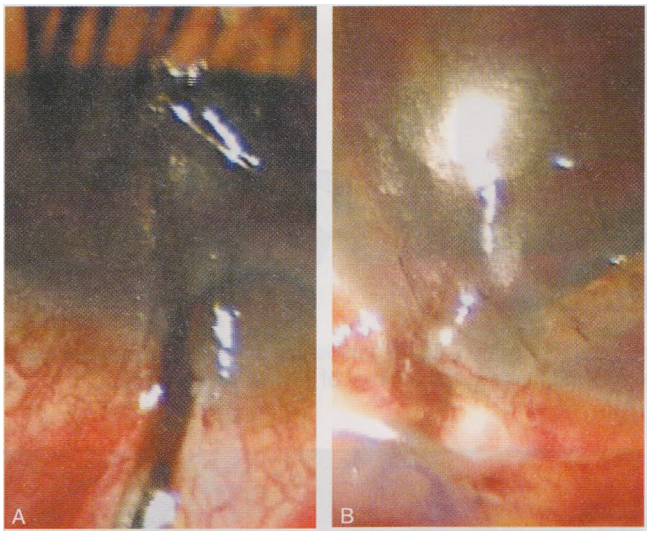


Fig. 24.13 (A) Corneoscleral penetrating injury; (B) a repaired corneoscleral wound. The first suture was placed at the limbus.

replacing fixed anatomical landmarks such as the limbus into continuity first and then suturing anteriorly and posteriorly as required. Scleral wounds more than 3-4 mm posterior to the limbus are sutured completely after a thorough exploration. They are also treated with surrounding cryoapplications to cause chorioretinal adhesions and prevent future retinal detachments.

Occasionally in a corneal wound caused by a dirty implement or vegetable matter, pyogenic organisms are carried into the eye, multiply there and cause rapid necrosis of the entire cornea. In these cases a ring of deep infiltration appears 2 or 3 mm internal to and concentric with the corneoscleral margin—the so-called *ring abscess.* If the organism is *Pseudomonas aeruginosa* (an anaerobic Gram-negative rod), there is extensive chemosis of the conjunctiva, sometimes with a greenish discharge. Enzymes released by the organism cause liquefaction of the cornea. Usually panophthalmitis sets in and the whole of the central part of the cornea is cast off. The institution of intensive treatment with appropriate local and systemic antibiotics and a therapeutic keratoplasty may occasionally save such eyes.

If it finds access into the anterior chamber, pyogenic infection leads to a *purulent iridocyclitis* with hypopyon, endophthalmitis and usually panophthalmitis.

Wounds of the lens

Such wounds cause traumatic cataract and are always a serious complication. If the wound in the capsule is small, the entry of aqueous causes a localized cloudiness in its vicinity and, irrespective of the site of the wound, opacities in the form of feathery lines appear in the posterior cortex, which later develop into a *rosette-shaped cataract* resembling that of early concussion cataract (Fig. 24.9B).

Occasionally the wound in the capsule becomes sealed, particularly if a posterior synechia develops, in which case these changes may be stationary. However, they usually progress until a complete cataract is formed. The integrity of the posterior lens capsule must be assessed pre-operatively so that appropriate surgery is planned. If the lens is damaged, it rapidly opacifies and flocculent grey masses protrude through the opening in the capsule, some-times filling the whole chamber.

A traumatic cataract of this type is liable to lead to serious complications if not aspirated at once. Traumatic iridocyclitis is invariable and may be severe. The swelling of the lens keeps the iris in contact with the cornea and a secondary glaucoma may ensue.

The *treatment* of traumatic cataract in association with penetrating wounds, especially if complicated by vitreous loss, is by the use of a vitrectomy instrument. The aim of surgery is to remove the cataract, perform an adequate vitrectomy, suture the globe as a *primary procedure,* and insert an intraocular lens in suitable cases.

Adequate steps are essential to ensure control of infection and inflammation by intraocular and topical antibiotics and steroids. Seriously injured eyes usually become atrophic or phthisical.

Two special infections should be noted. *Gas-forming organisms,* such as *Clostridium welchii,* are occasional contaminants. They excite a virulent panophthalmitis with a brownish discharge and gas bubbles in the anterior chamber. Although they are sensitive to penicillin, destruction of vision has always followed. *Tetanus* is a rare complication; if this infection is introduced into the eye, the localized cephalic type of tetanus often results. Whenever such a complication is suspected, as in agricultural or road accidents, if the patient is not already immunized, prophylactic treatment should be instituted.

Risk factors for poor visual return include a double penetrating or perforating injury, dense vitreous haemorrhage and blunt trauma as a causative factor.

PENETRATING WOUNDS WITH THE RETENTION OF FOREIGN BODIES

The retention of a foreign body adds considerably to the danger of a *penetrating injury.* The foreign bodies most likely to penetrate and be retained in the eye are minute chips of iron or steel (accounting for 90% of the foreign bodies in industry), stone, and particles of glass, lead pellets, copper percussion caps and, less frequently, spicules of wood. In chipping stone with an iron chisel, it is commonly a chip of the chisel and not of the stone which enters the eye.

The *size* and *velocity* of the missile are of importance. If the foreign body is large, severe damage is usually caused.



Fig, 24,14 Foreign body in the angle. (A) Small limbal granuloma seen at 3 o'clock position; (B) on gonioscopy a metallic foreign body with surrounding fibrosis is seen; (C) a diagrammatic representation of the correct approach to the removal of such a foreign body.

Very minute particles can, however, penetrate the cornea or sclera and lodge in the deeper parts of the eye.

A foreign body entering the eye may cause damage in one of three ways:

- by mechanical effects;
- by the introduction of infection and
- by specific action (chemical or otherwise) on the intraocular tissues.

Mechanical effects

The foreign body may enter the eye through either the cornea or sclera. Having penetrated the cornea, it may be retained in the anterior chamber where it may fall to the bottom and, if very small, lie deeply in the angle hidden by the scleral ledge where it can only be seen gonioscopically (Fig. 24.14). It is generally, how-ever, caught in the iris, and can be recognized with the slit-lamp. A piece of glass in the anterior chamber is exceptionally difficult to see because its refractive index differs so little from that of the surrounding media.

The foreign body may pass into or through the lens, either by way of the iris or the pupil (Fig. 24.15). In each case a traumatic cataract is produced. If the particle has passed through the iris there will be a hole in this structure which looks black by oblique illumination, but shows a red reflex when illuminated by the ophthalmoscope, unless the lens behind the hole is cataractous. A hole in the iris is of great diagnostic significance, since it rarely occurs, except as the result of perforation by a foreign body. The foreign body may be visible in the lens, either before or after dilatation of the pupil, but it is possible for it to pass through the iris and through the circumlental space without wounding the lens.

The foreign body may be retained in the vitreous to which it may obtain access by various routes: through the cornea, iris and lens; through the cornea, pupil and lens; through the cornea, iris and zonules; or directly through the sclera. If it comes to rest in the vitreous it may remain suspended for some time but eventually sinks to the bottom of the vitreous chamber owing to

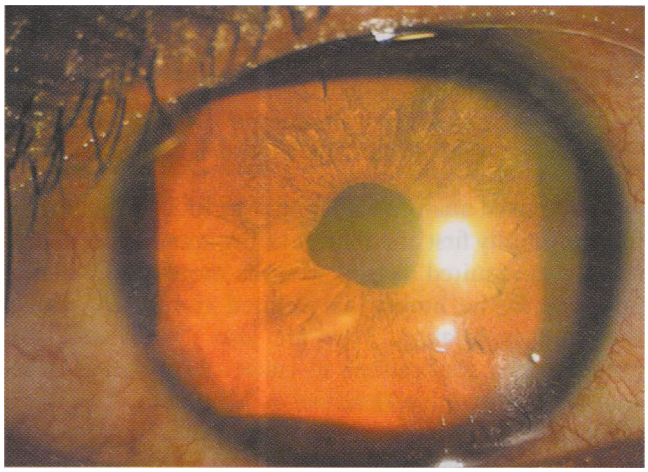


Fig. 24.15 Retained intraocular foreign body. The corneal wound of entry is seen as a leucomatous corneal opacity overlying a sphincter tear. The iris is golden-brown in colour due to siderosis.

degenerative changes in the gel, which lead to partial or complete liquefaction. If the particle is small, the lens clear, and there has been little haemorrhage, the foreign body may be seen ophthalmoscopically in the vitreous or retina, and the track through the vitreous often appears as a grey line. Most commonly, the particle has enough energy to carry it directly onto the retina where it may ricochet once or even twice before it comes to rest. Occasionally it pierces the coats of the eye and comes to rest in the orbital tissues, a condition known as a *double perforation* of the eye.

If it lies in the retina, the foreign body, generally black and often with a metallic lustre, is surrounded by a white exudate and red blood-clot, but eventually it is usually encapsulated by fibrous tissue and the retina in the neighbourhood becomes heavily pigmented.

Apart from its chemical nature, the lodgement of a foreign body in the posterior segment frequently leads to degenerative changes, which may damage sight considerably. These may entail a widespread degeneration, but most frequently fine pigmentary disturbances at the macula, often the result of concussion, diminish or

destroy central vision. The vitreous usually turns fluid, bands of fibrous tissue may traverse it along the path of the foreign body, haemorrhage may be extensive and retinal detachment may follow.

Infection

As with other perforating wounds, the introduction of infection is an ever-present danger when a foreign body enters the eye. Some types of foreign bodies are more likely to be associated with infection than others. Owing to the heat generated partly on their emission and partly by their rapid transit through the air, small flying metallic particles are frequently sterile, and infections are more likely to follow the introduction of pieces of stone or wood. Such eyes should be treated with antibiotics prophylactically as in penetrating wounds. Despite treatment, the prognosis in terms of vision is seldom good.

Reaction of the ocular tissues to a foreign body

This varies with the chemical nature of the foreign body.

Non-organic materials

These materials can (i) be inert, (ii) excite a local irritative response that leads to the formation of fibrous tissue, often resulting in encapsulation, (iii) produce a suppurative reaction or (iv) cause specific degenerative effects. Although inert materials cause little or no reaction at the time, iridocyclitis may eventually develop.

Glass, plastics and *porcelain* are inert. *Stone* may occasionally give rise to chemical changes, depending on its composition. Of the metals, *gold, silver, platinum* and *titanium* are inert. *Lead,* usually occurring as shot-gun pellets, becomes coated with the carbonate and excites little reaction. *Aluminium* frequently becomes powdered and excites a local reaction; so does *zinc,* which may excite suppuration—a reaction often associated with *nickel* and constantly with *mercury. Iron* and *copper,* the two most common materials found, undergo electrolytic dissociation and are widely deposited throughout the eye causing important degenerative changes.

Iron: This causes *siderosis,* so does *steel* in proportion to its ferrous content. The condition is probably due to the electrolytic dissociation of the metal by the intrinsic resting current in the eye, which disseminates the metal throughout the tissues and enables it to combine with the cellular proteins, thus damaging especially the epithelial cells and causing atrophy. The tissues are not uniformly affected. The earliest clinical manifestation is the deposition of iron in the anterior capsular cells of the lens, where oval patches of the rusty deposit are arranged in a ring corresponding with the edge of the dilated pupil. This appearance is pathognomonic and leads eventually to the development of cataract. The iris is also characteristically stained, first greenish and later reddish-brown. This is known as heterochromia iridis. Deposition of iron in the sphincter of the iris leads to a mydriasis. The vision of these eyes, however little affected by the primary injury, gradually fails owing to degenerative changes in the retina and lens. The retinal degeneration, associated with great attenuation of the blood vessels, eventually becomes generalized, taking the form of pigmentation resembling that of pigmentary retinal dystrophy. In early siderosis, the electroretinogram shows increased amplitude of the a-wave with a normal b-wave. As the condition progresses the b-wave diminishes and in advanced cases the electroretinogram is flat. Secondary glaucoma of the chronic type is a common late complication and, unless the foreign body becomes encapsulated or is removed in time, optic atrophy develops and most of these eyes go blind.

Pathologically, the deposits of iron are revealed by the Prussian blue reaction. The characteristic blue pigmentation is found particularly in the corneal corpuscles, in the meshes of the trabeculae, on the inner surface of the ciliary body, and in the retina where the entire retinal vascular system is clearly marked out. The anterior layers of the iris are impregnated and, in addition to subcapsular deposits in the lens, the fibres are also stained. There is always intense blue coloration immediately around the foreign body.

Copper: The reaction of *copper* or *brass* (as from percussion caps) varies with the content of pure copper. If the metal is relatively pure, a violent reaction ensues. Occasionally this results in the profuse formation of fibrous tissue so that the particle becomes encapsulated but, more often, a suppurative reaction follows which eventually results in shrinkage of the globe.

If, however, the metal is heavily alloyed, a much milder reaction ensues—*chalcosis.* The copper becomes electrolytically dissociated and is deposited particularly where resistance to its migration is offered by continuous membranes. The typical sites for deposition are in the deeper parts of the cornea at the level of Descemet's membrane where it accumulates mostly at the periphery causing the appearance of a golden-brown ring, which resembles the Kayser-Fleischer ring seen in Wilson disease *(see* Chapter 32), under the capsule of the lens where it is deposited to form a brilliant golden-green sheen aggregated in radiating formations like the petals of a flower *(sunflower cataract, see* Chapter 32), and occasionally on the retina at the posterior pole where lustrous golden plaques reflect the light with a metallic sheen. However, as there is no chemical combination with the proteins of the cells, as occurs with iron, degenerative changes do not appear and vision may remain indefinitely good.

Organic materials

Organic material tends to produce a proliferative reaction characterized by the formation of granulation tissue. Vegetable matter such as leaves, fronds and thorns may introduce a fungal infection into the eye. Wood and other vegetable matter produce a proliferative reaction characterized by the formation of giant cells. *Eyelashes* may be carried into the anterior chamber in perforating wounds of the cornea, and proliferation of the epithelium of the root of the hair frequently leads to the formation of intraocular cysts. *Caterpillar hair* may penetrate the eye, exciting a severe iridocyclitis characterized by the formation of granulomatous nodules (*ophthalmia nodosa).*

Diagnosis

The *diagnosis* of an intraocular foreign body is extremely important, particularly as the patient is often unaware that a particle has entered the eye. In all suspicious cases, particularly those with a history of having used a hammer and chisel, a careful search must be made for a wound of entry, which may be very minute and difficult to find. If the particle has passed through the cornea, however, the most minute scar can always be seen on careful examination with the slit-lamp, but its detection in the sclera may be much more difficult or sometimes even impossible.

The anterior segment of the eye must be thoroughly explored with the slit-lamp and the angle of the anterior chamber with the gonioscope. A hole in the iris or an opaque track through the lens is pathognomonic. These tracks, together with the position of the wound of entrance, are often valuable clues in localizing the foreign body. If the media are clear, the entire fundus must be similarly searched under full mydriasis.

Radiography is indispensable for the discovery and location of foreign bodies, which are radio-opaque. Caldwell and lateral views are commonly employed.

Fortunately, these particles are usually metallic and many—although by no means all—can thus be demonstrated. Many methods of localization are available. One of the most useful methods involves the suturing of a metal ring at the limbus or the use of a contact lens which contains a radioactive ring, and taking X-ray photographs in the anteroposterior and lateral axes. The foreign body can then be located in terms of the meridian and the number of millimetres behind the limbus or corneal apex.

A second method utilized is the *computerized axial tomography (CAT)* scan. The thinnest slices are used to localize a small foreign body with great accuracy. The extent of bony, soft tissue and intracranial injuries can also be assessed. *Magnetic resonance imaging (MRI)* scan is contraindicated in cases of magnetic or magnetizable foreign bodies, but is very useful in detecting a wooden foreign body and vascular changes.

Ultrasonography allows the detection of most foreign bodies, as well as associated intraocular conditions such as retinal detachment, suprachoroidal haemorrhage and a perforating injury of the eye.

A useful method of detection and localization in the operating theatre is to utilize the alterations in a secondary induced current produced by a metallic particle in its vicinity. This principle has been incorporated in instruments *(locators)* in which the searching element is a pointed probe and alterations in the current in the neighbourhood of the particle are revealed by the deflections of a needle on a dial or changes in the pitch of an audible signal amplified and transmitted to a loudspeaker.

Treatment

A foreign body should be removed unless: (i) it is inert and probably sterile; (ii) little damage has been done to vision and (iii) the process of removal will almost inevitably destroy sight. Magnetizable foreign bodies are more easily removed by using a magnet. Intraocular foreign bodies are often lightly magnetizable and always small. *Intravitreal magnets,* which can readily be manipulated by hand, are employed.

If the foreign body lies within the lens, it is better to treat such particles as if they were non-magnetic or remove the lens as a whole *(see below).*

If a magnetic foreign body is in the vitreous or retina, an intravitreal magnet or intravitreal forceps are necessary for its removal. Extraction is undertaken by the posterior route together with vitreoretinal surgery, whereby the particle is extracted directly. After excising any surrounding fibrous tissue and vitreous traction bands, areas of retinal breaks are treated at the same sitting. Subretinal foreign bodies are removed externally through an overlying scleral incision or internally by retinotomy as part of a vitreoretinal surgical procedure.

The immediate effect of extraction of foreign bodies is often good, but prognosis should be guarded. The tracks through the vitreous may become filled with fibrous tissue, and as this organizes and contracts, the retina may be pulled upon and its total detachment destroys vision. Modern sophisticated vitrectomy instruments have helped greatly in the better management of cases of penetrating wounds due to intraocular foreign bodies. Lens opacities and vitreous haemorrhage, bands and membranes can be removed at the time of initial surgery. Unfortunately, in these cases there is a tendency for the macula to pucker and for proliferative retinopathy to develop, which adversely affect the quality of postoperative vision. Prolonged and careful follow-up is a must.

The extraction of a non-magnetic foreign body from the anterior segment of the eye is often easy.

If the foreign body lies upon the iris it can usually be picked out by an iris forceps through a suitably placed keratome incision. If entangled in this tissue, it is removed by performing an iridectomy.

If it lies in the angle of the anterior chamber, it is impossible to grasp it with forceps through an ordinary incision immediately over it. The incision should be made 3 mm inside the limbus in the quadrant of the cornea lying over the foreign body, the point of the keratome being directed straight at it. The foreign body can then be lifted out with toothless forceps to minimize the risk of prolapse of the iris.

If the foreign body is in the lens, a few days should be allowed to elapse for the aqueous to act upon the lens fibres. An aspiration is then performed and the foreign body will probably be evacuated with the lens matter.

If a non-magnetizable foreign body lies on the retina, and *if accurate localization has been attained*, it may be removed directly by intra-vitreal forceps as part of a vitreoretinal procedure which includes a complete vitrectomy. Laser photocoagulation of the surrounding retina should be performed to prevent a late retinal detachment.

A foreign body retained in the eye has a serious prognosis, even if little mechanical damage has been done at the time of injury. Prognosis varies with the site and chemical nature of the particle. If the foreign body is allowed to remain and is inert, it may be retained indefinitely without affecting vision, although an iridocyclitis (sometimes appearing after many years) may be anticipated. If it is not inert and allowed to remain, the visual prognosis is bad. If the foreign body has been removed from the anterior chamber, the prognosis is usually good provided the lens was not injured. An injury of the lens adds to therapeutic problems owing to the immediate difficulties of its evacuation, the subsequent irritant reaction, and the tendency for the development of secondary glaucoma. Even if the foreign body has been successfully extracted from the posterior segment of the globe, a long-term follow-up is essential.

SYMPATHETIC OPHTHALMITIS

This is a condition in which serious inflammation attacks the sound eye after injury (including intraocular surgeries) to the other. In recent years it has become rare.

Sympathetic ophthalmitis or ophthalmia almost always results from a penetrating wound. Wounds involving the ciliary body and leading to its incarceration in the scar, have always been considered particularly dangerous. Incarceration of the iris or lens capsule are also more likely to set up sympathetic ophthalmitis than others. Sympathetic ophthalmitis very rarely occurs if actual suppuration has taken place in the exciting eye. It can also occur rarely following elective surgery for cataract or glaucoma where iris tissue has been left incarcerated in the wound. Sympathetic ophthalmia has also been reported after proton beam irradiation, Nd:YAG cyclophotocoagulation and cyclocryotherapy.

Children are particularly susceptible, but it occurs at any age. It usually begins 4-8 weeks after the injury to the first eye (the exciting eye) has taken place, rarely earlier. The onset has been reported to occur as early as 9 days after the accident and may be delayed for many months or even years.

Aetiology

The aetiology of the condition is unknown but is considered to be an autoimmune, T cell-mediated disease. Uveal pigment can act as an allergen and those who suffer from sympathetic diseases show a skin sensitivity to it. Viral infection may be the initiating factor and act by modifying uveal proteins to the extent that they become unusually antigenic or, by damaging the cells directly, uncover intracellular previously 'sequestered' antigens.

Pathology

Pathologically, the microscopic features in both the exciting and the sympathizing eyes are the same. In the earliest stages, examination shows nodular aggregations of lymphocytes and plasma cells scattered throughout the uveal tract. The pigment epithelium of the iris and ciliary body proliferates to form nodular aggregations (Dalen-Fuchs nodules) and the tissues become invaded by lymphocytes and epithelioid cells. The retina is also heavily infiltrated, especially in the neighbourhood of the vessels. In the later stages the infiltrate becomes diffuse and giant cells appear; in fact, the condition is scarcely distinguishable from tuberculosis of the uveal tract, although caseation is never present. These are merely the signs of reaction to a relatively mild form of irritation.

Clinical features

There is always iridocyclitis in the exciting eye. Usually it is a plastic iridocyclitis which has been set up by injury and has not subsided in the course of 3 or 4 weeks. Instead of quietening down, the ciliary injection remains, there is lacrimation and the eye is tender. Special attention should be directed to the presence or absence of keratic precipitates on the back of the cornea. In the rarer cases of delayed sympathetic

ophthalmitis, the exciting eye may have passed into a quiescent state. The exciting eye, while showing evident traces of old iridocyclitis, may still possess useful vision. In other cases the eye may have shrunk completely. The onset of sympathetic ophthalmitis in the second eye in such cases is then ushered in by return of irritation (ciliary injection, tenderness, etc.) in the shrunken globe.

In sympathetic ophthalmitis, the plastic iridocyclitis differs clinically in no respect from this form of iridocyclitis due to other causes. In rare cases it manifests itself as a neuroretinitis or choroiditis. Prodromal symptoms are sensitivity to light and transient indistinctness of near objects due to weakness of accommodation. The prodromal symptoms may occur in intermittent attacks, spread over a considerable period of time. In other cases, the patient first seeks advice for photophobia and lacrimation, or defective vision in the uninjured eye (sympathetic irritation). In cases which are prone to develop this condition, the first sign may be the presence of keratic precipitates on the back of the cornea or the presence of retrolenticular flare and cells, which are noticed at this early stage because they have been anticipated.

On examination at this stage, there may be lacrimation, slight ciliary injection, tenderness of the eyeball, as shown by the patient shrinking from an attempt at examination, precipitates on the back of the cornea and vitreous opacities; occasionally there is some oedema of the optic disc.

When fully developed, all the signs and symptoms of granulomatous uveitis are present, varying in degree according to the severity of the case. The prognosis as to vision is always doubtful, but if there is extensive deposition of plastic exudates in the pupillary area it becomes extremely grave. Cases showing little exudation but a deep anterior chamber and keratic precipitates have a more favourable prognosis, but they may at any moment develop into the severe plastic type. There is usually vitritis, multiple yellow-white lesions in the peripheral fundus, Dalen-Fuchs nodules and papillitis. Sympathetic ophthalmitis sometimes takes 2 or more years to run its course.

Treatment

The *treatment* of sympathetic ophthalmitis demands great judgement.

In the first place, it is prophylactic. In every case of penetrating injury, with or without the retention of a foreign body, prophylactic and long-term treatment, including the topical and systemic administration of steroids, may be adopted for a time. If the eye quietens down quickly it is unlikely to set up sympathetic inflammation. The chief causes which prolong irritation are entanglement of the iris or ciliary body or lens capsule in the wound. Every effort must therefore be made to obviate this. It must be remembered that children are more susceptible to the disease than adults. *Sympathetic ophthalmitis rarely occurs after the excision of an injured eye unless it has already commenced at the time of operation.*

It is even more difficult to decide the course to adopt in those cases in which sympathetic ophthalmitis has already supervened. If the case is seen early, shortly after the onset of inflammation in the sympathizing eye, and if the injured or exciting eye has no useful vision, this useless eye should be excised at once as this definitely has a good effect upon the process in the sympathizing eye if performed early. At a later stage, there is no evidence to show that it exerts any influence.

The treatment of sympathetic iridocyclitis is that of iridocyclitis in general with the proviso that steroid preparations have a more dramatic effect than in most other ocular inflammations. At the earliest suggestion of inflammation, steroids should be given systemically in large doses—intravenous methylprednisolone 1 g followed by 100 mg of prednisone orally tapered off slowly. This should be reinforced by the topical use of dexamethasone 0.1% drops and topical cycloplegics. In all cases, 15-20 mg of prednisone should be continued for many months lest relapses follow its cessation, and the eye should be watched over a period of years. Daily doses of oral steroids are employed initially but later it should be possible to change to alternate day steroid therapy. The use of steroids has completely altered the prognosis of this disease *if such treatment is commenced early.* If, however, the inflammation has taken a firm hold and the uvea is heavily infiltrated, the outlook for vision is much less hopeful. Steroid-resistant cases or those with severe corticosteroid-related side-effects require immunosuppressive therapy. Oral cyclosporin A specifically affects T cell-mediated immuno-inflammation and is useful in severe cases of sympathetic ophthalmitis as an adjunct to corticosteroids.

SUMMARY

Ocular injuries can occur in various ways. The eyes being small and delicate structures, sometimes even apparently minor trauma can have devastating effects. Children and young adult males are particularly prone. The importance of prevention through health education and precautions in hazardous occupations cannot be overemphasized.

First aid at primary care level for chemical burns is important. The eyes must be thoroughly irrigated with water or physiologic solutions like saline or ringer lactate, if available. After instillation of an antibiotic ointment, the eye should be patched and the patient referred to an

ophthalmologist. In case of lacerating injuries, a booster dose of tetanus toxoid and an intravenous dose of broad spectrum antibiotic should be administered, no topical medications are to be applied, the eye patched and patient referred urgently to the nearest eye specialist. Such cases should be asked to remain fasting to enable prompt repair under general anaesthesia as soon as possible.

Sympathetic ophthalmia is a delayed type-IV hypersensitivity reaction that takes place in the sound fellow eye about 4-8 weeks after penetrating wounds that affect the ciliary body and leave uveal tissue incarcerated in the wound, with persisting inflammation in the injured eye. Though rare, the disease is potentially sight threatening. Prompt recognition with early institution of steroid therapy helps to salvage vision.

Section V

Disorders of Motility

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Anatomy and Physiology of the Motor Mechanism

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THE MOTOR APPARATUS OF THE EYE

If each eye is to be rapidly and accurately fixed upon any object so that its image is thrown upon the fovea, and if both eyes, in their every movement, are to move in unison so that binocular vision is to be attained, it is obvious that their motility and coordination must be subserved by an unusually accurate and responsive neuromuscular apparatus. We shall first study the extraocular muscles and then their central nervous control.

The extraocular muscles

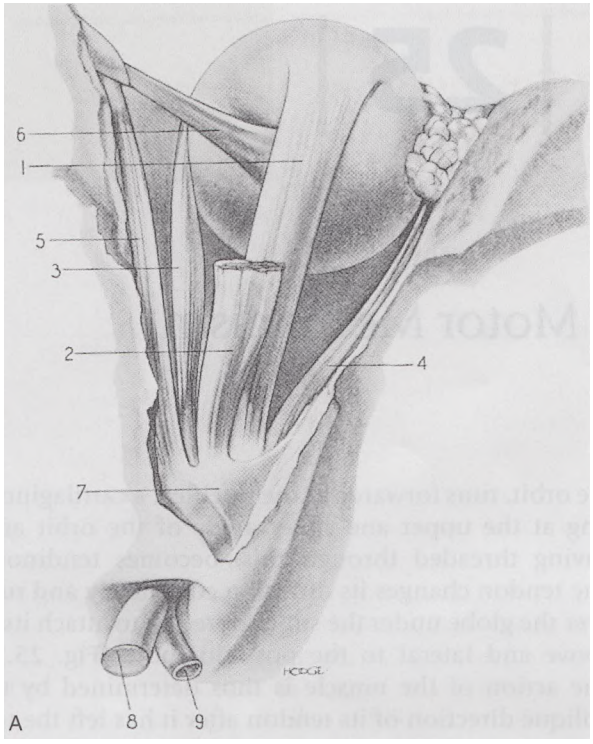
A team of six muscles controls the movements of each eye. Four of them, the *rectus muscles,* have the primary action of rotating the eye in the four cardinal directions—up, down, out and in (Fig. 25.1). They arise in a fibrous ring around the optic foramen to the nasal side of the axis of the eye and are inserted in the sclera by flat tendinous insertions about 10 mm broad. The medial rectus is inserted into the sclera about 5.5 mm to the nasal side of the corneoscleral margin, the inferior rectus 6.6 mm below, the lateral rectus 7 mm to the temporal side, and the superior rectus 7.75 mm above (Fig. 25.2). The *oblique muscles,* the primary function of which is rotation of the globe, are differently arranged (Figs 25.1 and 25.3). The superior oblique arises from the common origin at the apex of the orbit, runs forwards to the trochlea, a cartilaginous ring at the upper and inner angle of the orbit and, having threaded through this, becomes tendinous. The tendon changes its direction completely and runs over the globe under the superior rectus to attach itself above and lateral to the posterior pole (Fig. 25.3). The action of the muscle is thus determined by the oblique direction of its tendon after it has left the trochlea. The inferior oblique maintains a similar direction throughout its course and is the only muscle not arising from the apex of the orbit. It arises anteriorly from the lower and inner orbital walls near the lacrimal fossa and, running below the inferior rectus (i.e. the inferior rectus lies between the globe and inferior oblique muscle), finds an insertion in the sclera below and lateral to the posterior pole of the globe.

The extraocular muscles are different from other striated muscles in the body in certain important aspects. They are small in size with a small motor unit and one motor axon supplying only six muscle fibres. They have specialized muscle spindles and there are two different types of muscle cells, small and large within each muscle. The small fibres are located peripherally, have a slow twitch response, are capable of graded contractions in absence of action potential and have multiple motor end plates known as *'en grappe.* The large fibres are located centrally, have a fast twitch response and have a single motor end plate. Proprioception is via the fifth cranial nerve controlled by the mesencephalic nucleus.

To control their movements all these muscles are provided with fascial *check ligaments* intimately connected with the perimuscular sheath, Tenon capsule and the periosteum.

The action of the extraocular muscles

These rotate the eye around a *centre of rotation,* which lies in the horizontal plane some 12 or 13 mm behind the cornea, and in every movement of the globe each muscle is involved to some degree, either by contraction



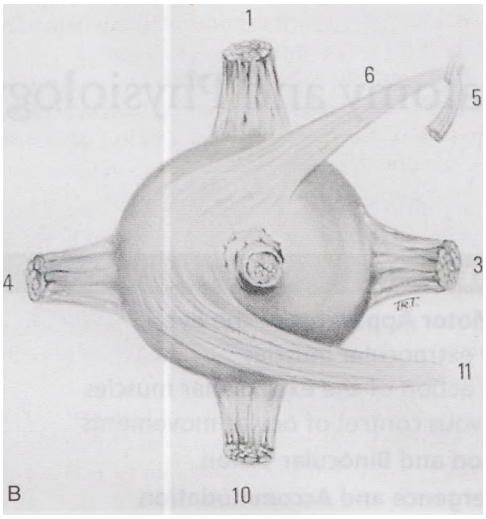


Fig. 25.1 The extraocular muscles. (A) View from above (right eye); (B) view from behind (left eye): 1, superior rectus; 2, levator palpebrae superioris; 3, medial rectus; 4, lateral rectus; 5, superior oblique; 6, reflected tendon of superior oblique; 7, annulus of Zinn; 8, optic nerve; 9, ophthalmic artery; 10, inferior rectus; and 11, inferior oblique.

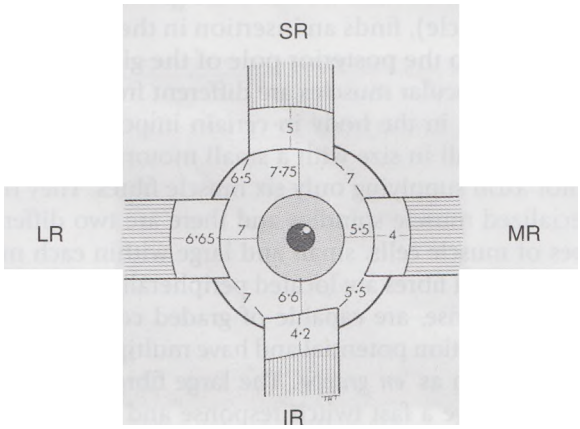


Fig. 25.2 Lines of insertion of the rectus muscles of the right eye seen from the front.



Fig. 25.3 Lines of insertion of the superior and inferior oblique muscles and of the superior, medial and lateral recti of the right eye, seen from above.

or inhibition (Table 25.1). Three types of rotation or 'degrees of freedom' are possible around the centre of rotation:

1. rotation around the vertical axis whereby the globe is turned from side to side;
2. rotation around the horizontal axis whereby the globe is turned upwards and downwards and
3. rotation around the anteroposterior axis—an involuntary movement of *torsion;* intorsion when the upper pole of the cornea rotates nasally, extorsion when temporally.

When the medial or lateral rectus acts, it rotates the eye horizontally inwards (adduction) or outwards (abduction). Owing to the obliquity of their course, however, contraction of the superior and inferior recti must involve some torsion (Fig. 25.4A and B). Thus, when the superior rectus acts upon the globe in the primary position, it not only pulls the eye upwards but also inwards and intorts

Table 25.1 Actions of the extraocular muscles

Muscle	Primary action	Subsidiary actions
Medial rectus (MR)	Adduction	None
Lateral rectus (LR)	Abduction	None
Superior rectus (SR)	Elevation (best when eye is in abducted position)	Incycloduction (intorsion) and adduction
Inferior rectus (IR)	Depression (best when eye is in abducted position)	Excycloduction (extortion) and adduction
Superior oblique (SO)	Incycloduction (intorsion)	Depression (best when eye is in adducted position) and abduction
Inferior oblique (IO)	Excycloduction (extortion)	Elevation (best when eye is in adducted position) and abduction

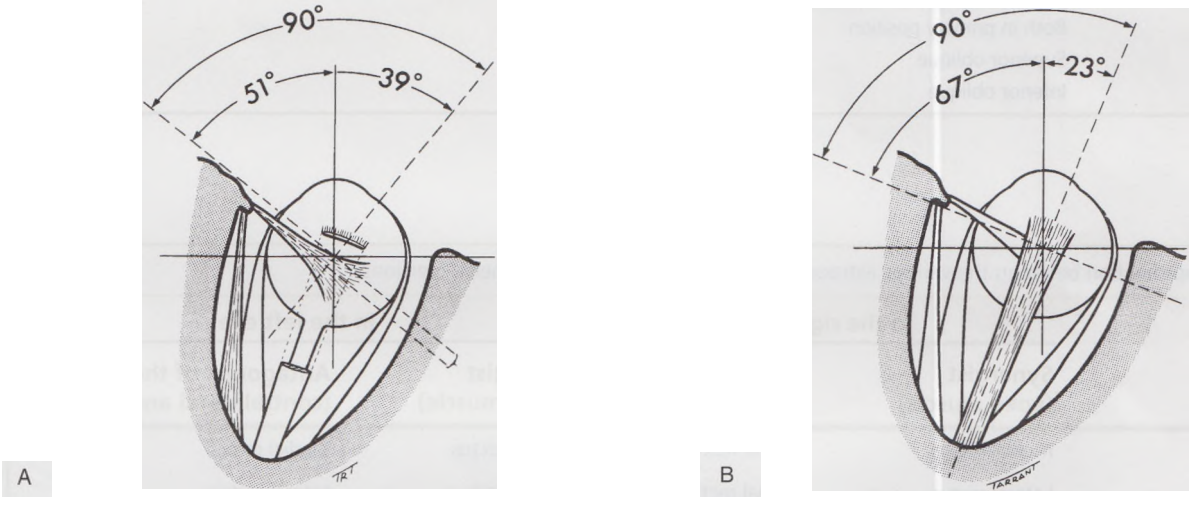


Fig. 25.4 The effectivity of the vertical rotators in elevation. When the visual axis lies in the muscle plane, rotation vertically will be maximal; in this position there is one direction of movement only—upwards and downwards; the further the visual axis is removed from this position, the more effective the muscle becomes in torsion. (A) The superior (or inferior) oblique is 100% effective in depression (or elevation) when the eye is adducted 51°. It is ineffective when the eye is abducted 39°. (B) The superior (or inferior) rectus is 100% effective in elevation (or depression) when the eye is abducted 23°. It is ineffective when the eye is adducted 67°. In the primary position, three-quarters of its efficiency is devoted to vertical rotation and one-quarter to torsion.

it. Similarly, when the inferior rectus acts the eye is pulled downwards and inwards and extorted. Since the obliques are inserted behind the centre of rotation, their effective action is to pull the back of the eye from behind forwards and inwards. Therefore, when the superior oblique contracts, if the globe is in the primary position, the main effect is intorsion but it also rotates the eye downwards and outwards; the inferior oblique primarily causes extorsion but also rotates the globe upwards and outwards. The mechanism is so arranged that when the superior rectus and inferior oblique act simultaneously the eye moves directly upwards, the upward movement caused by each muscle being summated, while the inward movement and torsion of the superior rectus is exactly compensated by the outward movement and contrary torsion of the inferior oblique. Similarly, when the inferior rectus and superior oblique act simultaneously the eye moves directly downwards (Tables 25.2 and 25.3).

Every movement of the eyeball is thus a synkinesis. Not only is there uniocular synkinesis but also in normal circumstances there is always binocular synkinesis. Abduction of one eye is accompanied by adduction of the other—which is known as a *conjugate* movement. The only exception to this rule is the bilateral adduction of the eyes in convergence and abduction of both eyes in divergence *(dysconjugate* movements). Elevation or depression of one eye is always accompanied by elevation or depression, respectively, of the other. Elevation of both eyes is accompanied by slight abduction (divergence), depression by slight adduction

Table 25.2 Uniocular eye movements (ductions)

Movement	Main muscle	Other muscles
Abduction	Lateral rectus	Superior oblique Inferior oblique (Both muscles are inserted behind the centre of rotation and pull the posterior pole of the globe medially when they contract and hence the anterior portion of the eye is abducted)
Adduction	Medial rectus	Superior rectus Inferior rectus (Both muscles are inserted anterior to the centre of rotation and pull the anterior portion of the globe medially in adduction)
Elevation	Superior rectus in abduction Inferior oblique in adduction Both in primary position	
Depression	Inferior rectus in abduction Superior oblique in adduction Both in primary position	
Intorsion	Superior oblique	Superior rectus
Extortion	Inferior oblique	Inferior rectus

Table 25.3 Coordination between the various extraocular muscles in binocular movements (versions)

	In the right eye		In the left eye	
Movement	Synergist (yoke muscle)	Ipsiiateral antagonist	Synergist (yoke muscle)	Antagonist of the synergist (contralateral antagonist)
Laevoversion	Medial rectus	Lateral rectus	Lateral rectus	Medial rectus
Dextroversion	Lateral rectus	Medial rectus	Medial rectus	Lateral rectus
Dextroelevation*	Superior rectus	Inferior rectus	Inferior oblique	Superior oblique
Dextrodepression*	Inferior rectus	Superior rectus	Superior oblique	Inferior oblique

*Laevoelevation and laevodepression are similar.

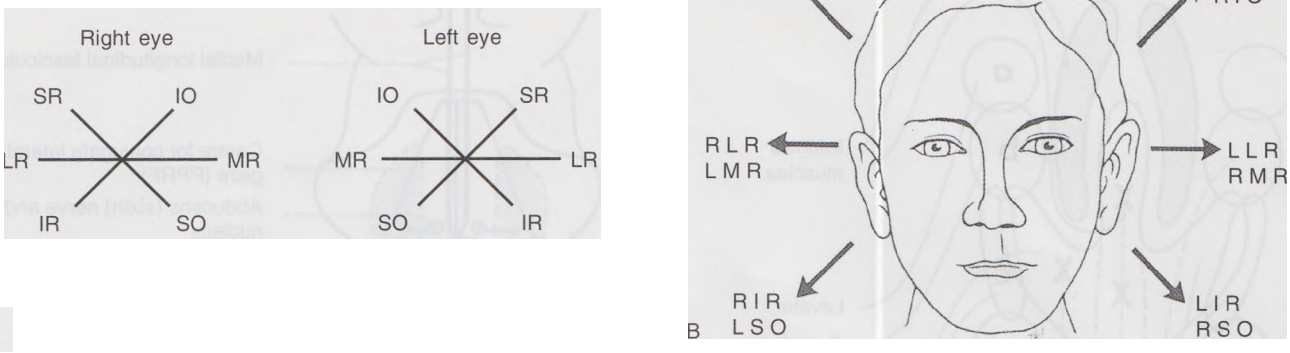
(convergence). In these movements the muscles which contract together are called *synergists;* those which suffer inhibition, antagonists. Their correlation has been summarized in Table 25.3 and Fig. 25.5. Muscles contracting together to move both the eyes in the direction of any of the arrows in Fig. 25.5(A) are synergists and the muscles that would work in a directly opposite direction are relaxed and called antagonists for that particular action. Thus *in rotation to the right* (*dextroversion*) the synergists are the right lateral rectus and left medial rectus, while the antagonists are the right medial rectus and left lateral rectus.

In rotation upwards synergists are the right and left superior recti primarily and the right and left inferior obliques secondarily. The antagonists are the right and left inferior recti and right and left superior obliques.

The testing of eye movements (Table 25.4) is complete only if the examination of all types of eye movements is done systematically.

Table 25.4 Categories of eye movements to be tested

- *Versions* (both eyes open, attempting to fixate a target, and moving in the same direction)
- *Vergences* (both eyes open, fixing a target but moving in opposite directions synchronously, e.g. convergence or divergence)
- *Ductions* (only one eye is open, the other covered or closed)
- 5accad/cmo\/e/T)enfs(quickfixation movements)
- *Pursuit* moi/emenfs (slow following movements)
- *Voluntary movements*
- *Involuntary movements*



Fig, 25.5 (A) The range of movement of each muscle is graded as −4 (no movement); −3 (can move but does not reach the midline); −2 (can reach midline), and so on till 2+(overaction). 10, inferior oblique; MR, medial rectus; SO, superior oblique; IR, inferior rectus; LR, lateral rectus; SR, superior rectus. (B) The fields of action of the ocular muscles in binocular eye movements (versions). For example, the maximum effectivity as elevators is attained by the RSR and the LIO when acting as right-hand elevators.

Nervous control of ocular movements

Laws governing the neural control of ocular movements are as follows.

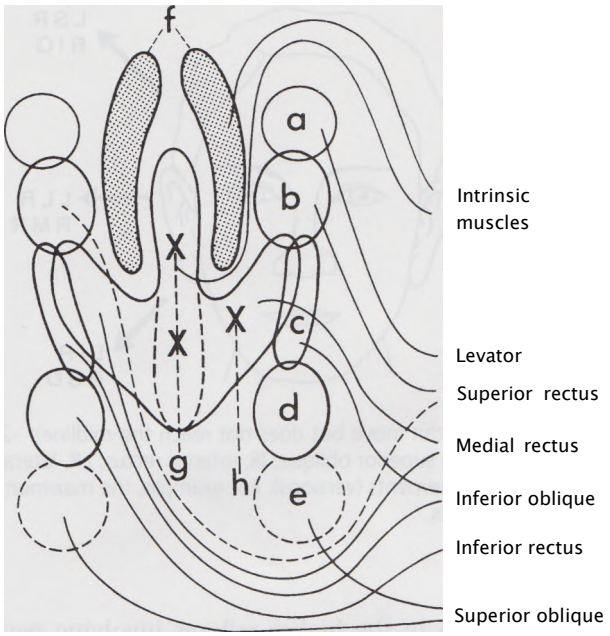
Hering law of equal innervation applies to both eyes. Equal and simultaneous innervation flows from the brain to a pair of synergistic (yoke) muscles which contract simultaneously in conjugate binocular movements. For example, in laevoversion, the lateral rectus of the left eye and medial rectus of the right eye receive an equal and simultaneous flow of innervation; during convergence, both medial recti; and so on. In the case of a paretic squint, the amount of innervation to both eyes is always determined by the fixating eye so that the angle of deviation will vary according to which eye is used for fixation *(see* Chapter 27).

Sherrington law of reciprocal innervation: During the initiation of an eye movement, increased innervation to an extraocular muscle is accompanied by simultaneous inhibition (a reciprocal decrease in innervation) of the direct antagonist of the contracting muscle of the same eye. If the left medial rectus muscle receives innervational flow to initiate adduction of the left eye, there is simultaneous decreased and inhibitory flow to the left lateral rectus muscle to make it relax and enable the eyeball to move medially.

The *nervous* control *of ocular movements* is complicated. The muscles are supplied by nerves arising from nuclei in the mid-brain. Their action is coordinated by intermediate 'centres' situated in this region by which reflex activities are governed. Finally, these intermediate centres are linked with the vestibular apparatus whereby they become associated with the equilibration reflexes and the cerebral cortex so that voluntary movements and participation in the higher reflexes involving perception become possible.

The *oculomotor,* or *third cranial nerve,* supplies all the extrinsic muscles except the lateral rectus and superior oblique. It also supplies the sphincter pupillae and ciliary muscle. The superior oblique is supplied by the *trochlear (fourth) nerve* and the lateral rectus by the *abducens (sixth) netve.*

The *oculomotor nucleus* is located in the mid-brain and forms a large, continuous mass of nerve cells situated near the midline in the floor of the aqueduct of Sylvius beneath the superior colliculus (Fig. 25.6). The cells nearest the midline towards the anterior part of the third nucleus are smaller than the others: they form the *Edinger-Westphal* (and *Perlia) nucleus* which supplies fibres to the ciliary muscle (accommodation) and sphincter pupillae (constriction of the pupil). The main mass of the large-celled nucleus is composite and divided into cell masses or subnuclei subserving the individual extrinsic ocular muscles, as is seen in Fig. 25.6. A single, central, caudally located nucleus innervates both levator palpebrae superioris muscles. Paired bilateral subnuclei that innervate the superior recti have crossed projections that pass through the opposite subnucleus and join the nerve of the opposite side. The decussation of the fibres takes place mostly posteriorly. Paired bilateral subnuclei with uncrossed projections innervate the medial recti, inferior recti and inferior oblique muscles. Parasympathetic input to the sphincter muscle of the iris and ciliary body arises from the single Edinger-Westphal nucleus. The clinical relevance of knowing this innervation pattern is to distinguish nuclear from non-nuclear third nerve palsy. A bilateral third nerve palsy without ptosis indicating sparing of the single levator subnucleus and a unilateral third nerve palsy with contralateral superior rectus



Fig, 25,6 Schematic diagram of the third nerve nucleus and its associated cell groups (after Brouwer): a, levator palpebrae; b, superior rectus; c, inferior oblique; d, inferior rectus; e, superior oblique–fourth nerve nucleus; f, intrinsic ocular muscles (sphincter of the iris and ciliary muscles); g, medial rectus for convergence; h, medial rectus for inward movement. Note: The diagram shows the various subnuclei but is not directly representative of the actual location; for example, 'a' is in reality a single, central, caudally located nucleus.

involvement and bilateral ptosis are both indicative of obligatory nuclear involvement. Unilateral ptosis, unilateral internal ophthalmoplegia and unilateral external ophthalmoplegia with normal contralateral superior rectus function are conditions that exclude a nuclear lesion. The levator palpebrae is represented most caudally.

The *fourth nerve nucleus* is located more caudally in the mid-brain. It is unique among the motor cranial nerves in having a dorsal decussation. Nearly, if not quite, all the fibres decussate in the superior medullary velum and are distributed to the superior oblique muscle of the opposite side.

The *sixth nerve nucleus* is situated much further caudally in the brainstem (Fig. 25.7) in the immediate vicinity of the facial (seventh) nucleus, the fibres from which make a large bend around it. Hence, vascular and other lesions of the sixth nucleus are very liable to be accompanied by facial paralysis on the same side. All the fibres of the sixth nerve are distributed to the ipsilateral lateral rectus.

The peculiarities of distribution of the fibres from the third, fourth and sixth nuclei to muscles partly on one side and partly on the opposite side of the body show that the nervous mechanism of coordination of these muscles is extremely complex.

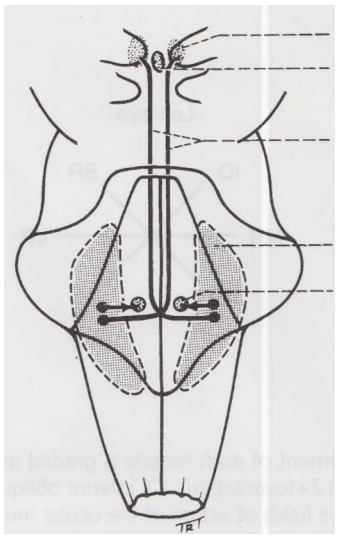


Fig. 25,7 Diagrammatic representation of the dorsal surface of the brainstem showing the connection of the pontine centres for conjugate lateral gaze (pontine paramedian reticular formation or PPRF) with the abducens nuclei and the oculomotor nuclei by way of the medial longitudinal fasciculus.

The *intermediary mechanism* coordinating the activities of these nuclei is also complex. The nuclei are interconnected to a considerable extent by fibres participating in the *posterior longitudinal bundle* (Fig. 25.8), a large and important tract of nerve fibres derived in part from the anterior columns of the spinal cord, lying in close relation to the third, fourth and sixth nuclei. These fibres have important functions in the coordination of movements and equilibration, which are so intimately related with vision. The nuclei are also interrelated through this bundle so that coordination of the two eyes is maintained. One of the most important among such connections is the group of fibres which link up the sixth nucleus of one side with the third nucleus of the other (i.e. the medial longitudinal fasciculus or the MLF).

There are 'centres' which control conjugate movements. The supranuclear centres are in the cerebral cortex. The frontal cortex has an area which controls quick fixational eye movements to the opposite side. The occipital cortex has an area which controls slow pursuit eye movements to the ipsilateral or same side. Both supranuclear areas send impulses to the brainstem to the centres which control conjugate eye movements by sending appropriate impulses to the relevant lower motor neuronal cells in the nuclei from which the nerves which supply the extraocular muscles originate. The centres controlling eye movements in the brainstem are the final common pathway conveying impulses for movement in a particular direction, irrespective of whether the movement is voluntary or involuntary, a saccade or a pursuit, or a vestibular reflex eye movement.

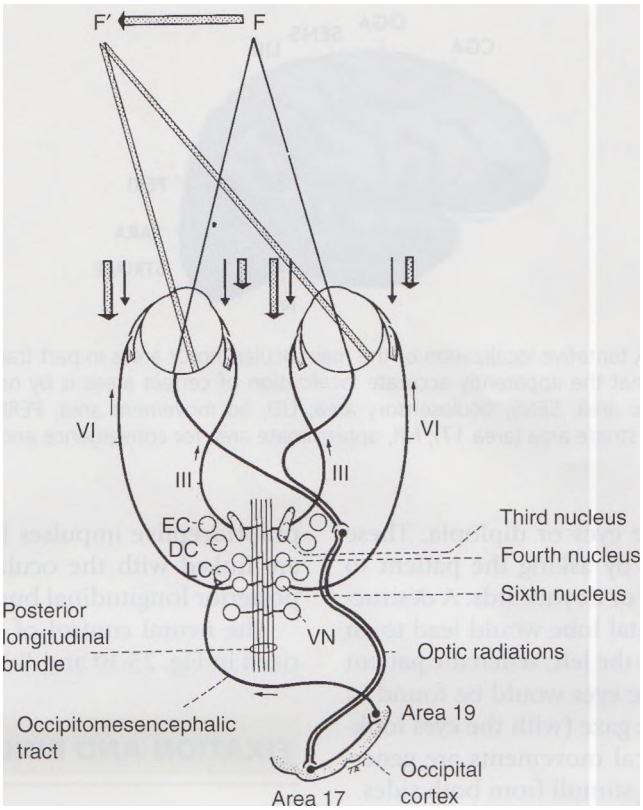


Fig. 25.8 The organization of the psycho-optical reflexes (fixation, refixation, fusional, etc.). So long as the fixation point (F) is imaged on each macula, the fixation reflex maintains the posture of the eyes steady by an equality of muscular tone (thin solid black arrows). If, however, F is moved to F', the retina on the right of the macula is stimulated and sets up a refixation reflex. The afferent path is: (a) retinae optic nerve -> chiasma -»right optic tract; (b) lateral geniculate body —> right optic radiations -> striate area of occipital cortex; (c) peristriate occipital cortex. The efferent path is conjectural, but traverses the posterior part of the optic radiations and reaches the opposite cerebral peduncle where connection is made with the vestibular nucleus (VN), the mid-brain ocular motor centres governing conjugate elevation, depression and lateral movements (EC, DC, LC), from where impulses are relayed through the posterior longitudinal bundle to the ocular motor nuclei (third, fourth and sixth). In the present case, acting essentially through the left sixth nerve and the branch of the right third nerve to the medial rectus, the muscular tone is altered (hollow arrows) to orientate the eyes so that F' again falls on each macula.

The centre controlling horizontal conjugate movements in the neighbourhood of the sixth nucleus is the pontine paramedian reticular formation (PPRF, Fig. 25.7) and it controls conjugate horizontal movement to the ipsilateral side.

An area controlling vertical movements lies just above the two third nerve nuclei (Fig. 25.7) and is involved in the early development of a pinealoma *(see* Chapter 31); the centre for convergence (Perlia nucleus) is associated with the third nerve nucleus and lies in the region of the Edinger-Westphal complex (Figs 25.6 and 25.7), and an area coordinating divergence possibly exists.

This elaborate mechanism in the mid-brain and pons is controlled by three sources, one voluntary and three reflex.

Movements can be voluntary or involuntary (reflex). All voluntary movements are initiated by the cerebral cortex which sends impulses to the specific centres for a particular type of movement. The cerebral cortex represents a movement of gaze involving both eyes and not individual muscles. If a lesion affects an individual muscle or group of muscles the lesion has to be a lower motor neurone lesion.

Voluntary ocular movements are initiated in the pyramidal cells of the motor area of the *frontal cortex* in the second and third frontal convolutions of both sides (Fig. 25.9). The fibres enter the knee of the internal capsule as part of the pyramidal tract close to the fibres governing facial movements and break off in the mid-brain, first the fibres for vertical movements (and movements of the upper lid) and then those for lateral movements. These fibres control conjugate movements, vertical and horizontal, of both eyes; movements of individual muscles are not represented in the cortex. Stimulation of the cortex or the tracts unilaterally therefore produces horizontal conjugate movements of the eyes to the opposite side; destruction, paralysis of voluntary conjugate movements away from the side injured, in either case without

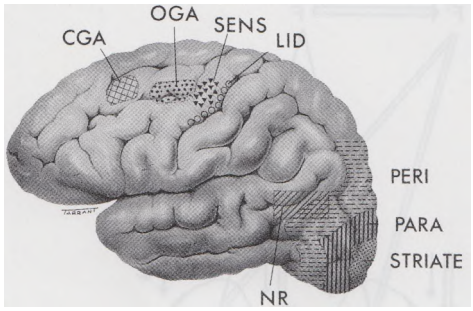


Fig. 25.9 The ocular motor areas. A tentative localization of the main ocular motor areas in part transferred from the brain of primates to that of man. It is to be noted that the apparently accurate localization of certain areas is by no means factual or constant. CGA, cephalogyric area; OGA, oculogyric area; SENS, oculosensory area; LID, lid movement area; PERI, peristriate area (area 19); PARA, parastriate area (area 18); STRIATE, striate area (area 17); NR, approximate area for convergence and the near reflexes (in the macaque) (areas 19 and 22).

involving disalignment of the eyes or diplopia. These pathways are tested clinically by asking the patient to look to the right, left, upwards or downwards. A destructive lesion in the right prefrontal lobe would lead to an inability to look conjugately to the left. When the patient is asleep or if unconscious, the eyes would be found in the position of right conjugate gaze (with the eyes looking towards the lesion). Vertical movements are generated by bilateral simultaneous stimuli from both sides.

The involuntary reflexes, which depend on vision (fixation, fusional movements, convergence, etc.)—the *psychooptical reflexes*—are centred in the visual cortex of the *occipital lobe* (Fig. 25.9). The afferent path for these reflexes is the visual pathway; the efferent runs down the optic radiations to the posterior longitudinal bundle (Fig. 25.8) and from there to the ocular motor nuclei. These pathways are tested by asking the patient to follow an object, which is passed horizontally and vertically so that the conjugate following movements of the eyes may be elicited.

An elaborate system of *statokinetic reflexes* coordinates the position of the eyes when the head is moved in space; their afferent path runs from the semicircular canals of the inner ear to the mid-brain centres. They induce conjugate movements of both eyes, a slow tonic movement in the direction of equilibration and a quick return (nystagmus). This pathway is tested by passive movements of the head. If the chin is depressed the eyes normally elevate if fixation is maintained, and if the head is rotated on a vertical axis the eyes maintain fixation as a result of the statokinetic reflexes. These movements are often referred to as *'doll's-head'* movements and they may be selectively maintained when voluntary and saccadic conjugate gaze and pursuit (following) conjugate gaze are disturbed as in the Sylvian aqueduct syndrome *(see* Chapter 31). Optokinetic movements are initiated by rotation or movement of the environment or the visual target.

A similar system of *static reflexes* coordinates movements of the eyes in respect to movements of the head upon the body. They are mediated mainly by proprioceptive impulses from the neck muscles, which are linked with the ocular motor centres through the posterior longitudinal bundle.

The neural control of ocular movements is summarized in Fig. 25.10 and Table 25.5.

FIXATION AND BINOCULAR VISION

We have already seen that the location of the image of an external object on the retina is determined by a line passing from the object through the nodal point of the eye. Conversely, an object is *projected* in space along the line passing through the retinal image and the nodal point. When a distant object is looked at the visual axes are practically parallel; the object forms an image upon each fovea centralis. Any other object to one side forms its retinal images upon the temporal side of one retina and upon the nasal side of the other; these retinal areas are coordinated visually in the occipital cortex so that such an object is seen with both eyes as a single object. These are known as *corresponding points,* the most important pair of which, of course, is the foveae. Points on the two retinae, which are not corresponding points in this sense of the term, are called *disparate points,* and if an object forms its retinal images on these, it will be seen double (binocular diplopia). If the disparity is slight there is a tendency to move the eyes so that the images may be fused by means of the fusion reflexes from the occipital cortex.

Since the most accurate vision is attained by the foveae it is necessary that the eyes be rapidly orientated so that the image of an object of interest falls upon them or that of a moving object be retained on them. This ascendancy of the foveae is maintained by the *fixation reflex* (Fig. 25.8) and whenever the image leaves the foveae, the eyes are at once re-oriented so that it falls upon them. This continues till the object moves outside the binocular field of vision and the eyes then refixate on another object. The activity of this reflex is

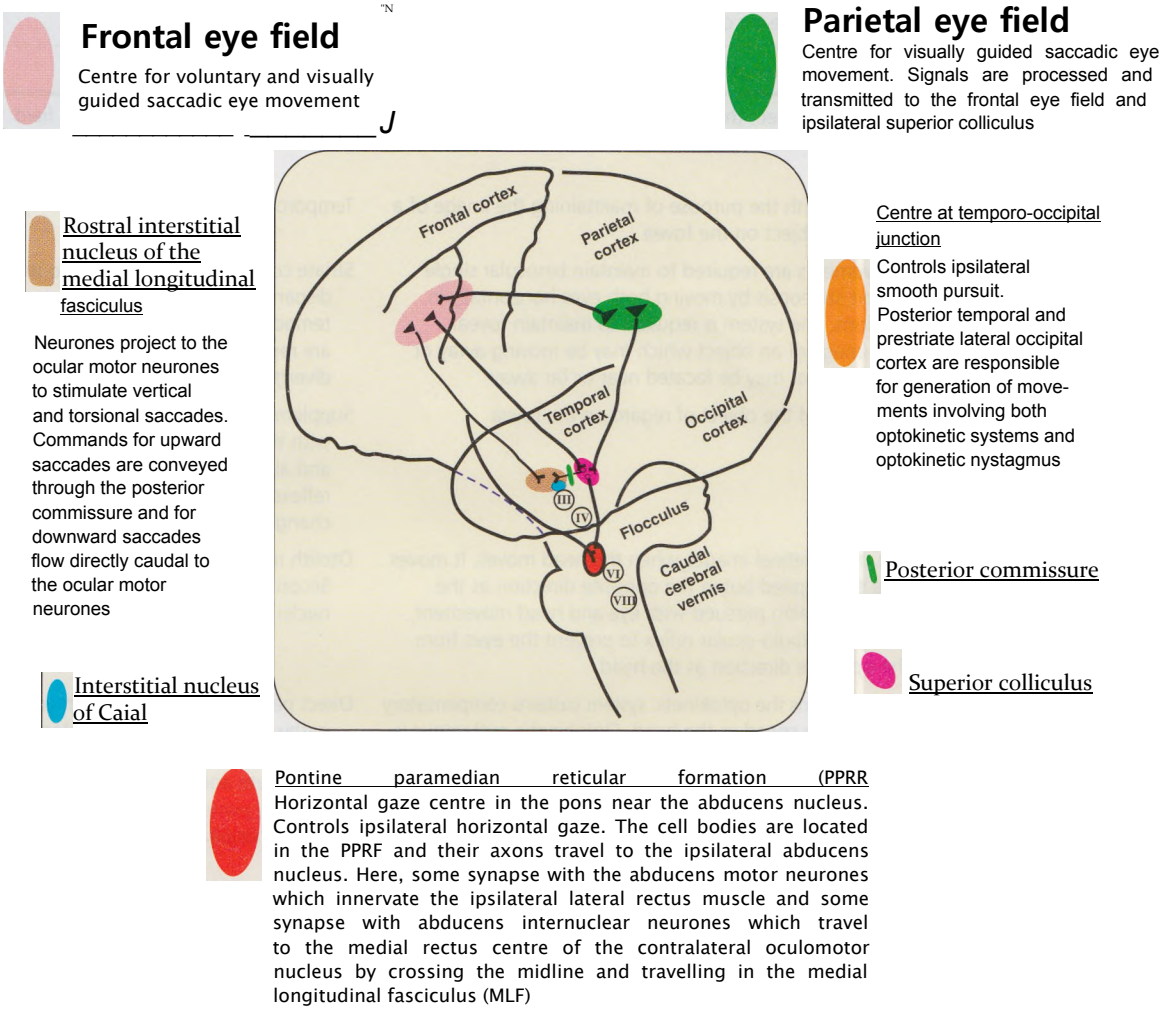


Fig. 25.10 Schematic diagram depicting the ocular motor systems and their neural control.

demonstrated by the rapid to-and-fro movements of the eyes of a person watching passing objects such as trees or electric poles while looking out of the window of a moving train, and can be demonstrated clinically by regarding a revolving drum or a moving tape on which black and white stripes are painted (*optokinetic nystagmus).* The latter phenomenon can be used as a test to demonstrate the integrity of the reflex paths.

The same reflex produces *involuntary fusional movements* of the eyes to maintain single binocular vision. This may be demonstrated clinically by placing a small prism in front of one eye while the patient regards a distant light. The eye will at once turn away from the primary position to allow the deflected rays to fall again upon the fovea. The strongest prism whose deviating effect can be tolerated without developing diplopia or double vision is a measure of the *reflex fusional capacity* (Fig. 25.11). A prism bar consists of a battery of prisms

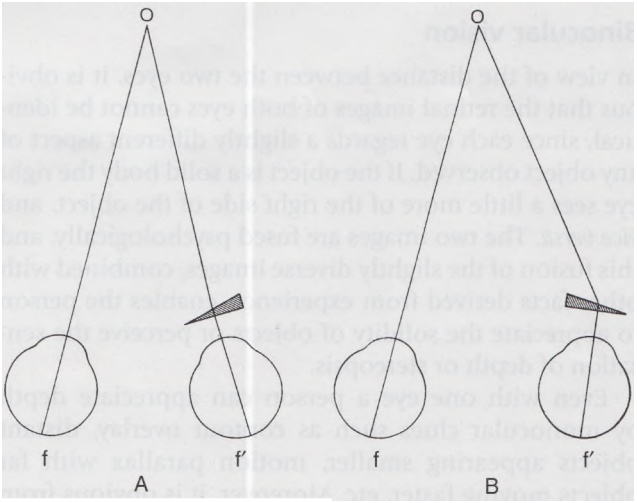


Fig. 25.11 The action of adducting and abducting prisms: o, object of fixation: f, *f″* left and right foveae centrales, respectively.

Table 25.5 Control of eye movements. There are six ocular motor systems

System	Purpose and description of movement	Initiation
Saccades	Rapid eye movements to direct the fovea to a target whose image is falling peripherally on the retina or a voluntary command eye movement	Frontal eye field and parietal eye field
Smooth pursuit	Following movements with the purpose of maintaining the image of a slowly moving small object on the fovea	Temporo-occipital junction
Vergence	Vergence eye movements are required to maintain binocular single vision and permit stereopsis by moving both eyes horizontally in opposite directions. The system is required to maintain foveal position of the image of an object which may be moving away or towards the observer or may be located near or far away	Striate cortex neurones respond to retinal disparity. The peristriate, posterior temporal and dorsal prefrontal cortex are regions which send convergence and divergence impulses
Fixation	Maintaining the image of the object of regard on the fovea	Supplementary eye field maintains fixation with the eyes in specific orbital locations and also inhibits visually evoked saccadic reflexes. The frontal eye field is involved in changing fixation (disengaging)
Vestibulo-ocular reflex (VOR)	Prevents slipping of the retinal images when the head moves. It moves the eyes at the same speed but in the opposite direction as the head. If an object is being pursued with eye and head movement, vision cancels the vestibulo-ocular reflex to prevent the eyes from moving in the opposite direction as the head	Otolith receptors and semicircular canals. Second-order neurons are in the vestibular nuclei
Optokinetic movements	During prolonged rotations the optokinetic system sustains compensatory eye speed at the same speed as the head. Optokinetic nystagmus is evoked during head motion with the environment stable and with the head still, but the visual image in motion. If the target is small and attention voluntarily guided, smooth pursuit is induced followed by opposite quick phases. The optokinetic nystagmus induced by rotating a striped drum is due to activation of both smooth pursuit and optokinetic systems	Direct pathway in the brainstem and indirect pathway involving the brainstem, cerebellum and cerebral hemispheres, parts of the striate and extrastriate visual cortex, parietal, posterior temporal, prestriate and lateral occipital cortex

Both the frontal eye field and superior colliculus (SC) are obligatory routes for cerebral cortex-initiated saccadic commands and project to the contralateral pontine paramedian reticular formation (PPRF). Each frontal eye field or superior colliculus can generate horizontal saccades to the opposite side. Vertical saccades are generated by simultaneous stimuli from bilateral frontal eye fields or superior colliculi.

of increasing strength and is a convenient instrument in clinical testing (Fig. 25.12).

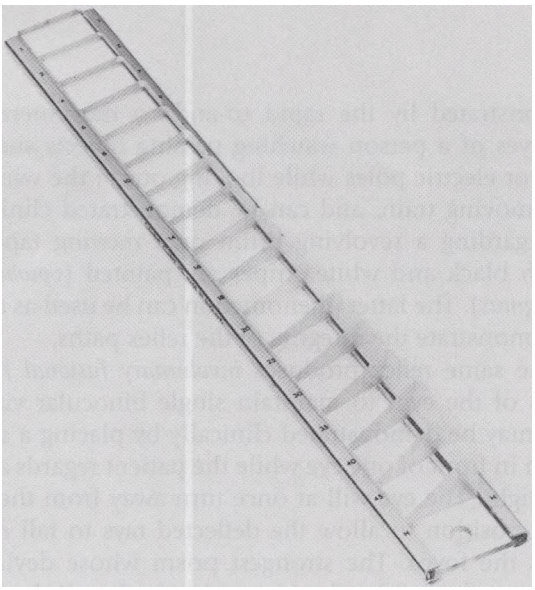
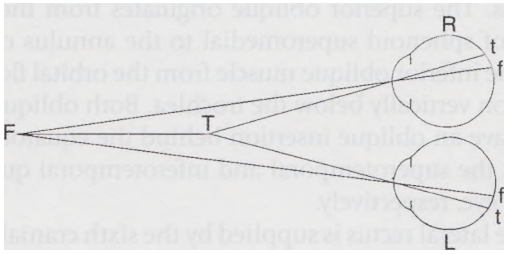


Fig. 25.12 Prism bar. (By courtesy of Clement Clarke International Ltd.)

Binocular vision

In view of the distance between the two eyes, it is obvious that the retinal images of both eyes cannot be identical, since each eye regards a slightly different aspect of any object observed. If the object is a solid body the right eye sees a little more of the right side of the object, and *vice versa.* The two images are fused psychologically, and this fusion of the slightly diverse images, combined with other facts derived from experience, enables the person to appreciate the solidity of objects or perceive the sensation of depth or stereopsis.

Even with one eye a person can appreciate depth by monocular clues such as contour overlay, distant objects appearing smaller, motion parallax with far objects moving faster, etc. Moreover, it is obvious from Fig. 25.13 that if both eyes are fixing upon a particular object, the images of other objects nearer or further



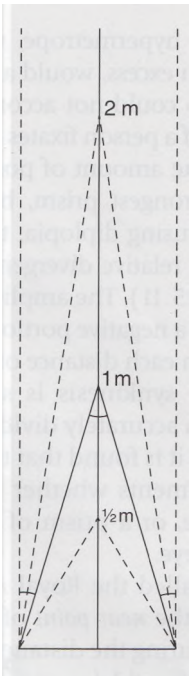
Fig, 25.13 Physiological binocular double vision. For the sake of clarity the distances are out of proportion. The images of the fixation point (F) fall on each fovea (f); those of an object near the eye (T) will fall on t, giving rise to crossed diplopia.

away cannot fall upon corresponding points. If their projection through the nodal point is continued to the retina, it is seen that the images of objects nearer than the object of fixation fall on the temporal side, those farther away to the nasal side of the fovea. This can be easily demonstrated by holding a pencil in front of the eyes: if the pencil is fixated, more distant objects appear doubled; if a distant object is fixated, the pencil appears doubled. It will thus be found that near objects suffer a *crossed* (*heteronymous*) *diplopia;* distant objects an *uncrossed* (*homonymous*) *diplopia.* This diplopia is physiological and is perceptually suppressed in actual vision, but produces a psychological impression, which is translated into appreciation of distance. It follows that accuracy of stereoscopic vision depends upon good sight with both eyes simultaneously.

CONVERGENCE AND ACCOMMODATION

When a distant object is observed by an emmetropic person, the visual axes are parallel and no effort of accommodation is made. If, however, a near object is regarded, the eyes converge upon it and an effort of accommodation corresponding to the distance of the object is made. These movements are reflex and are controlled, as we have seen, by a centre in the occipital cortex (Fig. 25.9), the afferent path being the visual pathways, the efferent path running to the Perlia nucleus region of the Edinger-Westphal nucleus. The associated pupillary contraction is a purely low-level reflex arc, the afferent path running from the medial recti to the Edinger-Westphal nucleus and the efferent by the parasympathetic fibres in the third nerve *(see* Fig. 4.8).

Convergence is usually measured by employing the *metre angle* as a unit. Suppose an object is situated in the median line between the two eyes at a distance of one metre from them. Then the angle which the line joining the object with the centre of rotation of either eye makes with the median line is called one metre angle (m.a.) (Fig. 25.14). With an interpupillary distance of 60 mm this angle is about 2 °. If



Fig, 25.14 Diagram of the metre angle. Cr, Cl: centres of rotation of the right and left eyes, respectively.

the object is 2 m away the angle is approximately half as great, or 1/2 m.a. If the object is 50cm away the angle will be 2 m.a. Now, the amount of accommodation which an emmetropic eye exercises to see clearly an object 1 m away is 1 D, 2 m away 0.5 D, 50 cm away 2 D, etc. Hence, with an emmetropic person, the amount of convergence, reckoned in meUe angles, is the same as the amount of accommodation reckoned in dioptres. Just as the difference in the amount of accommodation between the far point and the near point is called the amplitude of accommodation, the difference in convergence between the far points and the near point is called the *amplitude of convergence.*

Clinically, convergence can be tested roughly by making the patient fix a finger or pencil which is gradually brought nearer to the eyes in the midline. The eyes should be able to maintain convergence when the object is 8 cm (3 Vi inches) from the eyes. If outward deviation of one eye occurs before this point is reached, the power of convergence is deficient.

More accurate measurements can be made by instruments, held in front of the eyes, in which a vertical pointer slides along a scale. The amount of convergence can also be measured by prisms, as an extension of the method described to measure fusional capacity (Fig. 25.11). In this case, the prism is directed base outwards; the strongest prism that can thus be used without inducing diplopia when a *distant* object is regarded, is a measure of the amplitude of convergence.

Although related, it is obvious that the association between convergence and accommodation must be

elastic—otherwise a hypermetrope, whose accommodation is always used in excess, would always have diplopia, or a presbyope, who could not accommodate, would be unable to converge. If a person fixates (and accommodates for) a near object, the amount of positive convergence is measured by the strongest prism, base out, which can be borne without causing diplopia; the amount of negative convergence (or relative divergence) by the strongest prism, base in (Fig. 25.11). The amplitude of convergence, therefore, consists of a negative portion and a positive portion, which vary with each distance of the object fixated.

The convergence synkinesis is so coordinated that the energy exerted is accurately divided between the two medial recti. Hence, it is found that the effect is the same in the above experiments whether the prism is placed before only one eye, or a prism of half the strength is placed before each eye.

An instrument called the Royal Airforce (RAF) ruler is used to measure the *near point* of *accommodation* and *convergence* by measuring the distance at which the target appears 'blurred' or 'double', respectively.

SUMMARY

An understanding of the anatomy, physiology and neural control of the extraocular muscles is important for the clinical applications of examination, diagnosis and therapy of patients with ocular motility disorders.

There are six extraocular muscles, four rectus and two oblique muscles. All four recti originate from the annulus of Zinn and insert on the sclera 5.5-7.5 mm from the limbus. The superior oblique originates from the lesser wing of sphenoid superomedial to the annulus of Zinn and the inferior oblique muscle from the orbital floor at a location vertically below the trochlea. Both oblique muscles have an oblique insertion behind the equator of the eye in the superotemporal and inferotemporal quadrant of the eye, respectively.

The lateral rectus is supplied by the sixth cranial nerve, the other three recti, the inferior oblique and the levator palpebrae superioris are supplied by the third nerve and the superior oblique by the fourth nerve. The nuclei of these nerves are located in the brain stem.

Eye movements are of different types such as saccades, pursuit, voluntary, involuntary and so on. The supranuclear control of eye movements is very complex, but broadly one should know that there are various centres in the cerebral cortex and brain stem, each controlling different types of movements and transmitting signals to other centres for perfect coordination and the final command passes to the motor nuclei in the brain stem so that the motor impulses can be executed via the appropriate nerves and muscles.

The concepts of fixation and binocular vision help to understand the way visual information obtained separately from the two eyes is processed to give an integrated image in the brain which is projected in space to give the final picture. Convergence with accommodation for near viewing and divergence with relaxation of accommodation for looking at distant targets are other components of the complex sensorimotor coordination that is required for all our visual needs.

Chapter 26

Comitant Strabismus

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Strabismus (crooked eye or squint) is a generic term applied to all those conditions in which the visual axes assume a position relative to each other different from that conforming to physiological conditions. In simple terms, squint or strabismus is the condition where the visual axes of the two eyes do not meet at the point or object of regard.

COMITANT VERSUS INCOMITANT STRABISMUS

Squints can either be *comitant* or *incomitant.* In cases with comitant squint, as opposed to incomitant squint, although the eyes are misaligned, they retain their abnormal relation to each other in all directions of gaze. In comitant squint the efferent pathways are normal and can still maintain coordination of the eyes, but either the afferent path is defective (usually due to poor visual acuity owing to a defect in the eye) or the central mechanism mediating the fixation and fusional reflexes is undeveloped or has broken down. The breakdown may be due to peripheral causes, such as the excessive effort of convergence required with the sustained accommodation necessary in hypermetropes or a slight weakness in an extraocular muscle such as is not sufficient to cause a paralytic squint. Incomitant squints may be paralytic or restrictive (Table 26.1).

In paralytic squint the afferent pathways and centres are intact, but the efferent mechanism breaks down. In restrictive squints there is a mechanical factor such as a tight or fibrosed muscle or a local space-occupying lesion in the orbit or an innervational anomaly with simultaneous co-contraction of antagonist muscles which leads to limitation of movement and squint.

AETIOLOGY OF COMITANT STRABISMUS

We have already seen that in comitant strabismus, the visual axes, although abnormally directed, retain their abnormal relation to each other in all movements of the

Table 26.1 Differentiating features between incomitant and comitant squint

Clinical features	Incomitant squint (paralytic or restrictive)	Comitant squint
Magnitude of squint	Varies with eye position	Same in all positions
Diplopia	Usually present	Usually absent*
Ocular movements	Restricted	Full
False projection	Present	Absent
Abnormal head posture	Usually present	Absent
Secondary deviation	More than primary	Equal to primary

'Except in acute onset esotropia or intermittent divergent squint in a child old enough to understand and report the symptom.

eyes. The final lower pathway in the efferent tracts controlling ocular movements is undisturbed, but either the visual impressions arriving at the cortex from one eye are defective or the fusional reflexes have not or have been weakly developed and have broken down so that an ocular deviation results. The cause or causes of this failure are unknown and various theories have been stated and restated so frequently that they are often accepted as proved. The fact remains, however, that no theory of the fundamental causation has yet been advanced which satisfactorily explains the condition.

Nevertheless, many contributory factors in the aetiology of comitant strabismus are known, and a proper appreciation of them is essential for rational treatment. In the first place, *defective vision in one eye,* such as high ametropia, opacities in the media or ocular disease, makes it easy for the affected eye to lose fixation. If the defect exists from birth or early life, the cortical cells normally subserving both eyes may never develop binocular connections so that fusion is impossible. *Disturbances in muscular equilibrium,* usually due to a congenital malinsertion or defective development of one or more of the extrinsic muscles, may act in the same way, the squint being perhaps preceded by a period of heterophoria during which fusion was maintained. A *change in the normal balance between accommodation and convergence,* a matter originally pointed out by Donders, is also of importance. The continuous effort of accommodation in the hypermetrope to see clearly, even in the distance, stimulates convergence to a greater degree than is compatible with binocular fixation; faced with the dilemma of either relaxing his accommodation and not seeing clearly or converging too much and suffering diplopia, he chooses the latter, squints inwards and suppresses the image from the deviating eye. Conversely, the myope squints outwards. These relationships between the refractive condition and direction of the squint are, however, by no means invariable.

If the fusion mechanism is well-developed and the deviation slight, visual alignment may be maintained in normal circumstances by a continued effort of fusion: the squint is then *latent* and can only be made manifest when fusion is made impossible (as by covering one eye). This condition is called *heterophoria* or *latent squint.* If, on the other hand, the maintenance of alignment becomes impossible, a true or *manifest comitant squint* develops.

Comitant strabismus may be *intermittent (periodic*) or *constant, convergent* or *divergent.*

Convergent strabismus (esotropia) is more common in hypermetropes and is more common than divergent squint in Caucasians. It always commences in childhood. It may become manifest after an attack of whooping cough, measles or other debilitating illness, and is often popularly attributed to some such cause. There is an undoubted tendency for the deviation in all cases of convergent strabismus to diminish with the diminution of accommodation with age. The deviation is not always purely horizontal; in many cases the eye deviates upwards as well as inwards. In cases where there is a vertical element it is hypothesized that the deviation may have been originally primarily paretic. Congenital esotropia may also be associated with neurological disorders and may be hereditary.

Divergent strabismus, on the other hand, is most common in myopes, often commencing at a later age; it may, indeed, arise late in life when one eye loses most or all of its vision. The better eye is then used and the other is allowed to take up the position of rest, which is usually one of divergence. Spontaneous cure rarely if ever occurs in divergent strabismus, which tends to increase with time.

SYMPTOMS OF COMITANT STRABISMUS

Apart from the loss of binocular vision and the cosmetic disfigurement, comitant squint is asymptomatic. Diplopia may be present in the initial stages, the history of which is not available, as the onset is usually early, in small babies or very young children, and it rapidly disappears due to psychological suppression of the macular image of the squinting eye. In most cases suppression is aided by an actual visual defect in the eye, but it also occurs in alternating squint, in which both eyes have normal

vision or have the same degree of ametropia. Suppression is undoubtedly aided, in all cases, by the peripheral situation of the image in the squinting eye, but the essential seat of suppression is the brain. Since the image of any object falling on disparate points results in diplopia and since the brain finds this intolerable, it actively inhibits the image of the squinting eye. This prolonged active suppression results in a permanent lowering of the vision of the squinting eye—*amblyopia.* In contrast, it is noteworthy that, because this purposeful and active inhibition is not involved in a visually mature eye, an eye which has been blinded for many years by cataract in adults, attains good vision after a successful operation.

Amblyopia is a developmental defect of spatial visual processing that occurs in the central visual pathways of the eye. It is defined as a condition with unilateral or bilateral subnormal vision (at least two lines less than 'normal' or two lines less than the fellow eye in unilateral cases) without any local ophthalmoscopic abnormality, which is reversible if treated appropriately at the proper time. Amblyopia commonly results from conditions that produce a blurred image on the retina (*amblyopia ex anopsia* or *stimulus deprivation amblyopia)* or cause diplopia (image of the same object falling on disparate retinal points) or confusion (images of different objects falling on the foveae of the two eyes as occurs in strabismus, *strabismic amblyopia)* and in high anisometropia with aniseikonia (a difference in the retinal image size between the two eyes), leading to abnormal binocular interaction. Amblyopia occurs during the critical or sensitive period of development and maturation of the visual system, which is estimated to be 0-8 years in children (0-3 years is the most vulnerable period). The major amblyopiogenic factors are summarized in Table 26.2.

Vision in amblyopic eyes has certain characteristic features:

1. Single letter vision is better than if the letters are presented in a row as is the norm in visual acuity charts. This is known as *crowding phenomenon.*
2. Visual acuity drops less when viewed through grey neutral-density filters compared to normal eyes.
3. Decreased recognition, Vernier and grating acuity.
4. Decreased contrast sensitivity and spatial localization.
5. Impaired pursuit eye movements.
6. Decreased saccadic amplitudes.

Suppression affects mainly the fovea, and the acuity of vision may become greater at an eccentric point of the retina where the new fixation axis falls in the squinting position, which results in the development of a 'false macula' with abnormal retinal correspondence and abnormal projection, maintained only when both eyes are in use. When only the squinting eye is used, the fovea is usually (but not invariably) used again for fixation. This abnormal system may become so fixed that the fovea remains suppressed and the eccentric retinal point may gain prominence such that the eye may continue to fix with the eccentric point when the other eye is covered. When the fixing eye is covered with the screen the deviating eye usually moves so as to take up fixation. In unilateral squints of long standing, this eye may remain motionless or move only slightly, a condition which is called *eccentric fixation.* Since it occurs only with marked deviation of long standing, there is generally no difficulty in distinguishing it from apparent squint.

If the eyes are surgically straightened, diplopia may result and the eyes naturally tend to return to their old squinting position. The elimination of false correspondences is therefore of importance before operation is attempted. In some cases, instead of developing eccentric fixation, eventually all power of fixation may be lost by the amblyopic eye leading to unsteady fixation or no fixation.

Treatment of amblyopia by occlusion of the fixing eye: To allow an amblyopic eye to be used, the other must be prevented from seeing, or at any rate from seeing clearly. The only satisfactory method of ensuring this

Table 26.2 Classification of amblyopia

		Amblyopiogenic influence	
Type	Examples	Deprivation of form vision	Abnormal binocular interaction
Stimulus deprivation	Unilateral media opacity	Present	Present
	Bilateral media opacity	Present	Absent
Anisometropic	Hypermetropia of +1 Dsph in one eye and of +6 Dsph in the other	Present	Present
Ametropic	Hypermetropia of +7 Dsph in both eyes	Present	Absent
Meridional	−5 Dcyl x180° in one eye	Present	Present
Strabismic	Unilateral convergent squint	Sometimes	Present

is by complete occlusion, effected by a patch covering the better eye fixed on the skin by adhesive material to prevent the child removing it. The patch is changed when it becomes dirty or loose. *Occlusion should be total* since, if both eyes are used together, active inhibition of the squinting eye rapidly undoes any improvement achieved. This should be continued for 6-12 weeks, but if there is little improvement after this interval, the practice may be discontinued. In children younger than 8 years, i.e. in the amblyopiogenic age, there is a danger of occlusion amblyopia in the good eye due to constant occlusion of that eye. This is avoided by alternating occlusion proportional to the age of the child. The good eye is occluded for the number of days corresponding to the patient's age, e.g. a 4-year-old would have a 4:1 occlusion, the amblyopic eye being occluded every fifth day for a day. The younger the child, the higher the risk of occlusion amblyopia; the alternation should be more frequent. In very young children less than 1 year of age, part-time occlusion is tried initially, i.e. for a few hours a day. Beyond 8 years of age, constant occlusion can be prescribed.

In cases of eccentric fixation the good eye should be occluded for a time in the hope that foveal fixation will develop in the other. In some cases the deviation is transferred to the occluded eye which is a good sign, as it indicates that the vision of the originally squinting eye is only slightly worse than that of the fixing eye.

An alternative method is to activate the entire population of visual neurones in the visual cortex by a range of spatial frequency gratings covering all orientations. This may be accomplished by slowly rotating a disc with black and white lines of varying widths before the amblyopic eye in which the vision may thus improve faster and more completely than with other techniques. Patients observe the gratings with the amblyopic eye for 7 minutes and play drawing games on a Perspex plate over the rotating grating. Children are treated at weekly intervals and the non-amblyopic eye is not occluded.

In very young children or in recent squinters in whom the habit of suppression has not become fixed, the less drastic procedure of instilling atropine into the *fixing* eye (penalization of the normal eye) every 2 days may be sufficient; as this forces the squinting eye to be used for seeing near objects.

THE INVESTIGATION OF STRABISMUS

After taking the history, the first step in evaluating a patient with squint is the assessment of visual acuity, followed by assessment of ocular motility and general examination of the eye including the fundus (Table 26.3). Refraction under cycloplegia and repeat fundus examination with a dilated pupil is mandatory in all children with squint.

Table 26.3 Outline of clinical and investigative evaluation of a patient with strabismus

Case history	Chief complaint Onset and duration Previous treatment Family history Treatment goals and expectations
Diagnostic tests	Visual acuity and monocular fixation pattern Cycloplegic refraction and fundus examination Look for any change in head posture and test ocular movements Determine details of deviation (Table 26.4) Tests for binocularity Forced duction test (if movements are restricted)
Management plan	Estimate prognosis Patient/parent counselling

In assessing the deviation an important step is to ensure that any apparent deviation is indeed real. An *apparent squint* may be due to the configuration of the palpebral aperture. If, for example, as commonly occurs in children, a flat nasal bridge with epicanthus is present and the medial canthi approach the cornea, the appearance of a convergent squint results.

The optic axis upon which the cornea and lens are centred passes through the centre of rotation of the eye and approximately through the centre of the pupil. The visual axis passes through the nodal point and the fovea centralis, thus crossing the optic axis and making a small angle with it. This angle (although the convention is slightly inaccurate) is commonly spoken of as the angle gamma (Fig. 26.1). Clinically this angle is assessed at the pupillary plane and is referred to as the angle kappa. In the emmetropic eye, the angle kappa is said to be positive, since the optic axis usually cuts the retina internal to the fovea centralis. In hypermetropic eyes the angle kappa is also positive but greater than in emmetropia and gives the appearance of pseudoexotropia or pseudodivergent squint. In myopia the angle kappa is absent or negative, for the visual axis and the optic axis coincide or the latter cuts the retina external to the fovea centralis giving rise to a pseudoesotropia.

Neither of these lines can be seen, and the direction of the line of vision is judged by the position of the pupil. Hence the greater the size of a positive angle gamma and kappa the more the eye will appear to look outwards. If the angle gamma is negative the eye will appear to look inwards. In high hypermetropia, therefore, there will be an apparent divergent squint, in high myopia an apparent convergent squint. The latter is the more striking because the emmetropic eye usually has a positive angle gamma

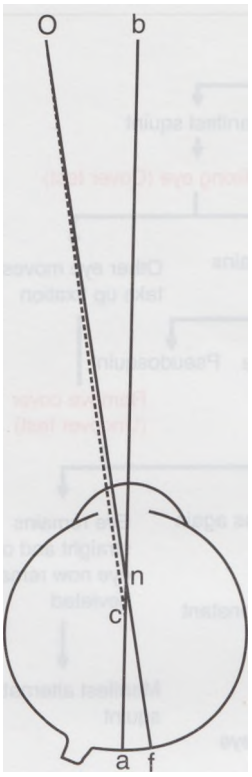


Fig. 26.1 Apparent strabismus, ab, optic axis upon which the refractive surfaces are centred; f, fovea centralis; n, nodal point; c, centre of rotation; O, point of fixation; Oc, line of fixation; Onf, line of vision; Ocb, angle gamma. It is practically equal to Onb, which can be measured. In actual practice the guide to ab is taken from the centre of the pupil; ab does not usually pass accurately through the centre of the pupil, so that the result is always only approximate. The angle gamma is to the nasal side in hypermetropia and emmetropia.

of 5°, thus producing an apparent divergence of 10°, which, however, is often regarded as the normal position of the eyes.

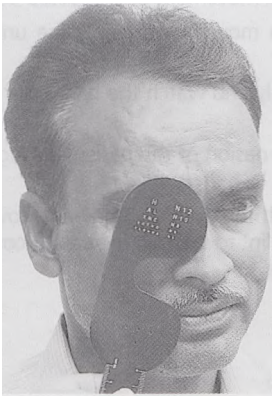
Small-angle strabismus and detection of amblyopia is difficult in infants. The Bruckner test may prove valuable in such cases. The infant is seated on the mother's lap while the lights are dimmed. The examiner sits at arm's length in front of the patient and shines the beam of a direct ophthalmoscope onto the patient's eyes. The light beam must be wide enough to illuminate both eyes simultaneously. Attention is directed to the fundus reflexes. When the patient is orthotropic, the colour and especially the brightness of the fundus reflex is equal in the two eyes. When strabismus is present, the fundus reflex of the fixing eye is darker, while that of the non-fixing eye is a brighter, lighter, red-yellow or white colour. The difference in brightness is more important than the difference in colour.

In establishing the presence of a true deviation or squint and further determining if it is latent or manifest, intermittent or constant, alternating or unilateral, convergent or divergent, comitant or incomitant the *cover test* is useful *(see* Flowchart 26.1 and Fig. 26.2).

In an apparent squint there is no deviation, so there is no restitutional movement when either eye is covered and then uncovered. The characteristics of the ocular deviation must be determined as outlined in Table 26.4. If one eye habitually fixes and the other squints the case is usually termed as one of *unilateral strabismus.* Sometimes fixation is retained by either eye in which case the squint is said to be *alternating.* Usually, in a divergent squint an object towards the right in the field of vision will be fixed with the right eye, in the left of the field by the left eye, while the converse may occur in convergent squint (cross-fixation). Occasionally, patients with alternating strabismus can fix with either eye voluntarily, but are usually unconscious of which eye is fixing.

The next step is to differentiate a comitant squint from an incomitant squint. This is done by the *cover-uncover test.* In incomitant squint, we have already seen that the secondary deviation is greater than the primary, while in comitant squint, both deviations are equal. In comitant squints, when either eye is covered and then uncovered, the deviation suffered by each is the same in any direction. Moreover, the movements of the eye are found to be full in all directions, and there is no complaint of diplopia if the





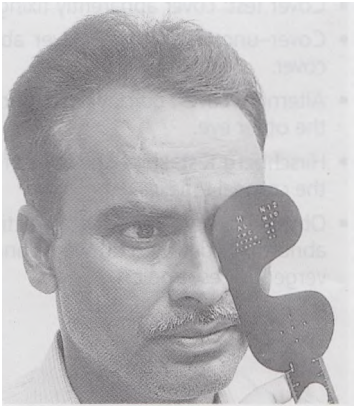
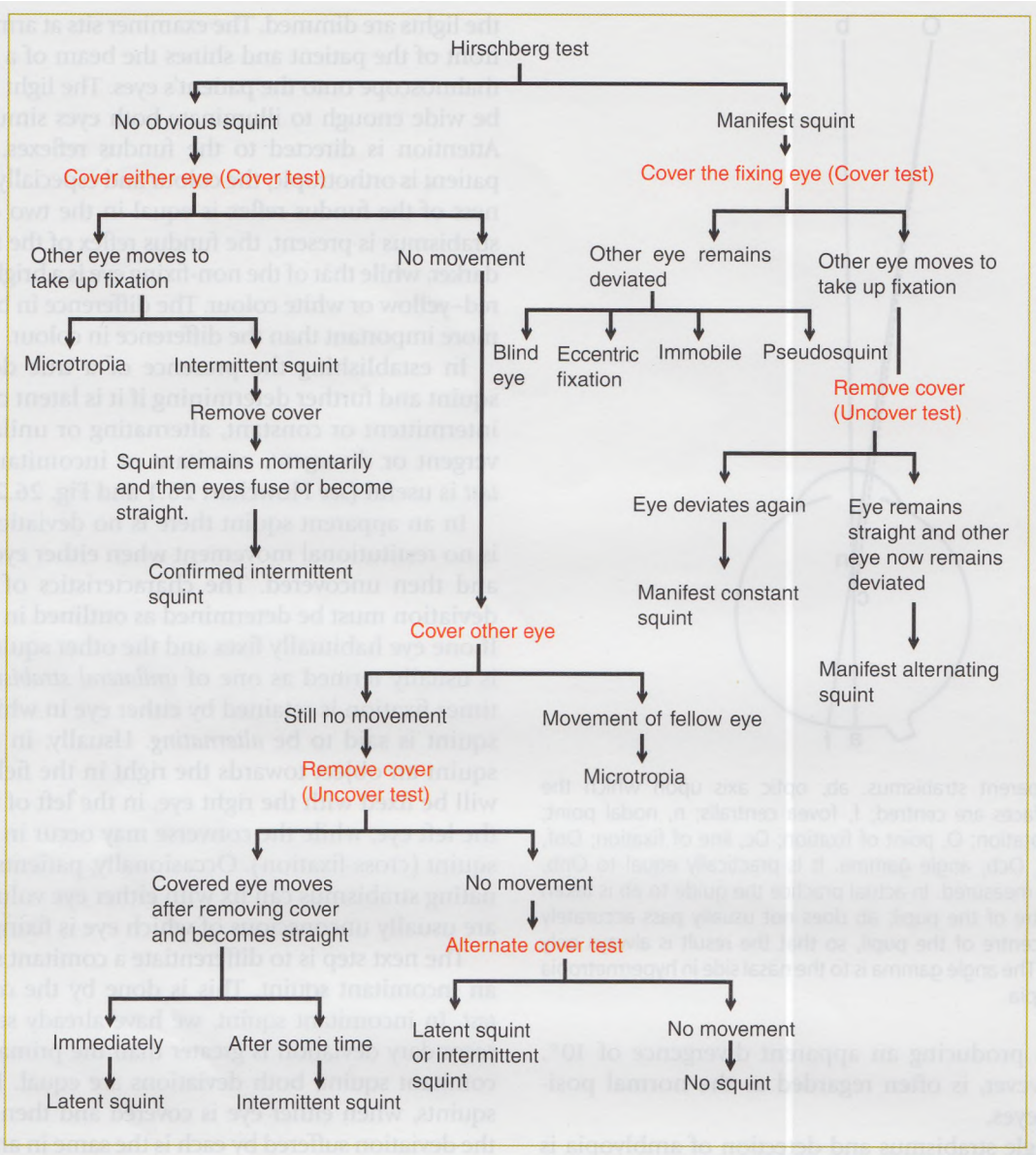


Fig. 26.2 Cover test. Observe the alignment of the eyes. Cover the apparently fixing eye with an occluder and observe the response of the other eye. Repeat test with the other eye if required.



Flowchart 26.1 Interpretation of cover, cover–uncover and alternate cover tests.

- Cover test: cover apparently fixing eye and watch movement of suspected deviating eye.
- Cover–uncover: remove cover above and watch movement of only the uncovered eye, i.e. covered eye immediately after removing cover.
- Alternate cover: quickly cover each eye alternately and watch the behaviour of each eye when the cover is removed and transferred to the other eye.
- Hirschberg test: shine the light of a torch on the nasion of the patient asking him/her to fixate on the light, and watch for symmetry of the corneal reflexes.
- Observe direction of each corrective movement. If the eye moves inwards towards the nose it is a divergent squint because the eye was abnormally deviated outwards and had to move 'in' to take up fixation. If corrective movement is outwards, the squinting eye was convergent or esotropic.

Table 26.4 Clinical parameters of ocular deviation

Direction	Convergent (esotropia) Divergent (exotropia) Vertical (hypertropia or hypotropia) Torsional (incyclotropia or excyclotropia)
Frequency	Latent (heterophoria) Manifest (heterotropia) Intermittent Constant
Magnitude	For distance and near fixation with and without glasses
Comitancy	Comitant or incomitant
Laterality	Unilateral Alternating (which eye is preferred for fixation or which eye is dominant)
Accommodative convergence/ accommodation (AC/A) ratio	Low, normal or high

squint is longstanding. In acute comitant squint a patient may report diplopia but the distance between the images is the same in all directions. It must be remembered, however, in performing this test in a marked squint of long duration that the eyes do not move as much as usual in the direction opposite to that of the deviation. Thus, in convergent squint it may be very difficult to get the eyes to move outwards to the full extent so that on maximum attempted abduction of the affected eye the margin of the cornea may still lie inside the lateral canthus. This defective movement may be due to contracture of the muscle synergistic to movement of the squinting eye in the direction of squint, for example, in a constant left convergent squint the medial rectus of the left eye may develop contracture and not allow full outward movement (abduction) of the left eye. This may mistakenly be diagnosed as a left lateral rectus paresis if one is not aware of this phenomenon.

A simple test to confirm if a defective range of eye movement is due to muscle weakness or a physical restriction is the forced duction test.

Forced duction test: It is simply an attempt to passively rotate an eyeball to its full extent of movement to judge if the limitation of the full range of eye movement is purely paralytic or whether there is some physical restriction. The test is performed under local anaesthesia, but sometimes under general anaesthesia in the case of very young children. The patient is asked to look in the direction in which movement is being tested and the maximum range noted. The eyeball is then held at the opposite limbus with a toothed forceps and rotated maximally further in the same direction.

Interpretation: The test is said to be positive if there is a resistance to full passive movement and negative if it is possible to passively rotate the eye fully with the forceps. A negative result on testing forced duction implies a paralytic or innervational squint. A positive forced duction test indicates a restriction due to contracture or fibrosis of the ipsilateral antagonist or an orbital space-occupying lesion preventing full movement.

Force generation test: An additional useful test in immobile eyes is the active force generation test. This is needed in situations where multiple problems exist such as post-traumatic blow-out fracture of the orbit, where both muscle entrapment and paralysis may coexist. The anaesthetized limbus is grasped with a forceps and a 'tug' is appreciated when the patient 'attempts' to move the eye in the affected direction if the muscle is not paralysed but only 'mechanically restricted' in making the eye move.

Assessment of binocular vision

Various tests using different mechanisms to identify the image seen by each eye are used to assess the status of binocular vision. Commonly used tests are Bagolini striated glasses, examination with a synoptophore, Worth 4-dot test and tests for stereopsis.

Measurement of the angle of deviation

Measurement of the angle of deviation is important in all cases of squint for diagnosis and as a guide to treatment. The commonly used methods are (i) the Hirschberg test, (ii) the prism bar test and (iii) the synoptophore.

Hirschberg test: A rough indication of the angle of the squint can be obtained from the position of the corneal reflex when light is thrown into the eye from a distance of about 60 cm with the ophthalmoscope or a focused light beam from a torch (Figs 26.2 and 26.3). The patient is asked to look at the light; an infant does this reflexly. In the fixing eye the corneal reflex will be in the centre of the pupil, or slightly to the inner side if there is a large angle kappa, to the outer side if there is a negative angle

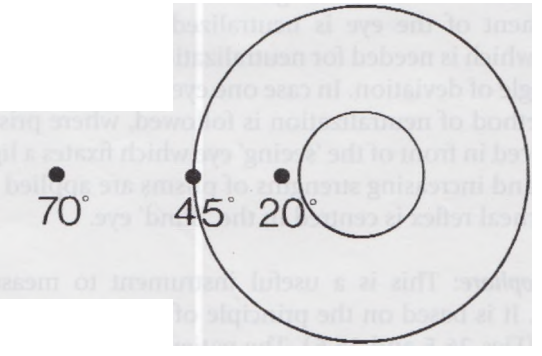


Fig. 26.3 Hirschberg test. Diagram of the position of the corneal reflex as a guide to the angle of the squint.

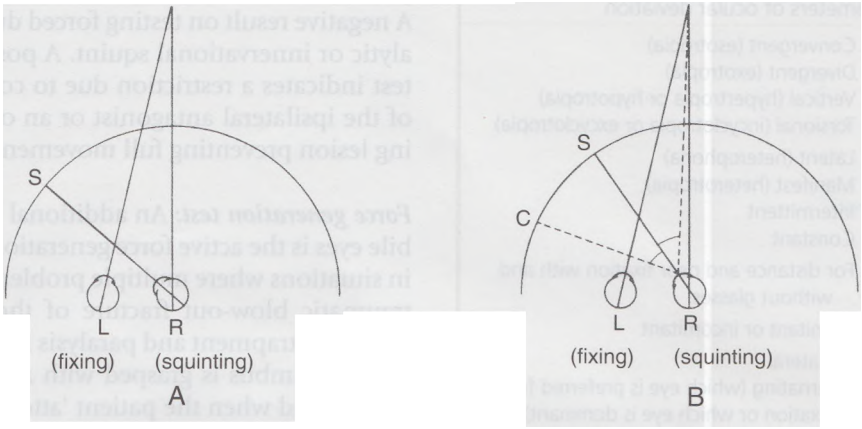


Fig. 26.4 Angular strabismometry. (A) Javal method. The right eye (squinting) is central in the perimeter. The left eye fixes F. The surgeon carries a light (S) along the arc of the perimeter until the corneal reflex in R is central. Angle SRF (less the angle gamma) is the angle of squint. (B) Charpentier method. The right eye (squinting) is central in the perimeter. The left eye fixes F. A light is placed on the perimetric arc on the line FR and the surgeon moves round the arc (to C) until he sees the corneal reflex in R central. Half the angle FRC (i.e. FRS) (less the angle gamma) is the angle of squint.

kappa (p. 394). The light is observed to be decentred in the squinting eye. If the reflex is about half-way between the centre of the pupil and the corneal margin, there is a deviation of about 20° if it is at the corneal margin, about 45 °. Roughly 1 mm deviation of the corneal light reflex is equivalent to 7° of deviation. This test gives only an approximate estimation.

The angle of deviation of the squinting eye can also be measured on the perimeter or the tangent scale; in either case the patient fixes the central point with the good eye, and the surgeon carries a light along the arc of the perimeter or the arm of the tangent scale until the corneal reflex thus obtained is centred on the pupil of the squinting eye. The angle at which this occurs is the angle of the squint (Fig. 26.4).

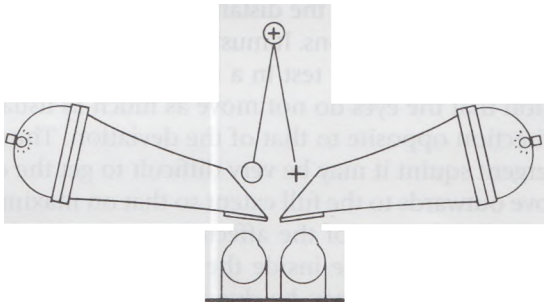


Fig. 26.5 The amblyoscope.

Prism bar test: This is the most commonly used method in routine clinical practice. The angle of deviation can be measured with the prism cover test using prisms of different strengths (either loose prisms or mounted prism bars) in front of one eye with the apex pointing towards the deviation and repeating the test till the corrective movement of the eye is neutralized. The strength of prism which is needed for neutralization gives the objective angle of deviation. In case one eye is blind the Krimsky method of neutralization is followed, where prisms are placed in front of the 'seeing' eye which fixates a light target and increasing strengths of prisms are applied till the corneal reflex is centred in the 'blind' eye.

Synoptophore: This is a useful instrument to measure squint. It is based on the principle of a simple amblyoscope (Figs 26.5 and 26.6). The patient looks down two adjustable tubes at two easily fixated small objects, and the angle between the tubes is altered until each eye attains

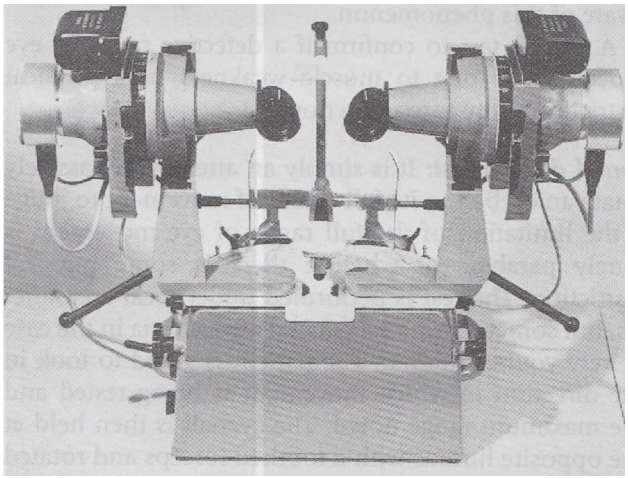


Fig. 26.6 A synoptophore for the examination of binocular vision, the capacity for fusion and the muscle balance. (By courtesy of Clement Clarke)

fixation when it is used separately, one rapidly after the other. This gives the position of the visual axes. The corneal reflexes are then centred on the pupil; this gives the position of the optic axes, and the difference between the two gives the angle of deviation. An attempt is then made to make both eyes fixate the objects simultaneously so that they appear superimposed; if the deviation is different from that obtained with each eye separately, the presence of abnormal correspondence is shown, and the difference gives the angle of false projection.

GENERAL PRINCIPLES OF MANAGEMENT OF STRABISMUS

The essential prerequisite for management of strabismus is the prescription of appropriate refractive correction and the treatment of attendant amblyopia if present. Binocular functions of the patient must be evaluated to determine the line of further management and prognosis. Patients without any degree of binocular function will be treated for purely cosmetic reasons. The treatment options for strabismus can be either conservative or surgical. Conservative therapy includes observation, optical (refractive or prisms) and orthoptic treatment (fusion exercises or pleoptics). Generally accepted indications for strabismic surgery are different in the various kinds of strabismus.

Usually, a constant deviation of more than 20 prism dioptres (10°) in convergent strabismus, more than 25 prism dioptres in divergent strabismus and 10 prism dioptres (5°) in vertical strabismus warrant surgery.

HETEROPHORIA OR LATENT STRABISMUS

Heterophoria is defined as a condition in which there is a tendency to misalignment of the visual axes, which is corrected by the fusional capacity. As with all deviations, the tendency is equally shared between the two eyes. Since the position of rest is usually one of slight divergence, some degree of heterophoria is almost universal and few people are *orthophoric.* If the latent deviation is one of convergence the condition is called *esophoria,* of divergence, *exophoria,* if vertical, *hyperphoria.* It is impossible to be sure whether there is absolute hyperphoria of one eye or hypophoria of the other, the condition being relative, so by convention the phoria is named according to the upwardly deviating eye, i.e. right hyperphoria or left hyperphoria. If the deviation is torsional the term *cyclophoria* is applied. Horizontal deviations are the most common, due often to overstimulation of convergence with accommodation in hypermetropia (*esophoria*) or understimulation in myopia (*exophoria*). Hyperphoria is also common and is probably often due to abnormal insertions or slight weakness of one or other of the vertically rotating muscles. Cyclophoria is rare.

The *symptoms* of heterophoria may be considerable since parallelism of the visual axes is only maintained by tonic contraction of the appropriate muscle. Symptoms of eyestrain are, therefore, encountered in the higher degrees; but lesser degrees give rise to little or no trouble. This particularly applies to eso- and exophoria since the muscles involved are accustomed to act unequally in convergence; only when the deviation is great, i.e. 5-10° or more, is asthenopia generally present. Slight degrees of hyperphoria, however, may cause considerable discomfort, for in these cases more complicated adjustments are necessary involving the non-physiological action of muscles (which are not accustomed to work together) to keep the visual axes in the same plane. For the same reason cyclophoria gives the greatest discomfort of all.

As might be expected, the deviation is liable to become manifest in conditions of fatigue and to vary in amount from time to time. Some periodic squints are due to this and the periodicity may be rhythmic. Thus a child may squint in the evening when he is tired, but after a good night's rest the squint may disappear and may not return until the second or third day, the sequence being accurately repeated. Often latent squints give no trouble until school age or adult life is reached, when the demands of near vision increase the strain. No symptoms arise, perhaps, until after reading or writing for an hour or two when 'the letters seem to run together'. This is due to relaxation of the over-strained muscles, when the eyes momentarily assume the position of rest, and diplopia, which is often not appreciated as actual double vision, causes blurring of the print. With effort, the blurring is overcome, but eventually this becomes impossible, headache supervenes, and the work has to be abandoned.

The *diagnosis* of heterophoria simply depends on abolishing fusion so that, without its control, the eyes assume their position of rest. Several tests are available for this.

The most simple is the *cover test* (Fig. 26.2). When a distant object is regarded, and both eyes are uncovered, there is no deviation. One eye is then covered so that the eyes dissociate and the latent deviation appears; when the screen is removed, this eye moves at once to regain the position of binocular fixation. The other eye reacts similarly, the deviation in both being the same.

Other tests depend on altering the appearance of the retinal image in one eye so that no stimulus is given to fusion. Of these the simplest is the *Maddox rod test.* The patient is placed in front of a bright spot of light in a dark room. A Maddox rod, which consists of four or five cylinders of red glass side by side in a supporting disc, is placed in the trial frame before one eye (the same effect is given by a disc of deeply grooved red glass—the Maddox groove, Fig. 26.7). The spot of light seen through the red



Fig, 26.7 Maddox groove. (By courtesy of Clement Clarke International Ltd.)

cylinders appears as a long red line perpendicular to the direction of the cylinders or grooves. If the cylinders are placed with their axes horizontal, the red line will be vertical. If there is orthophoria the bright spot will appear to be in the centre of the vertical red line; if there is eso- or exophoria the red line will be to one side of the spot. The angle of the deviation is measured by the strength of the prism which is necessary to be placed in front of the Maddox rod (or the other eye) to bring the red line and the spot together. The nature of the deviation is indicated by the position of the base of the prism, whether out (esophoria) or in (exophoria). The prism is placed with the apex pointing in the direction of deviation and is denoted by the position of the base. The Maddox rod is then rotated so that the cylinders are vertical, the red line now being horizontal. If there is no hyperphoria, the line will pass through the bright spot. If there is hyperphoria, the red line will be below or above the spot depending upon whether the relative hyperphoria is associated with the eye with the rod in front of it or with the other eye. In each case, the amount of deviation is measured either on a graduated tangent scale placed on a Maddox cross at 5 m distance set on the wall, or by the strength of the prism required to correct it.

The deviation in latent squint is often different in near vision as compared with that in distant vision. An exophoria, appearing when near objects are regarded is, in fact, an *insufficiency of convergence,* a condition that may give rise to symptoms when extensive near work is undertaken. This is the commonest type of latent squint seen in clinical practice. An exophoria, manifesting only for distance or showing a marked increase for distance as compared to near could be a manifestation of a mild sixth nerve paresis, particularly a mild bilateral sixth nerve paresis, which may occur in patients with raised intracranial pressure or multiple sclerosis.

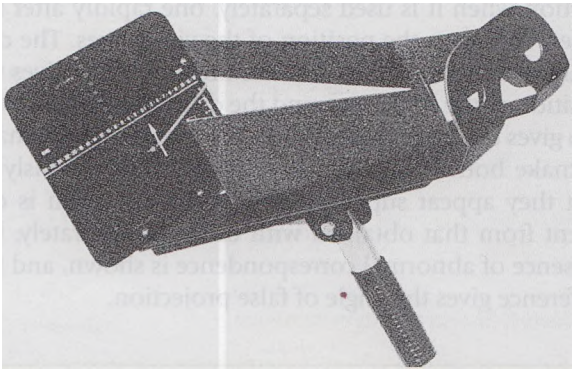


Fig. 26.8 The Maddox wing test.

The deviation in near vision is conveniently tested by the *Maddox wing* test (Fig. 26.8), in which the patient looks through the two slit holes in the eyepieces of the instrument. The fields which are exposed to each eye are separated by a diaphragm in such a way that they glide tangentially into each other. The right eye sees a white arrow pointing vertically upwards and a red arrow pointing horizontally to the left, whereas the left eye sees a horizontal row of figures in white and a vertical row in red. These are calibrated to be read in degrees of deviation. The arrow pointing to the horizontal row of figures and the arrow pointing to the vertical row should both be at zero; any deviation indicates an eso- or exophoria or a hyperphoria, the amount of which can be read off on the scale. There are several *diaphragm tests* on somewhat similar principles.

Besides the actual measurement of the deviation in latent strabismus, the strength of the muscles involved should also be tested by forcing them to a maximum effort against prisms *(prism vergence tests).* With the patient seated 6 m from a light, the highest prism which can permit single vision gives the *verging power* for the particular direction involved. The converging power varies greatly and with practice, can be raised to 50 prism dioptres (25°) or more; if it falls below 20°, it may be taken to be definitely insufficient. The diverging power should be 4-5°, and normal limits of super- and subduction are from 1.5° to 2.5°.

The range of fusional convergence can also be assessed using the synoptophore, which has two separate viewing tubes through which the patient views two images which are seen by each eye separately and fused by the brain. The images selected for viewing are different depending on the purpose for which the instrument is being used. When testing for fusion, each eye is presented with similar images which are incomplete in some aspects (Fig. 26.9). The tubes can be moved to a slight extent to see the range of separation of images which can be fused by the observer and viewed as single.

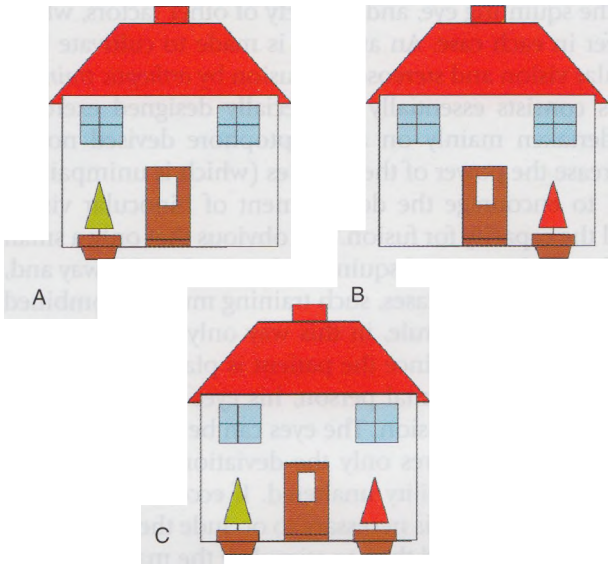


Fig. 26.9 Fusion slides. (A) and (B) are images seen by each eye separately; (C) fusion of images seen by the two eyes.

Treatment

The lower degrees of esophoria and, to a lesser extent, exophoria, cause no symptoms and need no special treatment. If symptoms are apparent after any error of refraction has been corrected with spectacles, a rational treatment of eso- or exophoria consists in exercising the weak muscles against prisms (with the base of the prism in the direction of deviation), or by the use of the synoptophore. Unfortunately, this is usually not or only temporarily beneficial, but relief, however, may be maintained by repeating the exercises at intervals, an activity which the patient can practice himself. If this is ineffective, the symptoms may be relieved by ordering prisms in spectacles to correct the defect, i.e. prisms with their bases in a direction opposite to those used for exercise. This should be avoided, if possible, since it generally tends to increase the defect, so that stronger prisms have to be ordered from time to time. The total prismatic error should be divided equally between the two eyes when ordering the correction. Hyperphoria in its lesser degrees should unhesitatingly be treated in this way, as exercises are useless in this condition.

Insufficiency of convergence may be treated by prism exercises. The following simple exercise is often sufficient without having recourse to prisms. A pencil is held in the hand and slowly approximated to the nose until, despite an effort of convergence, it appears double; this is repeated until the distance at which diplopia occurs is gradually shortened. At about every tenth time, the patient looks into the distance so as to relax his accommodation and convergence. The exercise should be repeated three or four times a day for several weeks but never at night when tired. After each session the patient should attempt to relax his muscles by either closing both eyes or looking into the far distance for a few minutes.

In all cases in which the deviation is large and unaffected by such treatment, operation may be considered, one or other muscle being recessed or resected and the case being treated as if it were a manifest squint. Even if not curative, the deviation may thus be reduced to such a degree as to abolish asthenopia.

HETEROTROPIA OR MANIFEST STRABISMUS

Convergent strabismus (esodeviation)

Aetiology

These are generally more common in childhood and hypermetropes. Racial differences in prevalence are possible. The aetiology is complex and is briefly outlined on p. 391.

Classification

Esodeviation can be classified according to the underlying aetiopathogenesis and according to the type of deviation (Table 26.5).

Treatment

The routine management of a case of comitant convergent strabismus in a child should be undertaken at the earliest possible age. It is summarized as refraction, occlusion and then operation and is explained below.

1. *Preliminary:* Record the distant vision of each eye by the appropriate method according to the age of the child (if not too young by the E Test or by the

Table 26.5 Classification of esodeviation

Type	Criterion
Non-accommodative	Esotropia at distance = near fixation. No change with refractive correction
Accommodative	
• Refractive (normal AC/A ratio)	Esotropia at distance > near fixation. Fully corrected by hyperopic correction for distance
• Non-refractive (high AC/A ratio)	Esotropia at near Fixation > distance or manifesting only at near. Fully corrected by an additional hyperopic correction for near work
• Mixed	
Partially accommodative	Esotropia partly corrected by the use of refractive correction

Sheridan-Gardner test-types), and the angle of deviation. Atropine 1% eye ointment three times a day is then prescribed for 3 days. At the end of this period estimate the error of refraction by retinoscopy and confirm the result subjectively if possible, though retinoscopy should be relied upon rather than subjective tests. Care should be taken to examine the fundus in detail as retinoblastoma or any other organic lesion may sometimes present as a squint in young children. The angle of the squint should be measured again which is likely to be less under atropine than without a cycloplegic in case of hypermetropes with a convergent squint or more in myopes with a divergent squint. Full *spectacle correction* should be ordered for constant use. In hypermetropes no deduction for the effect of atropine should be made. Great care must be taken to correct all astigmatism, especially in the squinting eye. The patient should be re-examined in a month's time (Fig. 26.10).

Children with non-refractive accommodative esotropia are prescribed bifocals with near addition of+3 D to eliminate accommodative convergence by removing the need to accommodate for viewing near objects.

2. *If the child refuses to wear glasses* or is unable to use spectacles such as a child who is less than 2 years old, has a flat nasal bridge, is a hypermetrope and has a convergent squint, it is sometimes easier to eliminate accommodation by temporarily treating him with *miotic drugs* with anticholinesterase activity such as di-isopropyl fluorophosphate (DFP) or echothiophate (phospholine iodide). The child should be examined at regular intervals to ensure that the squint is corrected by these measures until it is considered advisable to order spectacles. Anticholinesterase agents have systemic side-effects which include nausea, vomiting, diarrhoea, abdominal cramps, perspiration and ocular side-effects such as pain on instillation, conjunctival irritation, accommodative spasm, myopia, brow ache, headache, anterior subcapsular cataract, iris cysts and rarely retinal detachment. Hence, they are not popular and prescribed only when no other alternative is possible.

3. *Orthoptic training:* Further treatment depends upon the size of the angle of deviation, the condition of vision in the squinting eye, and a variety of other factors, which differ in each case. An attempt is made to cultivate binocular vision and stereoscopic fusion by *orthoptic training.* This consists essentially in specially designed exercises undertaken mainly on a synoptophore devised not to increase the power of the muscles (which is unimpaired) but to encourage the development of binocular vision and the capacity for fusion. It is obvious that only a small and recently acquired squint can be cured in this way and, in the majority of cases, such training must be combined with surgery. As a rule, in this way only can a complete 'cure' be attained since the patient is placed in the same condition as a normal person; his eyes are straight and he has binocular vision. The eyes can be put straight surgically, but this cures only the deviation and leaves the fundamental disability unaltered. If eccentric fixation is well established, it is necessary to occlude the affected eye for some weeks and then to stimulate the macula by special *pleoptic methods* (flashing devices, the production of after-images, etc.) but it must be pointed out that such treatment is time-consuming and exacting and not always successful.

There are three stages in orthoptic treatment:

- the production of simultaneous vision with the two eyes;
- the production of binocular vision and elimination of false projection and
- the production of stereoscopic vision, i.e. the fusion of two images of the same object seen in perspective, resulting in the perception of solidity and relief.

Although orthoptic treatment is of great value in inculcating correct visual habits such as the training of binocular vision and the abolition of false projection, it rarely (if ever), by itself, cures a squint of over 10° deviation or one of long standing. In many cases it is useless to attempt it, and in all cases it is useless unless carried out systematically and thoroughly. It is rarely worthwhile to persist with it as a sole method of treatment if the deviation is not corrected within 3 months. The only exception to this rule is accommodative esotropia. For the details of treatment, monographs on the subject must be consulted. Its most valuable function is as an



Fig. 26.10 Accommodative esotropia fully corrected with glasses. (By courtesy of M Gogoi)

adjunct to operative treatment—to develop binocular vision and reduce the intensity of abnormal projection before operation, to consolidate results and correct any residual deviation after surgery.

4. *Surgical treatment* of comitant unilateral convergent squint is indicated when the angle of squint is 10° or more with correcting lenses, and in children when orthoptic training has failed to correct the deviation within a reasonable time. As a general rule it should be undertaken early and certainly as soon as the child is old enough to cooperate in post-operative orthoptic treatment, usually between 4 and 5 years of age but preferably may be undertaken as early as 18 months if required. Better results are expected with regard to binocularity if the child is operated within 2 years of age. Postponement until the child is 10 years old or more usually results in permanent amblyopia and failure to establish binocular vision. The operation is then purely cosmetic.

The safest operations for general use are a recession or a resection of the appropriate muscle. There is often a considerable deviation so that surgery may be required on both eyes. Free tenotomy of the medial rectus tendon and its expansions into Tenon capsule is usually followed by divergence and retraction of the caruncle and plica semilunaris owing to failure of reattachment to the globe and are no longer recommended. A partial tenotomy of the lateral rectus muscle, however, is sometimes permissible but again not generally recommended. The medial rectus should not be recessed more than 5 mm, i.e. not beyond the physiological equator lest weak convergence occurs leading to discomfort in reading and near work and to headaches. An approximate guide to expected results is given in Table 26.6.

The treatment of alternating comitant convergent squint detected or presenting late without appreciable error of refraction is purely cosmetic. These patients have no binocular vision, and it is useless to attempt to develop it at this late stage. However, if the case is seen when the patient is very young (less than 2 years old) or immediately after the squint has been first noticed, proper treatment can produce good functional results with binocular vision. This emphasizes the importance of referring all infants with squint or suspected squint early to the ophthalmologist.

Flowcharts 26.2 and 26.3 summarize the steps of treatment for esodeviation and exodeviation.

Divergent strabismus (exodeviation)

Aetiology

This has been briefly described on p. 391.

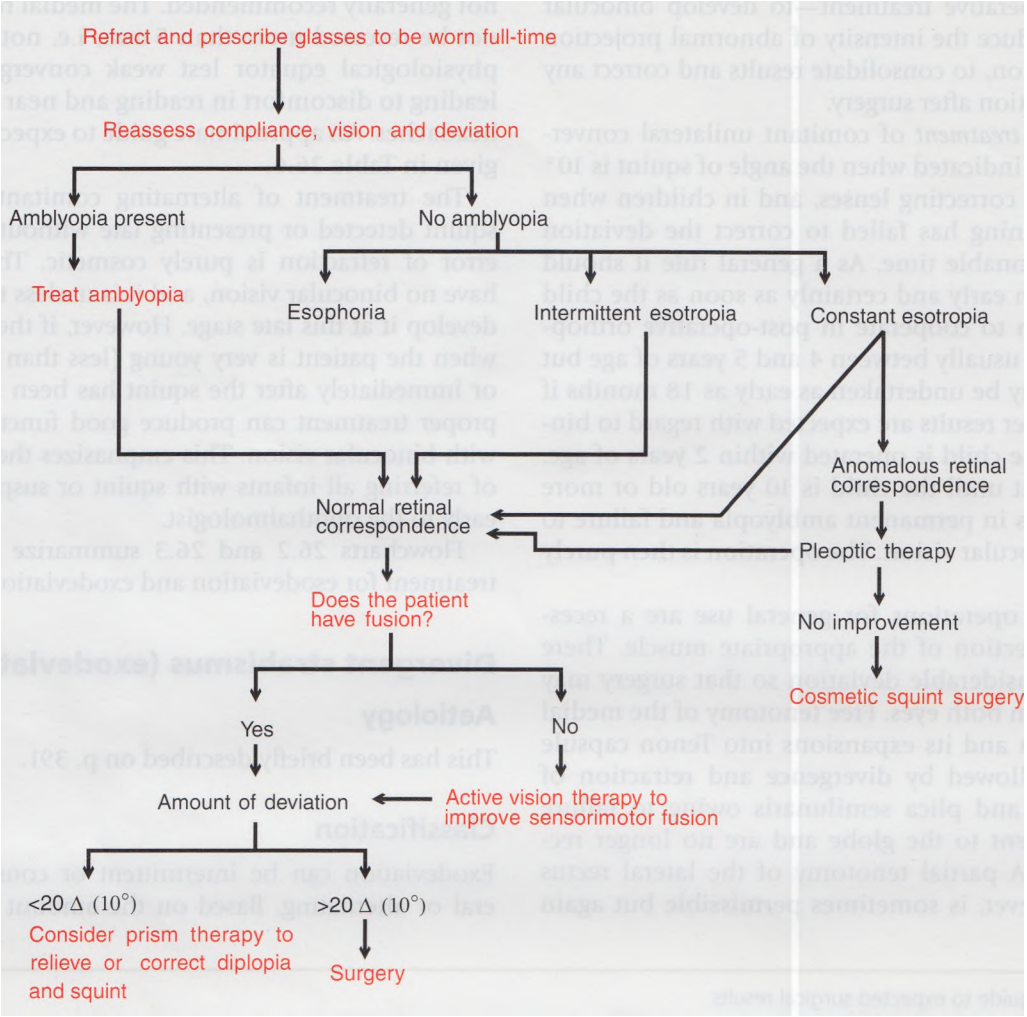
Classification

Exodeviation can be intermittent or constant, unilateral or alternating. Based on the amount of deviation

Table 26.6 A guide to expected surgical results

	Surgery (in mm)	Correction (in °)	Correction (in prism dioptres. Δ)
Esotropia			
Minimum MR recession each eye	3	12–15	20–30
Maximum MR recession each eye	5	Up to 25	Up to 50
Minimum MR recession & LR resection same eye	3 & 5	12–15	20–30
Maximum MR recession & LR resection same eye	5 & 8	30	60
Exotropia			
Minimum LR recessions each eye	5	15	30
Maximum LR recessions each eye	7	Up to 30	Up to 60
Minimum MR recession & LR resection same eye	5 & 4	12	20–25
Maximum MR recession & LR resection same eye	7 & 8	30	60
Vertical rectus surgery			
Minimum SR or IR recession	2.5	Up to 5	Up to 8–10
Minimum SR or IR resection	3	Up to 5	Up to 8–10
Maximum SR or IR recession (or resection)	4.5	Up to 8	Up to 15
Combined maximum vertical recti recession resection of same eye	4.5	15	25–30

MR, medial rectus; LR, lateral rectus; SR, superior rectus; IR, inferior rectus. (By courtesy of Fells)



Flowchart 26.2 Steps in planning the management of esodeviation.

measured at distance and near fixation they can be categorized as in Table 26.7.

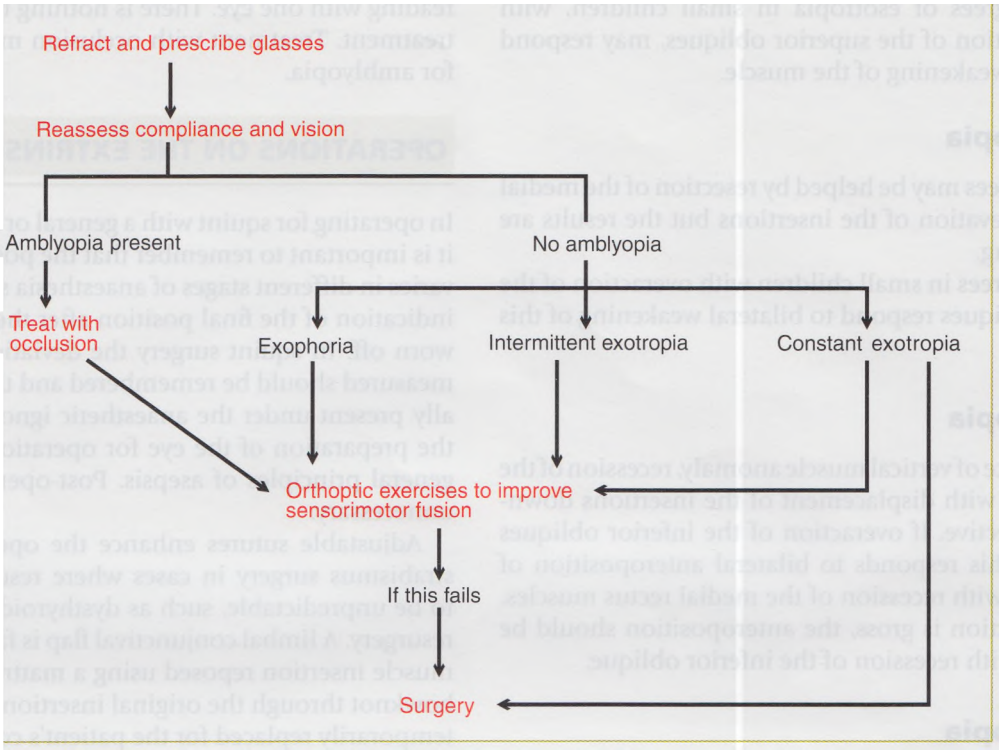
The principles and sequence in treatment of comitant divergent strabismus is similar to that of the convergent type. The treatment is outlined in the flowchart. The refraction must be first carefully and fully corrected for constant use unless the myopia is very high. Recession of the lateral rectus muscle alone or in combination with resection of the medial rectus is usually necessary. In divergent strabismus slight overcorrection is indicated, for these eyes show a strong tendency to revert to their former position.

Sometimes patients develop diplopia after the eyes have been straightened. This may be due to false projection but also occurs with alternating squints. It is a troublesome complication, usually persisting for some weeks or months, and is distressing to the patient, but it usually disappears eventually.

Table 26.7 Classification of exotropia (Duane 1896)

Type	Criterion*
Convergence insufficiency Exotropia at	near< distance fixation
Divergence excess type	Exotropic at distance > near fixation
Basic type	Exotropic at near= distance fixation

'Difference of at least 10 prism dioptres between the deviation recorded at near and distance.



Flowchart 26.3 Steps in planning the management of exodeviation.

'A' AND 'V' PHENOMENA

A tendency for the eyes to diverge on elevation is physiological. Any squint can show a variation in deviation in upward and downward gaze and, depending on the nature of the squint, an A' or V pattern can be recognized. For example, a V' pattern is seen in a convergent squint which increases on downward gaze but a divergent squint which is maximum in upward gaze and less in downward gaze. The A' and *V* phenomena should be assessed by the cover test in 25 ° upward and downward gaze. This test should be carried out for near and distance fixation. Glasses should be worn if required. In assessing the cover test for near vision a small target to stimulate accommodation is necessary.

If no binocular vision is achievable and therapy is desired only for cosmetic purposes the grosser amounts of A' and V phenomena may require surgical adjustment, but minor degrees can be ignored.

If useful binocular vision is present, and this is only maintained by a compensatory chin elevation (in A' esotropia or V exotropia) or chin depression (in *'V* esotropia or A' exotropia) then surgical adjustment is indicated. Binocular vision in the primary position and in downward gaze is more important than on upward gaze and surgery should be planned accordingly.

In general it is found that the oblique muscles are of more importance in the production of A' and V phenomena than are the vertical recti. Usually, over-action of the inferior oblique or weakness of the superior oblique leads to a V' pattern and overaction of the superior oblique or weakness of the inferior oblique to an A' pattern. Weakening or strengthening of the oblique muscles, therefore, are well-recognized methods of influencing A' and V' phenomena. If there is no definite overaction of the obliques, then the vertical recti are shifted (remembered by the mnemonic that both medial recti are moved towards the closed end or both lateral recti towards the open end).

'A' esotropia

In the absence of vertical muscle anomaly, resection of the lateral recti with displacement of the insertions downwards should be effective in patients with a greater deviation for distance than for near. In those with A' esotropia associated with convergence excess, recession of the medial recti with shifting of the insertions upwards is effective.

Large degrees of esotropia in small children, with gross overaction of the superior obliques, may respond to bilateral weakening of the muscle.

'A' exotropia

Smaller degrees may be helped by resection of the medial recti with elevation of the insertions but the results are disappointing.

Large degrees in small children with overaction of the superior obliques respond to bilateral weakening of this muscle.

'V' esotropia

In the absence of vertical muscle anomaly, recession of the medial recti with displacement of the insertions downwards is effective. If overaction of the inferior obliques is present, this responds to bilateral anteroposition of this muscle with recession of the medial rectus muscles. If the overaction is gross, the anteroposition should be combined with recession of the inferior oblique.

'V' exotropia

In the absence of marked vertical muscle anomaly, recessions of the lateral recti with displacement of the insertions upwards is effective. If overaction of the inferior obliques is present, bilateral anteroposition of the muscle is effective, with or without recession of the muscle, depending on the degree of overaction. Recession of the lateral recti may be performed at the same time.

MICROTROPIA

The features of microtropia are a small esotropia of less than 10 prism dioptres or 5^0 with a minor or moderate degree of amblyopia. There is eccentric fixation and harmonious anomalous retinal correspondence. The cover test is not always reliable in demonstrating a microtropia because of the small angle and the presence of eccentric fixation, and its detection is facilitated by the use of a prism of 4 dioptres, which demonstrates a small scotoma in one eye. If such a prism is placed base-out before the sound eye, this eye adducts to resume fixation and the fellow eye abducts without showing a fusional recovery movement. When the prism is placed base-out before the squinting eye, the image is moved on to the foveal scotoma so that no movement of either eye results.

The aetiology of microtropia is uncertain although anisometropia is a common finding. Patients are usually referred because of the discovery of a slight amblyopia in one eye on routine testing. Some patients may complain of reading difficulties because they experience the crowding phenomenon or become aware of their scotoma on reading with one eye. There is nothing to offer by way of treatment. Treatment with occlusion may be attempted for amblyopia.

OPERATIONS ON THE EXTRINSIC MUSCLES

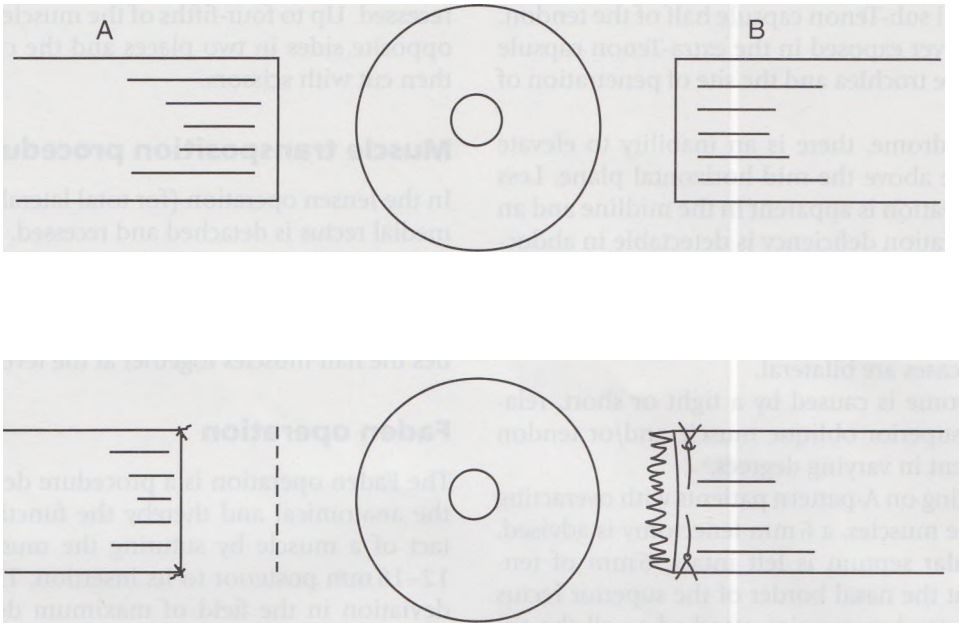
In operating for squint with a general or local anaesthetic it is important to remember that the position of the eyes varies in different stages of anaesthesia so that it gives no indication of the final position after the anaesthetic has worn off. In squint surgery the deviation as previously measured should be remembered and the position actually present under the anaesthetic ignored. In all cases, the preparation of the eye for operation should follow general principles of asepsis. Post-operative padding is unnecessary.

Adjustable sutures enhance the operative results of strabismus surgery in cases where results are expected to be unpredictable, such as dysthyroid eye disease and resurgery. A limbal conjunctival flap is fashioned and the muscle insertion reposed using a mattress suture with a bowknot through the original insertion. The flap is then temporarily replaced for the patient's comfort. Next day, if necessary, it is retracted, and a final adjustment made to the position of the muscle by tightening or loosening the bowknot. The flap is then replaced.

The following section briefly describes commonly used surgical procedures and includes operations useful for incomitant squint (*see* Chapter 27).

Recession of a rectus muscle (Fig. 26.11 A')

A vertical incision is made with scissors in the conjunctiva in front of the insertion of the muscle and a flap undermined towards the canthus or fornix exposing the muscle covered by Tenon capsule; alternatively a limbal conjunctival incision may be employed. Tenon capsule is then button-holed with scissors and slit for 7 mm along the upper and lower edges of the muscle: the part of the capsule covering the muscle should be preserved. The point of a strabismus hook is passed into Tenon capsule and passed deep to the muscle to hook it just behind the insertion. Calipers measuring the amount desired to set the muscle back are placed along the upper and lower borders of the muscle, the distance measured off from the tendon insertion, and marked on the sclera. Absorbable 5-0 or 6-0 vicryl sutures are passed through the upper and lower edges of the muscle 2 mm behind its insertion in the so-called 'whip- stitch' fashion. The tendon is divided, and the stitches passed through the superficial layers of the sclera at right angles to the long axis of the muscle at the points already marked as the new insertion.



Fig, 26.11 Squint surgery. As compared to the normal position of the muscles in the diagram above, the lower diagram shows A' recession and B' resection.

They are tied, and the conjunctival incision is then closed with a vicryl suture.

Resection of a rectus muscle (Fig. 26.11B')

An incision is made 2 mm behind and concentric with the corneoscleral junction in front of the insertion of the muscle, and the conjunctiva undermined. The muscle is exposed in the same manner as in recession. A strabismus hook is passed between the muscle and sclera, and the length of muscle and tendon for resection determined and marked with gentian violet. Whip-stitch sutures are passed through the upper and lower edges of the muscle just behind the mark, ensnaring a breadth of about 2 mm of the muscle fibres. The muscle is cut at the insertion, the distal part being held in a muscle resection clamp. The needles are passed through the base of the muscle stump at the level of the insertion. The muscle is drawn forwards, the sutures tied and the distal portion to be resected is divided at the mark. After ensuring haemostasis, the conjunctival incision is closed.

Surgical methods to weaken the inferior oblique

Anteropositioning of the inferior oblique muscle insertion effectively functions as a recession procedure and serves to weaken its action. The muscle is approached through the conjunctiva and separated at its insertion. It is re-attached closer to the inferior rectus muscle on an arc which joins the insertions of the lateral and inferior rectus muscles. In recession of the inferior oblique, the posterior end of the muscle is reattached 7 mm behind the lower end of the lateral rectus attachment and 7 mm downwards along a line concentric with the limbus. The anterior corner of the oblique muscle is attached 3 mm posterior to and 2 mm lateral to the lateral end of the inferior rectus insertion. Myectomy or transection and excision of a portion of the muscle have to be sometimes resorted to in extreme situations.

The superior oblique tendon weakening procedure

This procedure is carried out in two different clinical conditions:

1. An *A-pattern horizontal strabismus with overacting superior oblique muscles.*
2. *Brown syndrome,* secondary to a taut superior oblique tendon.

Tenon capsule is opened 10 mm posterior to the limbus. While the globe is depressed maximally with a muscle hook introduced temporally under the superior rectus muscle, Tenon capsule is retracted superiorly with a Desmarre lid retractor and the superior oblique is visualized 8 mm posterior to the nasal border of the superior rectus muscle insertion lying in its bed of intermuscular septum. A 1 mm hole in the intermuscular septum is made either immediately anterior or posterior to the tendon border so that a small hook may be introduced just nasal to the superior rectus muscle to isolate and pick up the superior oblique tendon. All surgery is performed

on the insertional sub-Tenon capsule half of the tendon. The tendon is never exposed in the extra-Tenon capsule space between the trochlea and the site of penetration of Tenon capsule.

In Brown syndrome, there is an inability to elevate the adducted eye above the mid-horizontal plane. Less restriction of elevation is apparent in the midline and an even smaller elevation deficiency is detectable in abduction. Slight downshoot of the adducting involved eye is often present. A widening of the palpebral fissure on adduction is associated with this restriction of elevation. Ten per cent of cases are bilateral.

Brown syndrome is caused by a tight or short, relatively inelastic superior oblique muscle and/or tendon and this is present in varying degrees.

When operating on A-pattern patients with overacting superior oblique muscles, a 6 mm tenectomy is advised. The intermuscular septum is left intact, 6 mm of tendon is excised at the nasal border of the superior rectus muscle and the tendon remains attached to all the tissues it is normally attached to—the sleeve of elastic tissue at the site of its penetration through Tenon capsule, its normal scleral insertion and the intermuscular septum which invests it between the point of penetration of Tenon capsule and the insertion. The pulling power of the proximal end of the severed tendon is transmitted through the contiguous intact intermuscular septum to the distal end of the severed tendon, reducing the possibility of muscle palsy after tenectomy.

For Brown syndrome a similar procedure is carried out, whereby 3 mm of tendon is tenectomized.

Enhancing the action of the superior oblique

This operation is performed on the lateral side of the superior rectus through a conjunctival incision running horizontally from the lateral edge of the superior rectus. A squint hook picks up the entire insertion of the superior oblique, which is then split half way along the fibres with a second hook. Two 6-0 collagen or vicryl sutures are placed in the anterior half of the superior oblique insertion before it is cut from the sclera. The anterior half of the superior oblique tendon is then swung anteriorly and this moves the line of muscle pull forwards, ensuring improved intorsion. It is a valuable operation when patients suffer from excyclophoria following trochlear (fourth) nerve paresis due to closed head injury.

Marginal myotomy

Marginal myotomy weakens a muscle without altering its attachment to the sclera and is usually applied to a medial rectus muscle which has already been fully recessed. Up to four-fifths of the muscle is clamped from opposite sides in two places and the crushed muscle is then cut with scissors.

Muscle transposition procedures

In the Jensen operation (for total lateral rectus palsy) the medial rectus is detached and recessed. The superior and inferior recti are split along their lengths and joined to the adjacent halves of the similarly split lateral rectus. A 5-0 ethibond polybutylate-coated braided polyester suture ties the half muscles together at the level of the equator.

Faden operation

The Faden operation is a procedure designed to change the anatomical and thereby the functional arc of contact of a muscle by suturing the muscle to the sclera 12-18 mm posterior to its insertion. This is to alter the deviation in the field of maximum deviation with no effect in the primary position, thus the dynamic angle is increased whereas the static angle of strabismus remains unaffected.

Conjunctival recession and hang-back sutures

When mechanical factors are important in the pathogenesis of a squint resulting from orbital trauma or poor surgery, simple recession-resection procedures do not usually suffice. The conjunctiva need not be closed at the end of an operation if, by its closure, the eye would be drawn back into its previous condition. Provided that it is sutured to the sclera, a bare crescent of sclera may be left between the conjunctival edge and the limbus.

A muscle, usually a medial rectus, can sometimes be recessed much further back than the maximum 5 mm by two 'hang-back' whip-stitches which are sewn through the insertion of the medial rectus. The muscle tendon itself is allowed to slip back as far as necessary into the orbit. This may produce a straight eye in the primary position and still allow for adequate adduction.

Complications

Complications that can occur during surgery are cardiac arrest due to the oculocardiac reflex induced by excessive pulling of the medial rectus muscle, slip or loss of a muscle and perforation of the globe.

Post-operative complications include overcorrection (known as consecutive squint), undercorrection (known as residual squint), chronic conjunctival inflammation, formation of excess scar tissue, formation of granulomas, anterior segment ischaemia, diplopia, endophthalmitis and orbital cellulitis.

SUMMARY

Strabismus or squint is the condition when the two eyes are not aligned properly and their visual axes do not meet at the point of fixation. In comitant strabismus there is no local defect in the oculomotor apparatus so the eye movements are full and the angle of deviation between the two eyes remains the same in all directions of gaze.

When assessing a case of squint careful history and examination is important. One must ascertain if the deviation is inwards (esotropia or convergent squint) or outwards (exotropia or divergent squint); if it is constant or intermittent; if intermittent, under what conditions does it manifest; the magnitude; which is the predominantly squinting eye or is it freely alternating; is there a refractive error and what effect it has had on the patient's visual acuity and binocular visual functions. All children with squint should be referred immediately to a competent ophthalmologist for further evaluation.

There are different types of comitant esodeviations and exodeviations depending on the pattern of deviation and associated clinical features. Some are correctable or controllable with proper refraction and prescription of spectacles and orthoptic exercises, while those not amenable to conservative management require surgery. Muscles are weakened by recession or strengthened by resection to correct the deviation.

27

Incomitant Strabismus

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Kinetic strabismus	433
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Incomitant squints are characterized by a variation in the amount of deviation in different directions of gaze. The classic example is paralytic squint, but this also occurs in restrictive squints and some special strabismus syndromes.

The motility of the eyes is controlled by voluntary and reflex mechanisms centred in the cerebral cortex and the brainstem. Lesions in the brainstem or in the supranuclear pathways produce *conjugate deviations* or *pareses of gaze* which affect both eyes equally. Although their movements or positions are abnormal, they maintain their relative coordination and diplopia is not produced. These deviations as well as the mixed palsies resulting from lesions in the mid-brain will be discussed in Chapter 31. If, however, the lesion is situated at the level of the lower neurones, affecting the nuclei, the nerves or the muscles, the relative coordination of the eyes is disturbed and diplopia and other symptoms appear. The usual result of such a lesion is paralysis *(paralytic strabismus*); however, at times it may be due to irregular or spasmodic activity of individual muscles or groups of muscles *(kinetic strabismus).* In some patients, the restriction of eye movement is due to mechanical factors such as musculofascial anomalies, muscle fibrosis, contracture or a space-occupying lesion in the orbit *(restrictive strabismus).* We saw in the previous chapter that a further type of squint exists when the visual axes, although abnormally directed, retain their relative position in all movements of the eyes; and is termed *comitant strabismus* (see Table 26.1).

PARALYTIC STRABISMUS

Aetiology

Lesions of the nuclei: Diseases of the central nervous system, which damage the ocular motor nuclei, are discussed in Chapter 31. The most common cause is a small haemorrhagic or thrombotic lesion in the midbrain associated with arteriosclerosis, diabetes or demyelination due to multiple sclerosis. Syphilis was earlier the most frequent aetiological factor. Other causes are tumours, infections of the central nervous system (encephalitis lethargica, polio encephalitis, etc.), toxins of endogenous (diphtheria) or exogenous (lead, botulism) origin, and thiamine deficiency.

Lesions of the nerves: The ocular motor nerves (third, fourth, sixth) traverse the cranial and orbital cavities, and can be damaged by various local pathological conditions as well as by changes in the microvasculature. They may be involved in infections of the meninges, cavernous sinus or orbit; by pressure from tumours or aneurysms; or trauma involving a fracture of the base of the skull. Among tumours, secondary invasion of the orbit or skull by malignant nasopharyngeal tumours *(see* Chapter 31) should be remembered as ocular palsies are a common early symptom. In raised intracranial pressure the nerve most frequently involved is the sixth; paralysis of the lateral recti is thus common in cases of intracranial tumours with high intracranial pressure, and generally has no localizing value. It may be due to traction on the nerves as they bend over the apex of the petrous portion of the temporal bone, or to pressure by the anterior inferior cerebellar and internal auditory arteries, which cross them at right angles and often lie ventral to them. The nerves are strangulated between the vessels and the oedematous and swollen pons. Following spinal anaesthesia, paralysis, generally of the lateral rectus, may be due to the same cause; the onset is rapid, and recovery usually takes many

weeks. Since the third nerve passes between the superior cerebellar and the posterior cerebral arteries, the same mechanism may account for ophthalmoplegic migraine *(see* Chapter 31).

Lesions of the muscles: Lesions of the muscles as well as of the branches of the nerves may occur with orbital disease or injury; the latter is relatively common. A weakness of the superior oblique owing to traumatic or inflammatory damage of the trochlea is one of the more common lesions of this type. Lesions of the muscles also include myositis, dysthyroid eye disease, hereditary myopathies and acquired myopathies such as myasthenia gravis.

Signs and symptoms

The signs and symptoms of paralysis of any extraocular muscle are: (i) squint; (ii) limitation of ocular movements; (iii) diplopia; (iv) false orientation; (v) abnormal position of the head and (vi) vertigo.

Squint: The *magnitude of squint* or abnormal alignment of the eyes may be of variable degree, depending on the degree of paralysis and in which direction the patient is looking. The amount of squint is quantified as the angle of deviation and will be

- more if the paralysis is severe;
- more if the patient is looking in the direction in Which the paralysed muscle comes into play, e.g. a left lateral rectus muscle palsy will produce a left convergent squint which will be more obvious when the patient looks to the left (laevoversion).

The *direction of squint,* i.e. whether the abnormal squinting eye is deviated inwards or outwards, is determined by the muscle involved. The eye deviates in the direction opposite to the direction in which the muscle moves the eye. The deviation is because of the unopposed action of the ipsilateral antagonist of the weak muscle.

Limitation of movement: In paralysis of an ocular muscle the ability to turn the eye in the direction of the normal action of the muscle is diminished or lost. In slight paresis the defect in mobility may be so small as to escape observation without special tests. In all positions in which the affected muscle is not brought actively into play the visual axes generally assume their normal relationship.

Limitation of movement is tested roughly by fixing the patient's head and asking him to follow the movements of a torch or the surgeon's finger. The finger should be held vertically in testing horizontal movements, horizontally in testing vertical movements.

An accurate record of the movements of each eye can be obtained by recording the *field of fixation* with the perimeter as for recording the field of vision. With the head immobile and the other eye screened the patient

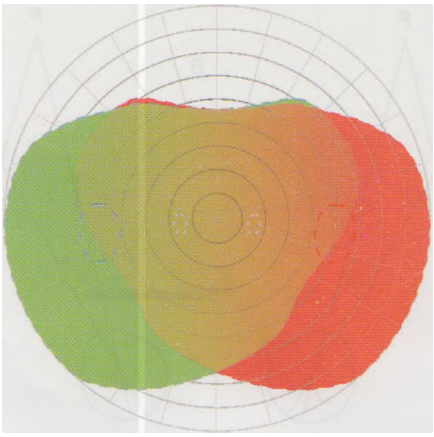
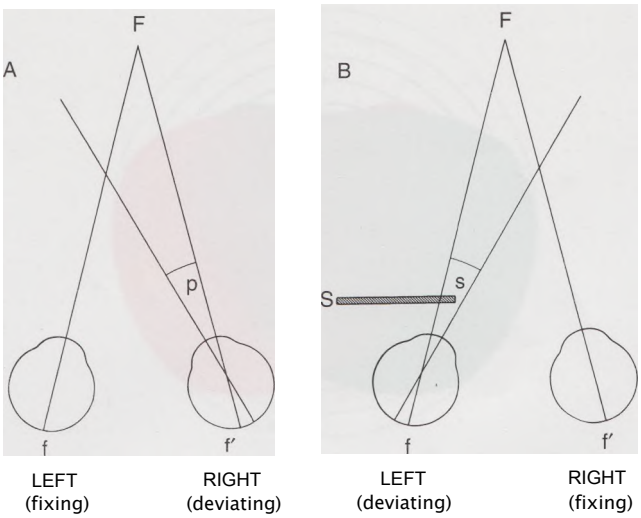


Fig. 27.1 Field of binocular single vision.

looks as far as possible along the arc of the perimeter, test-types being moved in from the periphery until he is just able to read them. The normal field of fixation is about 50° downwards and 45° in all other directions. The binocular field of fixation or field of binocular single vision (BSU) is plotted by moving an object along the arc of a perimeter (Fig. 27.1). The patient indicates when the single object appears double. If the patient is allowed to move the head and repeat the test, the result obtained is the practical field of binocular fixation, thereby indicating the field in which the patient is able to achieve single vision by compensatory head position.

The relative movements of the two eyes when each is used for fixation are of importance. This is most readily explored by the *cover test* which should be performed in the primary or straight ahead position and in all the other eight positions of gaze as well. When the eyes are turned in the direction of the normal action of the paralysed muscle, movements of the affected eye are impeded. It therefore deviates further relative to the other eye. The position of the eyes with the normal eye fixing is called the *primary deviation* (Fig. 27.2A). The angle of deviation is the angle which the line passing through the object of fixation and the nodal point makes with the visual line (Fig. 27.2).

If, on the other hand, the paralysed eye is used for fixation it will have difficulty in maintaining the straight ahead position by balancing the force of the normal antagonist and also have difficulty in moving in the same direction. Since the nervous energy required for movement is equally distributed between the two (Hering law, *see* p. 396), the normal eye will share in this abnormal effort. If, therefore, the sound eye is covered by a screen, and an attempt is made to fix an object so situated that the paralysed muscle is brought into play, it will be found that the normal eye behind the screen deviates more than the deviation of the paralysed eye (Figs 27.2 and 27.3). For example, if the right lateral



Fig, 27,2 Primary and secondary deviations. In comitant squint (affecting the right eye) the primary deviation (p, A) is equal to the secondary deviation (s, B) obtained when the non-squinting eye is occluded by a screen, S. F is the fixation point. In paralytic squint, the secondary deviation is greater than the primary.

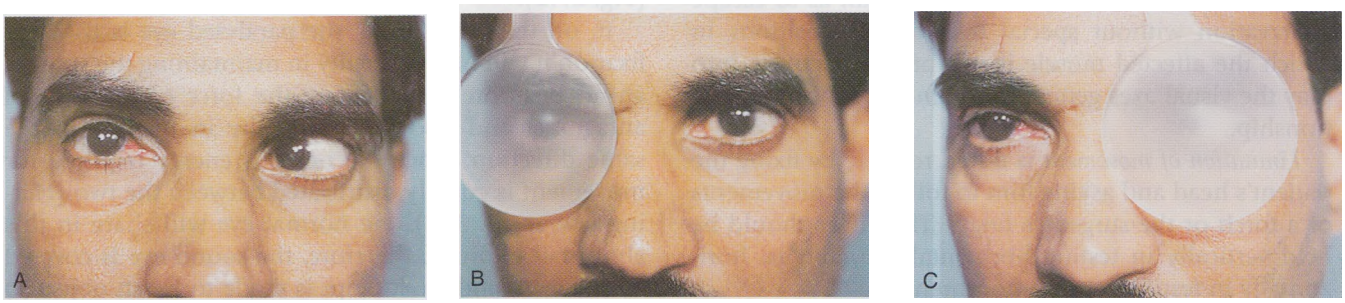
rectus is paralysed and the left eye is covered, then on attempting to fix an object situated to the right with the right eye, the left eye will deviate very much to the right, so much in fact that its line of vision is well to the right of the object fixed. Hence, if the screen is removed suddenly the left eye will spring back to the left so as to take up fixation. This deviation of the sound eye when the paralysed eye fixates the target eye is called the *secondary deviation* (Fig. 27.2B) and is due to overaction of the contralateral synergist (yoke muscle) of the palsied muscle. This feature is of great importance because when well marked it distinguishes paralytic squint from the comitant type in which the secondary deviation is equal to the primary.

Diplopia: The chief complaint of patients with paralysis of an extrinsic muscle is usually that they see double. If both eyes are functional and one deviates, *binocular diplopia* results. Diplopia occurs only over that part of the field of fixation towards which the affected muscle or muscles move the eye.

The image seen by the squinting eye *[false or apparent image*) is usually less distinct than that seen by the fixing eye (*true image),* because only in the latter case does the image fall upon the fovea centralis. The angular displacement of the false image is equal to the angle of deviation of the eye.

If the left eye fixes accurately while the right deviates inwards, a bright, sharply defined foveal image is seen with the left eye. The image formed by the object on the right retina, falling as it does upon the line joining the nodal point with the object, lies to the nasal side of the retina. The patient's brain, being unconscious of the malposition of his eye, orients the object subjectively as if the eye were straight. The patient knows from experience that objects which form their images upon the nasal side of the retina are situated to the temporal side because objects which stimulate the nasal visual fibres are projected by the occipital cortex in the temporal field. He therefore projects the object with this eye to the right of its actual position. This is called *homonymous diplopia,* because the object as seen by the right eye is to the right of the object as seen by the left eye (Fig. 27.4A). If the right eye deviates outwards, *heteronymous* or *crossed diplopia* results, because the object as seen by the left eye lies apparently to the right of the object as seen by the right eye (Fig. 27.4B).

False orientation: It will be seen from what has already been said that false orientation is a necessary accompaniment of binocular diplopia. If a patient whose right lateral rectus is paralysed shuts his left eye and attempts to fix an object situated towards the right with his right eye and is then asked to quickly point at the object with his extended index finger, the finger will pass considerably more to the right of the object. This is called *false projection.* It depends upon the same principle as the increase of the secondary deviation, for



Fig, 273 This patient with myositis of the right medial rectus muscle has: (A) restriction of abduction of the right eye due to the inflamed taut muscle; (B) the primary deviation with the normal left eye fixing; (C) secondary left nasal deviation which is greater with the affected right eye fixing. A Spielman occluder obstructs the patient's vision but allows the examiner to see the position of the eye behind the occluder.

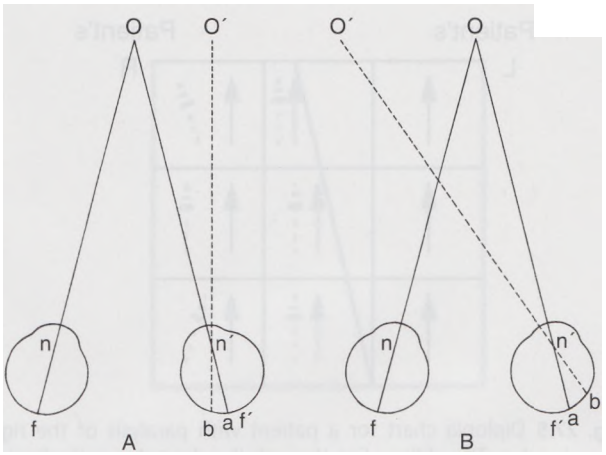


Fig. 27.4 (A) Homonymous diplopia and (B) diagram of heteronymous (crossed) diplopia; f, f', left and right foveae; n, n', left and right nodal points. The image of 0 formed at a is projected to 6 which is located further temporally in A and nasally in B. b is the retinal counterpart of 6 on the line passing from 0 through the nodal point.

the object is projected according to the amount of nervous energy exerted. As this is greater than that exerted in normal circumstances, the object is projected too far in the direction of action of the paralysed muscle. It is essential that the finger should be directed at the object quickly, otherwise the error is noticed and compensation is made. For example, if in the same circumstances the patient is told to walk towards an object situated at some distance to the right, he first steps too far to the right, then recognizes his mistake and corrects it. In long-standing paralysis the patient may learn by experience to compensate for the error.

Position of the head: The patient holds his head so that his face is turned in the direction of action of the paralysed muscle so that the eyes are rotated away from the field of action of the paralysed muscle and hence diplopia is eliminated. For example, in paralysis of the right lateral rectus the patient keeps his face turned to the right. The object of this manoeuvre is to lessen the diplopia and its attendant unpleasant consequences as much as possible. In complex paralysis the position of the head is still such as to relieve the diplopia to the maximum extent, the position being unconsciously adopted.

Ocular torticollis is a term sometimes applied to tilting of the head to compensate for defective vertical movements of one eye. It is distinguished from true torticollis due to contraction of the sternocleidomastoid muscle in that there is a simple tilting of the head without rotation of the chin towards the opposite shoulder; moreover, the sternocleidomastoid is not unduly contracted. It occurs chiefly in cases of congenital origin but it follows traumatic palsies if BSU can be obtained by appropriately adjusting the posture of the head (Fig. 27.8A). The vertical squint is made manifest by placing the head straight, when diplopia is also elicited. The most common isolated vertical muscle paresis which may present with ocular torticollis is fourth nerve or superior oblique muscle paresis.

Vertigo: Vertigo, leading to nausea and sometimes even vomiting, is due partly to diplopia, partly to false projection. It occurs chiefly when the paralysed muscle is called upon to exert itself. When the gaze is turned from the region of correct to that of false localization, objects appear to move with increasing velocity in the direction in which the eye is moving. The unpleasant symptoms are counteracted partially by altering the position of the head, or completely by shutting or covering the affected eye.

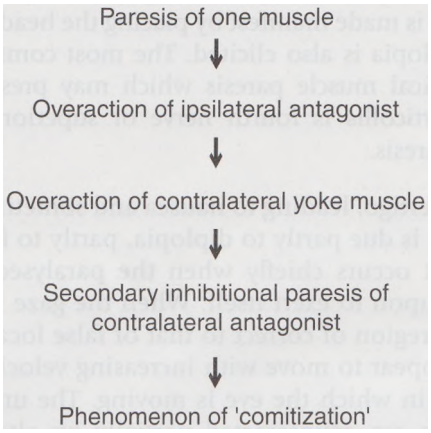
In congenital strabismus these symptoms are not obtrusive since the vision of one eye is suppressed or false retinal correspondences develop; in these cases marked contracture of the antagonistic muscles does not occur. In acquired cases they are at first very distressing and incapacitating. In paralyses of long standing, however, relief is gradually obtained. False orientation and diplopia tend to disappear or become less troublesome, for the patient learns to ignore the impressions derived from the affected eye. Moreover, contracture of the antagonists of the paralysed muscle gradually sets in, which has the effect of increasing the deviation. Since the retinal image is thus thrown further to the periphery of the retina where the sensitivity is less, its suppression is facilitated.

Changes in long-standing paralysis: In long-standing paralysis secondary contractures in the antagonist muscles and soft tissues such as the conjunctiva, Tenon capsule and muscle sheaths reduce the extent of incomitance and lead to clinical features that begin to resemble comitant squint (Flowchart 27.1).

Investigation of a case of ocular paralysis

This is essentially directed to (i) evaluation of the squint and determination of the involved nerves or muscles and (ii) investigations to find out the underlying cause based on history, ocular examination, orbital ultrasonography, neurological examination and computerized tomography (CT) or magnetic resonance imaging (MRI) as and when indicated.

The patient usually seeks advice on account of diplopia. In some cases the nature of the case is obvious immediately from the strabismus or from the manner in which the head is held. In other cases these features are too slight to decide the diagnosis and special examination techniques must be employed and tests carried out.



Flowchart 27,1 Sequence of secondary changes after muscle paralysis.

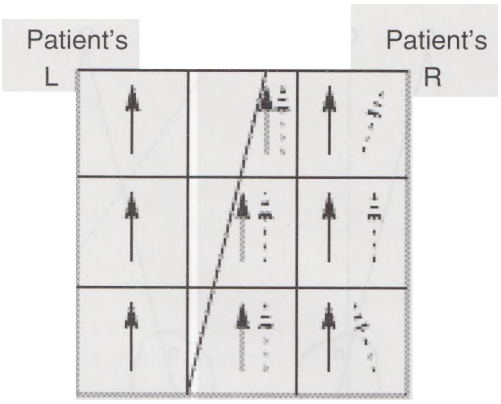


Fig. 27.5 Diplopia chart for a patient with paralysis of the right lateral rectus. The oblique line through the chart shows the limit of the fields of single vision and of diplopia. The dotted arrows show the positions of the false image in different parts of the field of diplopia. The chart depicts the patient's view of the images.

1. The first step is to cover one eye in order to determine whether the diplopia is uniocular or binocular.
2. If it is decided that the diplopia is binocular, the patient should fix the surgeon's finger, or a point source of light such as a pencil torch, and the field of fixation of each eye should be carefully investigated. In cases of complete paralysis of one or more muscles it may be possible to make an accurate diagnosis from the observation of the defective movements. Sometimes in cases of mild paresis the limitation of movement of the eye may be so slight as to be unidentifiable.
3. In such cases the diplopia must be investigated by more delicate tests. In a dark room a red glass is placed before one eye and a green one before the other to distinguish their images. A bar of light through a stenopaeic slit in a hand torch is then moved about in the field of binocular fixation at a distance of at least 120 cm from the patient, the patient's head being kept stationary. The positions of the images are accurately recorded upon a chart with nine squares marked upon it (Fig. 27.5). The examination may also be carried out by the surgeon turning the patient's head in various directions while the light is kept stationary. The following data are derived from this examination:
   - the areas of single vision and diplopia;
   - the distance between the two images in the areas of diplopia;
   - whether the images are on the same level or not;
   - whether one image is inclined or both are erect and
   - whether the diplopia is homonymous or crossed.

Diplopia charting is important in making the diagnosis, documenting the baseline defect and reviewing the improvement on follow-up. To complete the record, a note should be made of how far from the patient the test-object is located, because a change in distance will affect the separation of the images between the two eyes and may give rise to an erroneous interpretation on the progress of the paralysis on follow-up. The diplopia chart can also be recorded depicting the observer's view and the orientation of the recording should be specified (Fig. 27.6).

These data, if concordant, are sufficient to diagnose the paralysis. The false image, which is frequently tilted and the fainter of the two, is determined by the direction in which the images are most separated from each other, in which case it is displaced farthest in the direction of the normal action of the paralysed muscle. By covering one eye it can be shown which eye this image belongs to.

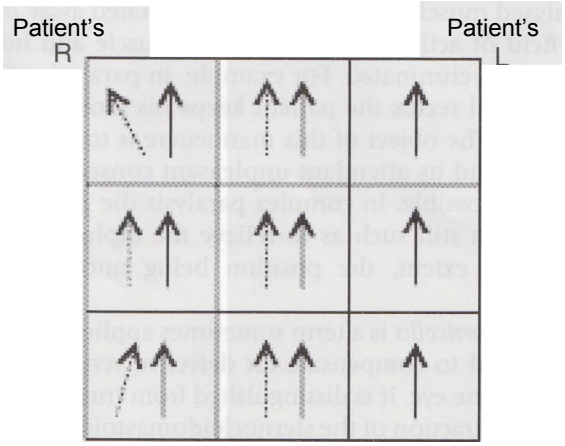


Fig. 27.6 Diplopia chart for a patient with paralysis of the right lateral rectus. The dotted arrows show the positions of the false image in different parts of the field of diplopia. The chart depicts the examiner's view of images reported by the same patient as in Fig. 27.5.

The charting of diplopia can very well be done in a normally lit room with a point source of light such as a hand-held torch and red-green glasses worn by the patient to distinguish the images seen by the two eyes. By convention, red is placed before the right eye and the red-coloured image is that of the right eye, and green in front of the left eye. However, by this method, fine details regarding tilting of the image cannot be recorded. In paralytic squint, the diplopia chart should be plotted with either eye fixing, if possible. It will be observed that there is a greater separation of images when the affected eye is fixing on the target (secondary deviation).

The deviation of the false image is most easily determined when the eye is turned in the *cardinal positions.* For horizontal muscle palsies where only two muscles are likely to be involved, the test is easy; greatest diplopia occurs in the horizontal line to the right in paralysis of the right lateral or left medial rectus, to the left for the left lateral or right medial rectus.

For vertical movements the action of four muscles must be analysed. They are most easily differentiated thus.

In view of the obliquity of their course the recti are most effective as vertical rotators as the eyes are abducted from the primary position, the obliques when adducted. On looking up and to the right, the right superior rectus and the left inferior oblique are therefore primarily involved, the false image being higher than the true (because the affected eye will always be lower) and tilted. Similarly, in looking down and to the right, the false image will be lower than the true and tilted. The relevant muscles in the six cardinal positions can be seen in Fig. 25.5B.

By careful study of the pattern of diplopia alone, the paralysed muscle can be identified, but it must be remembered that these tests are purely subjective. In many cases the patients are uncooperative or their intelligence is obscured by intracranial disease, or contracture of the antagonistic muscles may have set in. Consequently, the answers are not infrequently discordant, and accurate diagnosis may be extremely difficult or impossible. As additional complications, the paresis may unmask a latent squint or the patient may fix with the paralysed eye, especially if this eye has the greater acuity of vision.

Considerable ingenuity has been used to devise mnemonics for determining the position of the false image. One of the most satisfactory is that of Maddox shown in Fig. 25.5B. If the field is divided into areas as shown, in vertical palsies the paresis is due to failure of the 'same-named' rectus muscle (in the left superior area, the left superior rectus) or the most 'crossed-named' oblique muscle (right inferior oblique). In all cases the most peripheral image belongs to the palsied eye. In horizontal palsies, the failure is due to the same named muscle for the right eye on looking to the right and same named



Fig. 27.7 Child with left superior oblique palsy showing typical head posture. The second row demonstrates Park 3-step test. (By courtesy of P Sharma)

muscle for the left eye on looking to the left, and the opposite named muscle for the other eye in each case.

In clinical practice these principles are applied thus:

1. First decide whether the diplopia is horizontal or vertical from the history of the patient and by testing with red and green goggles, red in front of the right eye.
2. If horizontal,
   - Find the position of gaze where the separation of the images is maximal—right or left by moving a light in the horizontal plane.
   - In that position the furthest displaced image belongs to the eye with the muscle palsy.
   - Application of the mnemonic of Maddox will identify the palsied muscle.
3. If vertical,
   - Find the position of gaze where the separation of the images is maximal, moving the light vertically in the median plane. If the separation is greatest above there is an elevator palsy, if greatest below there is depressor palsy.
   - Find out if the separation is maximal to the right (above or below) or to the left (above or below).
   - The furthest displaced image belongs to the eye with muscle palsy.
   - The application of the mnemonic of Maddox will identify the paralysed muscle.
   - The diagnosis can be further confirmed by performing the 3-step test and the head tilt test.

Tests to help identify the affected muscle in a patient with paralysis of one of the vertically active extraocular muscles (four in each eye, i.e. eight total)

I. *Park 3-step test*

Step 1: Identify the hypertropic eye in the primary (straight ahead) position. This implies that either one of the two depressors of the hypertropic eye or one of the two elevators of the hypotropic eye is weak.

Step 2: Ask the patient to look horizontally right and then left and see in which position the deviation is more. Remembering that the deviation increases in the direction of action of the paralysed muscle, identify which two of the four muscles are likely to be affected (Fig. 27.7).

Step 3: Tilt the patient's head towards each shoulder and see in which direction the vertical squint increases. Remembering that on tilting the head towards one shoulder the eye on the same side intorts and the other eye extorts, the ipsilateral synergist of the paralysed muscle will try to intort or extort the globe as the case may be, and since the muscle also has a vertical action, that vertical effect will be more prominent in the paralysed eye.

II. *Bielschowsky head tilt test*

It is based on the same principle as the third step of the Park 3-step test and is useful for diagnosing superior rectus palsy. In a case of right superior oblique palsy, for example, the right hypertropia will become more prominent when the head is tilted to the right shoulder and will disappear when the head is tilted to the left shoulder (Fig. 27.8).

It may be pointed out that all the signs, with the exception of deviation of the eye—defective movement, false projection, increase of diplopia, secondary deviation and position of the head—are greatest towards the side of the paralysed muscle.

To measure the degree of deviation, especially if torsional, and particularly to measure any progressive increase or decrease, the *Hess screen test* (Fig. 27.9) is useful. It consists of a tangent screen marked in red lines on a black cloth with red spots at the intersection of the 15° and 30° lines with themselves and with the horizontal and vertical lines; over it three green threads are suspended in such a way that they can be moved over the screen in any direction by a pointer. The patient, wearing red-and-green glasses, is asked to place the junction of the three threads over the red spots in turn. Through the red glass he can only see the red markers and through the green, the green threads, so that he indicates the point at which one eye is looking when the other fixes a spot. The position on which the indicator appears to coincide with the spot gives a permanent record of the primary and secondary deviation. The test also provides an accurate measure of comitance. In a comitant squint the fields of each eye, although relatively displaced, are equal in area and undistorted; in paretic squint the area on the affected side is diminished away from the affected muscle and in spastic squint it is increased towards the affected muscle. Another test based on a similar haploscopic principle of separating the fields of view of both

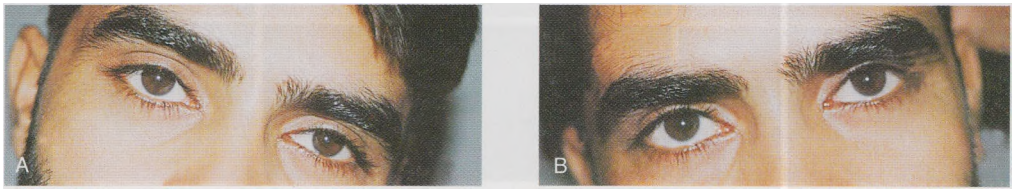


Fig. 27.8 Patient with left superior oblique paresis showing an increase in the hypertropia on tilting the head to the left and a reduction with the head tilted to the right. (By courtesy of M Gogoi)

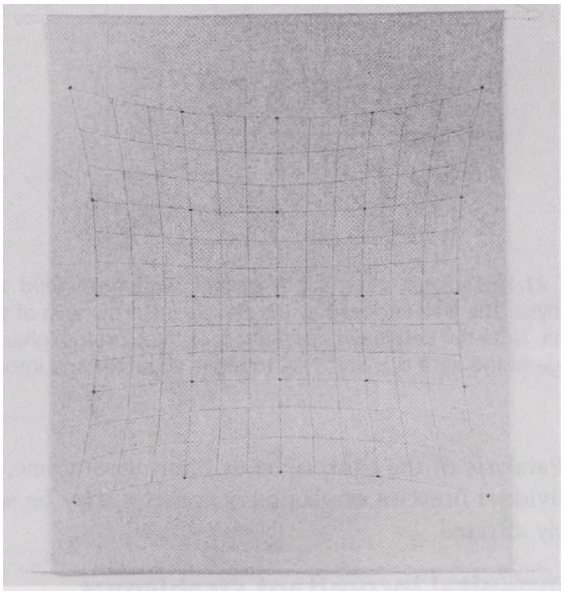


Fig. 27.9 Hess screen. A grey background reflects light well and is suitable for red and green torch markers.

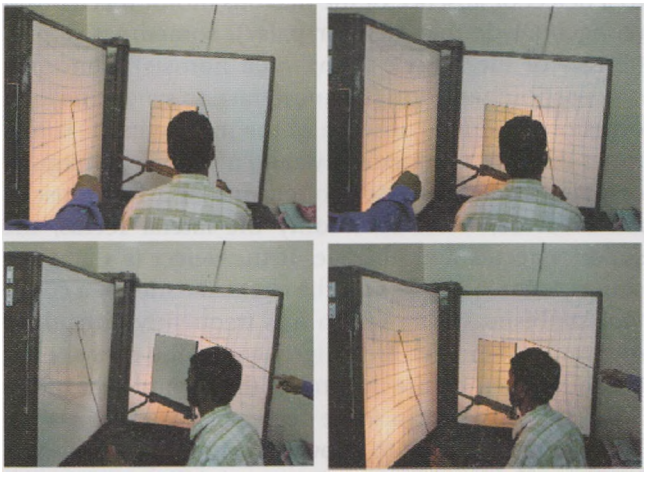


Fig. 27.10 A patient being examined with a Lee screen.

eyes is the Lee screen test, where a mirror is used with an illuminated screen (Fig. 27.10) to plot the field of movement of both eyes separately.

Varieties of ocular paralysis

If one muscle alone is affected it is generally the lateral rectus or the superior oblique, since each of these is supplied by an independent nerve. Affection of several muscles simultaneously is usually due to paralysis of the third nerve. All the extrinsic and intrinsic muscles of one or both eyes may be paralysed—*total ophthalmoplegia.*

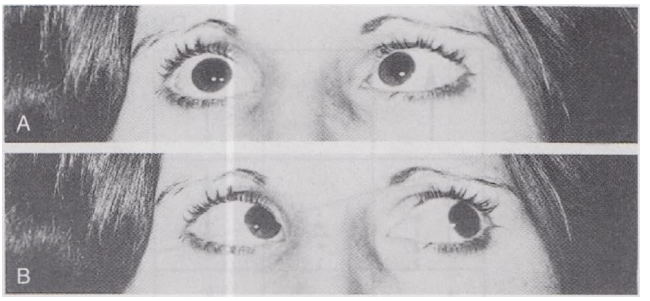


Fig. 27,11 Right sixth nerve palsy. (A) Looking to the right; (B) looking to the left. (By courtesy of Sanders)

If only the extrinsic muscles are affected the condition is called *external ophthalmoplegia*; if only the intrinsic muscles (sphincter pupillae and ciliary muscle) are affected it is termed as *internal ophthalmoplegia.*

Paralysis of the lateral rectus: There is an esotropia or convergent squint with limitation of movement outwards, and the face is turned towards the paralysed side, flomonymous diplopia occurs on looking to the paralysed side; the images are on the same level and erect, becoming more separated on looking more towards the paralysed side. The false image is slightly tilted on looking up or down towards the paralysed side because of the imbalanced effect of the oblique muscles in these positions (Figs 27.5 and 27.11).

Paralysis of the superior oblique: There is hypertropia of the affected eye with limitation of movement downwards and towards the sound side; the face is turned downwards and towards the sound side with a slight tilt of the head towards the shoulder of the sound or the normal side. Homonymous diplopia occurs on looking down (Fig. 27.12); the false image is lower and its upper end is tilted towards the true image (the image is intorted because the eye is extorted when the superior oblique is paralysed). The distance between the images increases on looking down and towards the sound side and the inclination of the false image increases on looking down to the *paralysed* side. The patient has great difficulty in going downstairs, and vertigo is usually a particularly prominent symptom.

A congenital left superior oblique palsy produces a compensatory head tilt to the right with chin depression and slight face turn to the right. Thus, binocular vision is maintained in the primary position. When the head is forcibly tilted to the left, reflex intorsion is excited. This can now only be undertaken by the left superior rectus which is stimulated to overact. The result is an unopposed overelevation of the left eye (Bielschowsky head tilt test).

Bilateral superior oblique palsy may follow head trauma and give rise to a form of diplopia which is often unrecognized because it is due to excyclotropia. It is diagnosed on the basis of a V pattern, e.g. when the two eyes

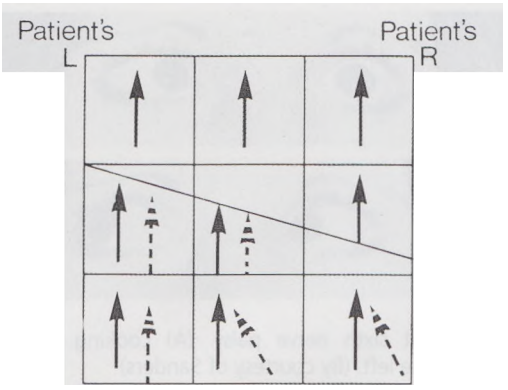


Fig. 27.12 Diplopia chart for a case with paralysis of the right superior oblique. The right eye is hypertropic, extorted and esotropic as the superior oblique is a depressor, intortor and abductor. The diplopia is thus homonymous and the false image belonging to the right eye is lower and intorted.

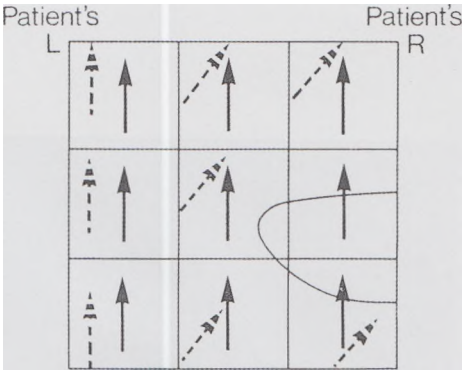


Fig. 27.13 Diplopia chart for a patient with right third nerve paralysis. The area enclosed by the curved line is the area of single vision. Note the heteronymous diplopia with extorted higher false image of the right eye which is exotropic, abducted and intorted.

are in a marked convergent position on attempted straight down gaze as opposed to a relative divergence on straight up gaze. This occurs because both superior oblique and inferior rectus muscles are involved in depression in the straight ahead position. Now, since the superior oblique is weak in both eyes the unopposed adductive effect of the inferior rectus (normally neutralized by the abductive effect of the superior oblique when healthy) produces an excessive adductive effect in straight down gaze, resulting in a V' pattern. It is relieved by symmetrical bilateral superior oblique surgery whereby the tendon of each muscle is split and the anterior half is advanced along the equator of the globe towards the upper border of the lateral rectus. This procedure eliminates the symptom of cyclodiplopia by reducing the degree of excyclotropia.

Paralysis of the third nerve: In complete paralysis of the third nerve there is ptosis, which prevents diplopia. On raising the lid with the finger the eye is seen to be deflected outwards (divergent squint or exotropia) and rotated internally (intorted), owing to the tone of the two unparalysed muscles. The pupil is semidilated and immobile, and accommodation is paralysed. There is a slight degree of proptosis, owing to loss of tone of the paralysed muscles. There is limitation of movements upwards and inwards; to a lesser degree, downwards. With the lid raised there is diplopia, which is crossed, the false image being higher, with its upper end tilted towards the paralysed side (the eye is intorted and the image extorted) (Figs 27.13 and 27.14). In the presence of third nerve paralysis, function of the fourth nerve is assessed by instructing the patient to attempt looking straight downwards. In the absence of inferior rectus action, the eye does not move down but 'intorts' because of the intorsional effect of the superior oblique. This is demonstrated by observing the inward movement of any of the bulbar blood vessels. If present, fourth nerve function is deemed to be intact (Fig. 27.14C and D).

Paralysis of the third nerve is often incomplete, and individual muscles or groups of muscles may be selectively affected.

Congenital incomitant strabismus

This is not uncommon. It is usually due to ineffectivity of a muscle owing to its malinsertion, sometimes due to a defect or absence of the nervous motor mechanism (congenital double elevator palsy), sometimes due to fibrosis of the muscle (congenital fibrosis), abnormal synergistic innervation (Duane retraction syndrome) and occasionally due to absence of the muscle itself. Sometimes the defects are extensive and movements irregular or grossly deficient. More often one or a few muscles are involved, most commonly the lateral rectus, the superior rectus and oblique. If the defect is slight the squint eventually takes on the characteristics of a comitant strabismus from which it is frequently difficult to differentiate in later life. Alignment of the eyes should be undertaken before the end of the second year of life if the aim is to obtain some degree of binocular vision. There is no evidence to show that surgery at 6 months is more effective than at 12 or 24 months.

Musculofascial anomalies: One of the common congenital defects is *Duane retraction syndrome.* It is due to a fibrosis of the lateral rectus or an innervational anomaly with co-contraction of the lateral and medial recti. In the primary position, the eyes are straight or show some latent convergence, but there is a restriction or absence of abduction. On adduction there is a retraction of the globe and a narrowing of the palpebral fissure while on attempted abduction there is a slight protrusion of the eyeball with widening of the palpebral fissure (Fig. 27.15).

The goal of surgery in Duane retraction syndrome is the elimination of any abnormal head posture and any

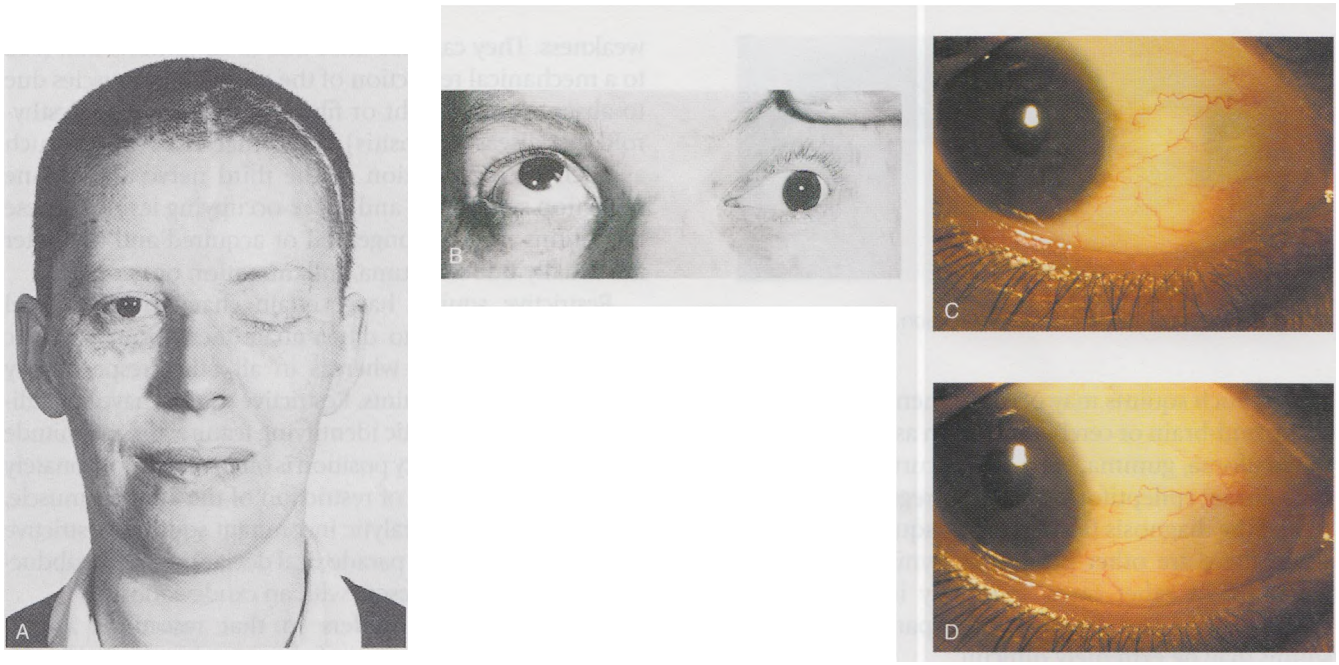


Fig. 27.14 (A) Complete left third nerve paralysis due to a posterior communicating artery aneurysm. Note the ptosis of the left eye and the craniotomy scar. (B) Complete left third nerve paralysis with the lid elevated and the patient attempting upward gaze to show the dilated and fixed pupil with failure of adduction and elevation on the left (By courtesy of Sanders). (C and D) Shifting of conjunctival vessel due to intorsion on attempted downgaze confirming normal fourth nerve function in a patient with right third nerve palsy.

significant deviation in primary position, or cosmetic misalignment of the eyes if fusion is not present. Simple recession of the appropriate muscle or muscles rids the patient of the abnormal head position without risking induced vertical tropias.

A second anomaly is the *superior oblique sheath syndrome* (Brown syndrome) in which there is a marked defect of elevation in the adducted position somewhat resembling the effects of a paresis of the inferior oblique muscle. Usually no active intervention is required particularly if there is no deviation in primary position. The condition becomes less noticeable as the child grows taller and needs to 'look up' less. However, if severe with significant strabismus in the primary position which is amblyopiogenic, the taut superior oblique tendon may be treated by a 3 mm tenectomy within the intermuscular septum. If postoperative palsy of the operated muscle occurs it can be managed by recession of the ipsilateral inferior oblique or the contralateral inferior rectus.

Treatment

Treatment should be directed to the cause of the palsy.

The diplopia, if minor, may sometimes be relieved by suitable prisms, but this treatment is rarely of much use owing to the variation in the amount of the deviation in different positions of the eyes. Surgery is indicated when the deviation has become stabilized—usually recession of the contralateral synergist muscle, followed, if necessary, by recession of the antagonistic muscle in the same eye, thus putting the affected muscle under better mechanical conditions. These operations should always be done in stages to assess the effects of each; the techniques of squint surgery have been described in the previous chapter.

Kinetic strabismus

Aberrant forms of strabismus occur as the result of irritative intracranial lesions, and are due, not to paralysis, but due to irregular action or overaction of certain muscles, caused by unequal stimulation of the nerve centres or



Fig. 27.15 Duane retraction syndrome (left eye). Note the marked limitation of abduction of the left eye (A), with minimal deviation in primary position (B) and narrowing of the palpebral fissure of the left eye on adduction (C). (By courtesy of P Sharma)

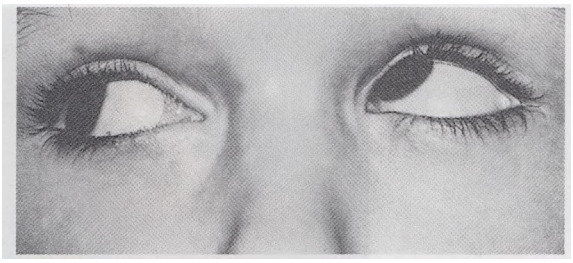


Fig. 27.16 Left inferior oblique overaction. (By courtesy of Fells)

nerves. Such squints may occur in meningitis and lesions of the mid-brain or cerebellum, such as tumours (glioma, tuberculoma, gumma, etc.). The occurrence of the squint only during epileptiform fits or its irregularity of type may render the diagnosis from paralytic squint easy, especially when there are other prominent symptoms of cerebral irritation. In other cases, especially in the early stages of the disease, the diagnosis from paralytic or comitant squint may be extremely difficult.

A second, more common, cause of such a squint is the spasmodic contracture which develops in the antagonist of a paretic muscle. The muscle usually affected is the inferior oblique following a paresis of the superior rectus or superior oblique, frequently congenital in origin. The deviation is typical. On looking away from the affected side, as the eye is adducted and the inferior oblique comes into play, it is suddenly jerked up and in (Fig. 27.16). Treatment is by myectomy or recession of the muscle *(see* p. 420).

RESTRICTIVE STRABISMUS

Incomitant squints, as partly already explained in the section on congenital incomitant squints, can be due to local disease in the orbit, apart from nerve paralysis or muscle weakness. They can also arise due to conditions that lead to a mechanical restriction of the extraocular muscles due to absent muscle, tight or fibrosed muscles (e.g. dysthyroid eye disease, myositis), abnormal innervation (such as aberrant regeneration of the third nerve and Duane retraction syndrome) and space-occupying lesions. These conditions may be congenital or acquired and the latter are usually due to trauma, inflammation or neoplasia.

Restrictive squints have certain characteristic clinical features which help to differentiate them from paralytic squints (Table 27.1) whereas in all other respects they resemble paralytic squints. Restrictive squints have an additional and characteristic identifying feature; the magnitude of squint in the primary position is often disproportionately less than the amount of restriction of the affected muscle, which is not so in paralytic incomitant squints. Restrictive squints may also have paradoxical deviations, i.e. an abduction deficit may be present with an exodeviation.

The management differs in that resections are to be avoided and recession of the muscles restricting the movements usually helps. If inadequate to relieve the symptoms then recession of the contralateral synergist (yoke muscle) is also undertaken. Results are likely to be unpredictable so surgery should be done in stages with the use of adjustable sutures if required.

Synkineses

The extrinsic muscles take part in many normal and pathological synkineses. When the eyes look up, the levatores palpebrarum raise the lids and in extreme upward movements the frontales also contract. In congenital ptosis upward movement of the eyes is often defective. On looking down, the lid follows the globe; in exophthalmic goitre the lid follows tardily or not at all *[von Graefe sign);* in total facial paralysis the lid follows

Table 27.1 Clinical features of paralytic and restrictive squints

Clinical features	Paralytic squint	Restrictive squint
Deviation in primary position	Present and is proportional to the degree of underaction of the affected muscle	May be present, absent or paradoxical. Is generally disproportionately mild compared to the degree of underaction and can even be paradoxical, e.g. an exotropia in Duane retraction syndrome with deficiency of abduction
Forced duction test or ability to move the eye mechanically using a forceps to hold the anaesthetized eye at the limbus	Negative, i.e. the eye can be easily moved in the direction of restricted movement	Positive, i.e. the eye cannot be mechanically moved in the direction of restricted movement
Active force generation test or estimation of the amount of force generated by the affected muscle by using a forceps to hold the anaesthetized eye at the limbus and assess the 'tug' induced by the contracting muscle	Negative or weak force generation	Positive or normal force generated by the muscle

the globe on looking down, although the eye cannot be closed voluntarily. On closing the lids, as in sleep, the eyes generally turn upwards and outwards (*Bell phenomenon).* The same movement of the eyes occurs on attempted closure in total facial paralysis.

Other pathological synkineses are probably due to congenitally abnormal associations between two nerves or to aberrant regeneration of nerve fibres along the wrong nerve sheath after disease or injury. The *'jaw-winking synkinesis* (of Marcus Gunn) is particularly striking. In these rare cases one levator palpebrae is thrown into spasm during eating, and sometimes on reading aloud. The upward lid movement is especially associated with lateral movements of the jaw, due to action of the pterygoid muscles, which are innervated by the fifth nerve. In most cases, but not all, there is slight ptosis of the affected lid, and in cases with congenital ptosis the synkinesis occurs on sucking. Patients requiring surgery are offered bilateral levator transection plus a bilateral frontalis suspension. Allied to the jaw-winking cases are others in which spasmodic lid movements occur on adduction of the affected eye (aberrant regeneration of the third nerve).

The convergence pupillary synkinesis has already been mentioned, to it may be added the contraction of the pupil on forced closure of the lids. In rare cases spontaneous rhythmical variations in the size of the pupil are accompanied by ocular or lid movements. They are usually associated with congenital or early infantile paresis of the third nerve. Of these, a rhythmic *cyclic oculomotor spasm* is one of the most dramatic. In the mydriatic phase there is total ophthalmoplegia with ptosis, and at intervals of a minute or less a miotic phase develops in which the upper lid retracts, the eyes converge, the pupil contracts and the accommodation undergoes spasm.

In lesions of the third cranial nerve trunk, when the fibres regenerate following trauma or following damage due to an aneurysm, sometimes the fibres get misdirected to supply the wrong muscle. Misdirection in the regeneration of the third cranial nerve is common after total interruption of function usually by head trauma. Misdirection can be identified by the following ocular signs:

1. Pseudo-von Graefe lid sign. As the eye attempts to move downwards the upper lid retracts, because some of the fibres originally supplying the inferior rectus muscle are now misdirected to supply the levator palpebrae superioris.
2. Pseudo-Argyll Robertson pupil. There is a slow light reflex and a better constriction of the pupil with the near synkinesis. Fibres supplying the sphincter are damaged and fibres to the ciliary muscle for accommodation are misdirected to the pupil.
3. Horizontal gaze lid dyskinesis. The upper lid retracts as the eye is adducted and falls as the eye is abducted (medial rectus fibres now supply the levator).
4. Difficulty in vertical gaze.
5. Adduction on attempted vertical gaze (superior rectus fibres misdirected to the medial rectus).
6. Monocular optokinetic response. As vertically moving optical targets are presented to the patient the normal eye develops good vertical optokinetic nystagmus whereas the affected eye does not.

SUMMARY

Incomitant strabismus results when there is a local abnormality of the oculomotor apparatus which results in the deviation between the two eyes varying in different positions of gaze. These squints can be neurogenic, myogenic, mechanical or a combination of these.

Neurogenic (paralytic) strabismus is due to paralysis of one or more extraocular muscles. *Myogenic* is due to myasthenia gravis, dysthyroid myopathy, ocular myopathies or ocular muscle inflammation or myositis such as with extraocular muscle cysticercosis. Myogenic conditions like dysthyroid eye disease and myositis may be followed by fibrosis later adding a mechanical component. *Mechanical (restrictive*) strabismus is due to fibrosis or other local orbital abnormality preventing free movement such as fracture of an orbital wall with muscle entrapment or an orbital space occupying lesion. This also includes special oculomotility syndromes called musculofascial anomalies like Duane retraction syndrome and Brown syndrome.

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Diseases of the Lids

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ANATOMY

The lids are covered anteriorly by skin and posteriorly by mucous membrane—the tarsal conjunctiva. They contain muscle, glands, blood vessels and nerves, all bound together by connective tissue which is particularly dense at the posterior part where it forms a stiff plate—the *tarsus* (Fig. 28.1).

The skin of the lids is peculiar in its thinness, its loose attachment and the absence of fat in its corium. It is covered with fine downy hairs, which are provided with small sebaceous and sweat glands. At the margins, these structures are specially differentiated. The cilia or eyelashes are strong, short, curved hair, arranged in two or more closely set rows. Their sebaceous follicles, like the cilia themselves, are specially differentiated and called *Zeis glands,* which, apart from being larger, are identical to other sebaceous glands. The sweat glands near the edge of the lid are also unusually large and known as *Moll glands.* They are situated immediately behind the hair follicles, and their ducts open into the ducts of the Zeis glands or hair follicles, not directly onto the surface of the skin as elsewhere.

The margin or free edge of the lid is called the *intermarginal strip (see* p. 16). It is covered with stratified squamous epithelium, which forms a transition between the skin and the conjunctiva. The anterior border is rounded and the posterior, which lies in contact with the globe, is sharp. The capillarity induced by this sharp angle of contact is important for proper moistening of the surface of the eye. Immediately anterior to the posterior border, the ducts of the meibomian glands form a single row of minute orifices, just visible to the naked eye. Between them and the anterior border is a fine grey line, which is important for operations in which the lid is split since it indicates the position of the loose, relatively avascular fibrous tissue between the orbicularis palpebrarum and the tarsus.

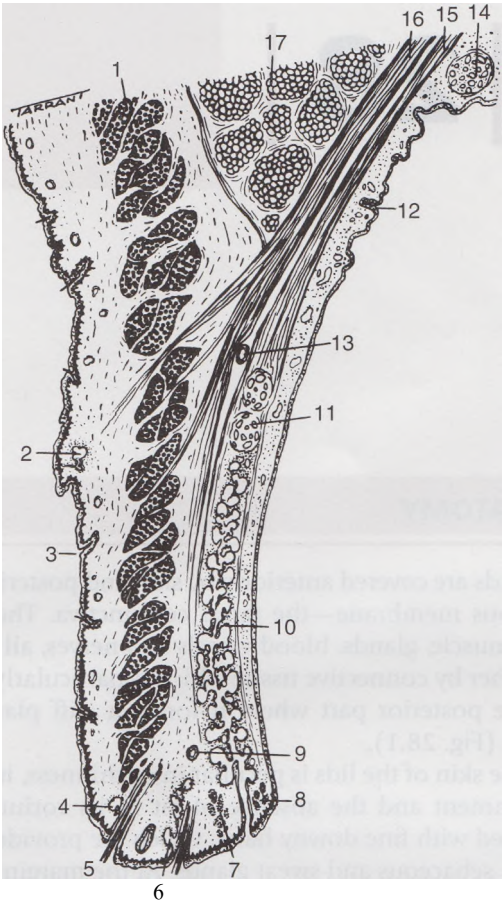


Fig. 28.1 Section through the upper lid. 1, orbicularis muscle; 2, sweat gland; 3, hair follicle; 4, gland of Zeis; 5, cilium; 6, gland of Moll; 7, pars marginalis of orbicularis muscle; 8, pars subtarsalis of orbicularis muscle; 9, inferior arterial arcade; 10, meibomian gland; 11, gland of Wolfring; 12, conjunctival crypts; 13, superior arterial arcade; 14, gland of Krause; 15, Muller muscle; 16, levator palpebrae superioris; 17, fat.

The tarsus consists of dense fibrous tissue, but no cartilage. Embedded in it are some enormously developed sebaceous glands, the *meibomian* (*tarsal*) *glands,* consisting of nearly straight tubes, directed vertically, each opening by a single duct on the margin of the lid. There are 20-30 glands in each lid. The orbicularis palpebrarum occupies the space between the tarsus and the skin. The main central band of the levator palpebrae superioris is inserted into the upper border of the tarsus, an anterior slip passes between the bundles of the orbicularis to be inserted into the skin of the middle of the lid, while a posterior slip is inserted into the conjunctiva at the fornix and laterally it is attached to the medial and lateral palpebral ligaments. The inferior rectus and oblique muscles send fibrous strands forwards into the lower lid and are attached to the tarsus and palpebral ligaments. The capsulopalpebral fascia (Whitnall ligament) originates from the inferior rectus muscle and is inserted by an aponeurosis to the inferior tarsal border.

Besides these striped muscles there are layers of unstriped muscle in each lid, constituting the superior and inferior tarsal muscles of Muller. The fibres of the former arise among the striped fibres of the levator, pass down behind it, and are inserted into the upper border of the tarsus, while the inferior tarsal muscle lies below the inferior rectus and is inserted into the lower tarsus.

The arteries of the upper lid form two main arches, the superior lying between the upper border of the tarsus and the orbicularis, the inferior in a similar position just above the hair follicles. In the lower lid there is one arch near the free edge. There are two venous plexuses in each lid—a post-tarsal passing into the ophthalmic veins, and a pre-tarsal opening into the subcutaneous veins.

The lymphatic drainage is to the submandibular nodes from the medial third of the upper lid and two-thirds of the lower lid and to the pre-auricular nodes from the lateral two-thirds of the upper lid and one-third of the lower lid.

The sensory nerve supply is derived from the trigeminal nerve. The upper lid by the ophthalmic division and the lower lid by maxillary division. The third nerve supplies the levator palpebrae, the seventh the orbicularis and the sympathetic nerves, Muller muscles.

OEDEMA OF THE LIDS

Oedema of the lids is common and, owing to the looseness of the tissue, may be so great as to close the eye. It may be of two types: (i) inflammatory or (ii) passive.

Inflammatory oedema

Inflammatory oedema may be caused by an inflammation of the lid itself (dermatitis, stye, insect bite, etc.), of the conjunctiva (when it may be associated with chemosis), of the lacrimal sac or by purulent inflammation in the eye, Tenon capsule, the orbit or the underlying nasal sinuses. Chronic thickening of the lids, resembling oedema but harder in consistency, so-called *solid oedema,* may follow recurrent attacks of erysipelas.

Passive oedema

Passive oedema is due to circulatory obstruction and is seen in general diseases (e.g. renal disease, cardiac failure) or local conditions such as cavernous sinus thrombosis. An intermittent and acute oedematous condition due to a general anaphylaxis is accompanied by swollen lids (e.g. angioneurotic oedema).

INFLAMMATION OF THE LIDS

Almost any inflammatory condition which affects the skin in general may attack the lids. In this region dermatitis is common and frequently marked, particularly allergic manifestations due to sensitization to innumerable allergens—cosmetics, dyes, drugs, etc. (Fig. 28.2). Atropine allergy is a typical example. Eczema may occur in association with a discharging conjunctivitis or where there is excess lacrimation. The ordinary coccal infections cause boils and abscesses, while specific infections such as anthrax or zoster may occur. Erysipelas is dangerous as it may spread to the orbit, leading to cellulitis, thrombosis of the cavernous sinus or meningitis.

Blepharitis

This is a chronic inflammation of the margins of the lids, appearing as a simple hyperaemia or as a true inflammation, which may occur in two forms: anterior and posterior. The anterior form may be (i) seborrhoeic or squamous; and (ii) ulcerative. The causes of blepharitis are very varied. The condition may follow chronic conjunctivitis due to staphylococci carried to the lid margins by infected fingers. Occasionally, parasites cause blepharitis—*blepharitis acarica,* due to *Demodex folliculorum,* and *phthiriasis palpebrarum,* due to the crab louse, very rarely to the head louse.

Anterior blepharitis

Seborrhoeic or squamous blepharitis

In this condition, small white scales accumulate among the lashes which readily fall out, but are replaced without distortion. If the scales are removed the underlying surface is found to be hyperaemic, but not ulcerated. The condition is often essentially metabolic and similar to seborrhoea associated frequently with dandruff of the scalp. Such aetiological factors require treatment. Daily cleaning with baby shampoo may ameliorate the condition. Infections need to be treated when they supervene.



Fig. 28.2 Contact dermatitis due to eye-shadow.

Staphylococcal or ulcerative blepharitis

This is an infective condition commonly due to staphylococcus. Yellow crusts or dry brittle scales glue the lashes together and on removing them small ulcers, which bleed easily, are seen around the bases of the lashes (Fig. 28.3). The symptoms are redness of the edges of the lids, itching, soreness, lacrimation and photophobia. This distinguishes the condition from a conjunctival discharge, which causes matting together of the lashes, but removal of the crusts reveals normal lid margins.

Treatment: The local treatment of ulcerative blepharitis must be energetic. The crusts must first be removed and loose, diseased lashes epilated. This is most easily done by thorough bathing of the eyes with 1:4 baby shampoo or with warm 3% bicarbonate of soda lotion. The application softens the deposits, so that they can be picked or rubbed off with a pledget of cotton-wool. When the crusts have been removed entirely, antibiotic drops, depending on the sensitivity of the organism, are prescribed. When the infection has been eliminated a simple daily habit of swabbing the lid margins with a warm bland lotion must be established. Rubbing of the eyes or fingering the lids with unwashed hands must be completely avoided. In most cases, if proper treatment is carried out, there is a speedy recovery.

Sequelae: The sequelae of the ulcerative form are serious. If not treated energetically and with perseverance, the



Fig. 28.3 Ulcerative blepharitis. The lower lid shows a loss of lashes in areas and an ulcer with surrounding mucopurulent discharge at the lash line.

disease is extremely chronic, causing or being accompanied by chronic conjunctivitis. The ulceration is liable to extend deeply, destroying the hair follicles so that the lashes that fall out are either not replaced (*madarosis)* or only by a few small, scattered, distorted cilia. When the ulcers heal the cicatricial tissue contracts. Neighbouring hair follicles are drawn out of place and a false direction given to the remaining cilia so that they may rub against the cornea (*trichiasis*). Occasionally the development of cicatricial tissue may be extreme so that the edge of the lid becomes hypertrophied and droops as a consequence of its weight *(tylosis).*

The lower lid is particularly liable to be displaced by prolonged ulcerative blepharitis. The contraction of the scar tissue drags the conjunctiva over the margin, and the posterior lip of the intermarginal strip, instead of being acute-angled, becomes rounded, so that its capillarity is impaired. Tears then tend to spill over *(epiphora),* a condition which is accentuated if the punctum becomes everted and ceases to lie in accurate contact with the bulbar conjunctiva. The continuous wetting of the skin with tears leads to eczema, which is followed by contraction. The condition is made worse by perpetually wiping the eyes, so that eventually *ectropion* develops, thus aggravating the epiphora and setting up a vicious circle.

Posterior blepharitis

This may lead to tear film instability and inferior punctate keratitis.

1. *Meibomian seborrhoea:* Oil droplets may be seen at the Meibomian gland openings which can be expressed out like foam.
2. *Meibomianitis:* Patients present with a diffuse rounded posterior lid margin and thickening around Meibomian gland openings. Lid massage expresses out an inspissated, toothpaste-like material. Cyst formation due to blockage of the ducts may also be seen.

Posterior blepharitis also presents commonly in two ways.

Treatment is again by warm compresses and lid massage, together with doxycycline or minocycline for 6 weeks.

Molluscum contagiosum

This is a small, white, umbilicated swelling, generally multiple, due to a large poxvirus from which a substance resembling sebum can be expressed. Histologically, large intracytoplasmic inclusion bodies occur within the acanthotic epidermis. It produces a severe conjunctivitis and occasionally a keratitis which are intractable to treatment unless the primary nodules on the lid margin



Fig. 28.4 Molluscum contagiosum.

are dealt with. Each should be incised and expressed and the interior touched with tincture of iodine or pure carbolic acid (Fig. 28.4).

Pre-septa l cellulitis

Pre-septal cellulitis is a bacterial infection of the eyelid anterior to the orbital septum, and is due to trauma, or spread of infection from surrounding structures. Patients complain of an acute onset of pain and swelling of the lids. On examination, the lid is oedematous with a raised temperature and tenderness. Visual acuity and ocular motility are normal and there are no signs of proptosis. If the infection spreads posterior to the orbital septum it can lead to visual disturbances, proptosis and even meningitis. It is imperative to treat this with broad spectrum oral antibiotics such as amoxycillin and a non-steroidal anti-inflammatory drug to contain the infection.

Allergic dermatitis

Airborne contact dermatitis or contact dermatitis due to local ocular medications or other applications such as cosmetics can lead to an inflammation of the skin of the lids and surrounding areas of the face (Fig. 28.5).



Fig. 28.5 Allergic dermatitis to hair dye.

INFLAMMATION OF THE GLANDS OF THE LIDS

Hordeolum externum or stye

This is a suppurative inflammation of a Zeis gland (Fig. 28.6). In the early stages the gland becomes swollen, hard and painful, and usually the whole edge of the lid is oedematous. An abscess forms which generally points near the base of one of the cilia.

The pain is considerable until the pus is removed. Styes often occur in crops, or may alternate with boils on the neck, carbuncles, or acne, usually indicating a deficient resistance to staphylococci. It is commonest in young adults, but may occur at any age, especially in debilitated persons.

Treatment: Antibiotics orally and the use of hot compresses are advocated for a few days. When the abscess points it may often be evacuated by pulling out the affected lash. Alternatively, it can be incised with a small knife. If the infection spreads to form a pre-septal cellulitis, oral antibiotics may be required. If crops of styes occur, conditions such as diabetes must be excluded and rubbing of the eye prevented. The patient should be investigated for any refractive errors. A general course of tetracycline may stop recurrences.

Hordeolum internum

This is a suppurative inflammation of a meibomian gland, and may be due to secondary infection of a chalazion. It is less common but the inflammatory symptoms are more violent than in an external stye, because the gland is larger and embedded in dense fibrous tissue. The pus appears as a yellow spot shining through the conjunctiva when the lid is everted. It may burst through the duct or the conjunctiva, rarely through the skin.

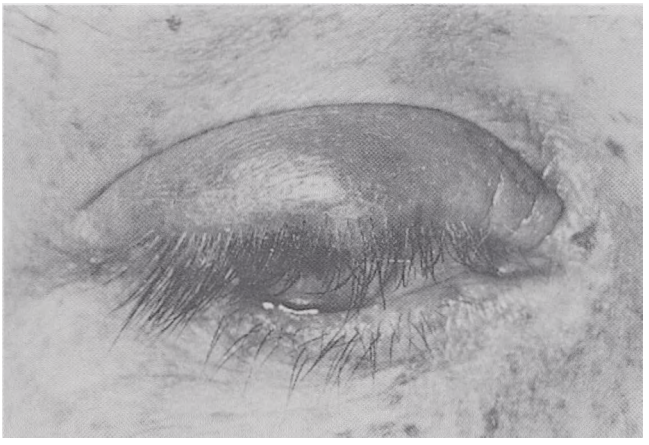


Fig. 28.6 Stye.

Treatment: It is the same as for the external type, except that the incision should be made exactly as for a chalazion.

Chalazion

Clinical features

Chalazion is also known as a tarsal 'cyst' or meibomian 'cyst'. This is not a cyst but a chronic inflammatory granuloma of a meibomian gland (Fig. 28.7). Chalazia are often multiple, occurring in crops, and are more common among adults than in children. The glandular tissue is replaced by granulations containing giant cells, plasma cells, histiocytes and polymorphonuclear leucocytes probably as a result of chronic irritation. Retention of meibomian secretions could lead to such a reaction. The patient often notices a hard, painless swelling in either lid, increasing very gradually in size and without inflammatory symptoms. The smaller chalazia are difficult to see, but are readily appreciated by passing the finger over the skin. If the lid is everted the conjunctiva is red or purple over the nodule, in later stages is often grey, or rarely, if infection has occurred, yellow (hordeolum internum). The grey appearance is due to alteration in the granulation tissue, which becomes converted into a jelly-like mass. Chalazia become smaller over months, but complete spontaneous resolution rarely occurs. The contents may be extruded through the conjunctiva, in which case a fimgating mass of granulation tissue often sprouts through the opening, causing the conjunctival discharge and irritation to continue. Sometimes the granulation tissue is formed in the duct of the gland, from which it projects as a reddish-grey nodule on the intermarginal strip *(marginal chalazion).*

Treatment: An intralesional injection of triamcinolone acetonide may help in the resolution of smaller chalazia.

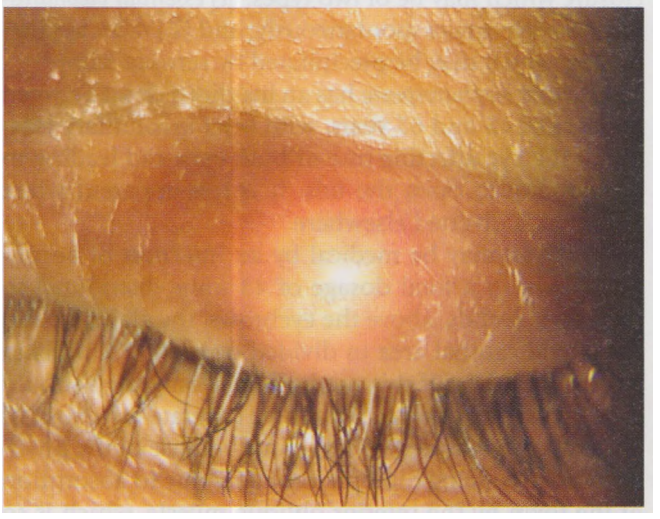


Fig. 28.7 Chalazion of the upper lid.

If the chalazion does not resolve, or there is a large chalazion, it should be incised and curetted.

The conjunctival sac and the lid are well anaesthetized by a submuscular injection of 2% lignocaine locally deep to the orbicularis and a topical anaesthetic. A chalazion clamp is applied around the nodule to help keep the lid everted and to provide a bloodless field for the surgery. The lid is everted and at the point of greatest discoloration a vertical incision made through the palpebral conjunctiva with a sharp scalpel to avoid damage to the adjacent meibomian glands. Any semifluid contents which may be present escape and the walls of the cavity are thoroughly scraped with a curette. In long-standing chalazia with pseudocapsule formation, this is also excised. The clamp is released and pressure is applied for a few minutes. Bleeding soon stops and no dressing is usually necessary.

The patient should be warned that the swelling will remain for some time since the cavity becomes filled with blood. Sometimes, especially if the curettage has not been sufficient, granulation tissue sprouts from the wound. This must be snipped off with scissors and the cavity again scraped out.

Very hard chalazia are occasionally met with, particularly near the canthi, which may be adenomata of the glands and require excision. Malignant changes occur but are rare. However, in all cases with recurrences or those occurring in elderly individuals, the lesion should be biopsied to rule out a meibomian cell carcinoma.

ANOMALIES IN THE POSITION OF THE LASHES AND LIDS

Blepharospasm

This consists of involuntary, sustained and forcible eyelid closure which may be of two types: (i) *essential blepharospasm,* which occurs spontaneously; and (ii) *reflex blepharospasm,* which may be precipitated by sensory stimuli.

Essential blepharospasm has an insidious onset between the ages of 45 and 65 years, with brief involuntary closing of the eye affecting one or both eyes and leading to an inability to open the lids. It is less apparent when attention is diverted elsewhere.

Treatment may be medical by an injection of botulinum toxin in a total dosage of 43 units distributed to the upper eyelids, above the eyebrows, the glabellar and the lateral canthal area in divided doses of 2.5 units in 0.05 ml of saline. If this method fails, only then should the lower lid be injected with three separate injections of 2.5 units of toxin in 0.05 ml saline, because of the possibility of producing diplopia probably due to absorption of the toxin by the inferior oblique muscle, which is so closely associated with the lower lid. The mean time for relief of blepharospasm is 10.5 weeks.

Surgical treatment consists of facial denervation. All temporal-zygomatic and buccal branches of the facial nerve, which cause contraction of the upper facial muscles, are avulsed. The mandibular branch of the facial nerve is identified and the function of its branches assessed by electrical stimulation. Excision of the orbicularis and corrugator muscles may also be done.

Sensory or *reflex blepharospasm* is commonly caused by bright light, corneal or eyelid irritation. Patients may complain of photophobia, a vague discomfort and a foreign body sensation.

Treatment of sensory blepharospasm constitutes removal of the sensory stimulus.

Trichiasis

Trichiasis is a misdirection of the cilia so that they are directed backwards and rub against the cornea (Fig. 28.8). Any condition causing entropion will cause trichiasis, trachoma and spastic entropion being among the most common, while other causes are blepharitis, pemphigoid and scars resulting from injuries, chemical burns, operations, or destructive inflammations such as Stevens-Johnson syndrome and diphtheria. A few of the lashes may be affected or the condition may be due to entropion involving the whole margin of the lid. It may also be caused by congenital distichiasis.

The *symptoms* are those of a foreign body continually present in the eye with irritation, pain, conjunctival congestion, reflex blepharospasm and lacrimation. Recurrent erosions, superficial opacities, vascularization of the cornea and frequent, recurrent corneal ulcers are eventually produced. Trichiasis may prevent corneal ulcers from healing despite therapy, thereby threatening vision.

Treatment: Isolated misdirected cilia may be removed by epilation which must be repeated every few weeks. Destruction of the hair fol licle by diathermy or electrolysis

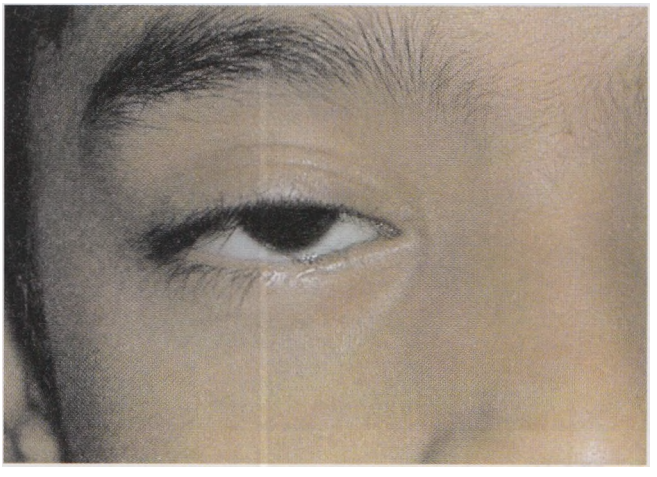


Fig. 28.8 Trichiatic lashes.

is preferable. The follicles may also be destroyed by cryosurgery and argon laser applications. Cryosurgery may be used to treat segmental trichiasis, but can lead to necrosis and depigmentation of the lid.

In diathermy, a fine needle is inserted into the hair follicle and a current of 30 mA applied for 10 seconds. In electrolysis, the flat positive pole is applied to the temple, while the negative, a fine steel needle, is introduced into the hair follicle and a current of 2 mA is used. The negative pole is determined by placing the terminals in saline—bubbles of hydrogen are given off by it. The strength of current can be gauged by the rate of evolution of gas. It should be remembered that electrolysis is both painful and tedious, but pain may be avoided by injecting local anaesthetic into the margin of the lid. If the current is of the proper strength, the bubbles produced at the puncture site cause the formation of slight foam, and the lash with its bulbous root can be easily lifted out.

If many cilia are displaced, operative procedures, as for entropion, must be undertaken.

Entropion

Positioning of the sharp posterior lid margin against the cornea is essential for the integrity of the tear film and the health of the ocular surface. Rolling inwards of the lid margin is called entropion, and is produced by a disparity in length and tone between the anterior skin-muscle, and posterior tarsoconjunctival laminae of the eyelid. The pathogenesis of an entropion may be different in different cases, and the management has to be tailored to the cause (Fig. 28.9). Entropion may be classified as

- involutional,
- cicatricial,
- spastic or
- congenital.

Clinical features: The symptoms are those of disturbances of the stability of the tear film and the induced trichiasis *(see* p. 89).

Involutional entropion

There is a general instability of the lid structures with age. A weakness or dehiscence of the posterior retractors of the lid occurs, together with a laxity of the medial and lateral canthal ligaments. This is accompanied by a loss of posterior support, as atrophy of the orbital fat leads to enophthalmos. The pre-tarsal orbicularis is attached to the tarsus, but the pre-septal orbicularis has more tenuous attachments and a tendency to override the pre-tarsal orbicularis. The lower border of the tarsal plate is therefore rotated forward and the margin of the lid onto the globe.

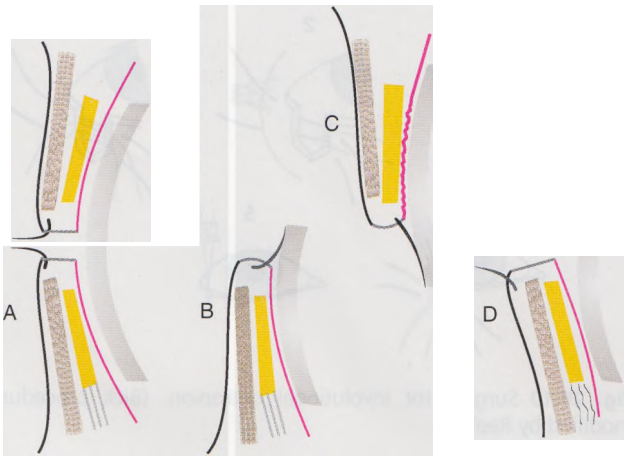


Fig. 28.9 (A) Normal position of the upper and lower lid margins; (B) spastic entropion; (C) cicatricial entropion; (D) senile ectropion.

Surgery for involutional entropion addresses the pathogenesis—reattachment of the retractors to the tarsal plate, shortening of the horizontal width of the tarsal plate and forming a cicatrix between the pre-tarsal and pre-septal parts of the orbicularis. The aim of the surgery is to restore the vertical and horizontal tautness of the lid.

In involutional entropion affecting bed-ridden patients or those for whom surgery is a medical risk, a simple suturing of the lower lid with double-arm 5-0 vicryl chromic catgut may prove efficacious. The needle is passed through the lid from the conjunctiva to the skin adjacent to, but not through, the inferior border of the tarsus. Slight downward traction is applied to the skin when the needle is passed through the muscle and skin. The second needle is placed 3 mm horizontally from it. The suture is tied firmly and left to fall out spontaneously in 3 weeks. Tissue reaction to the gut suture helps to create a cicatricial barrier that maintains the eyelid in the everted position.

In patients with significant horizontal laxity of the lower lids and entropion it is necessary to remove some of the excessive lid tissue next to the lateral canthus. In the *Bick procedure modified by Reeh,* an inverted house-shaped lid shortening is performed as shown in the diagram (Fig. 28.10: 1). One 4-0 silk suture is brought through the skin of the medial edge 2 mm from the wound margin. The suture is carried through two-thirds of the thickness of the tarsus and does not penetrate the conjunctiva. The needle is then carried through the equivalent tissue of the lateral margin before piercing the lateral canthal tendon. A similar 4-0 silk suture is carried through the skin and lower tarsus on the medial margin of the wound and through the orbicularis laterally before being fixed to the periosteum of the lateral orbital rim (Fig. 28.10: 2). These sutures are left *in situ* and 6-0 chromic catgut sutures used to close the tarsus and the equivalent tissue laterally (Fig. 28.10: 3). A marginal 6-0 silk suture is passed through the grey line of

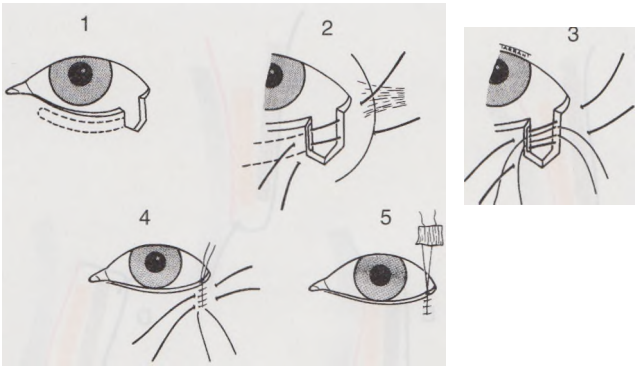


Fig. 28,10 Surgery for involutional entropion. (Bick procedure modified by Reeh)

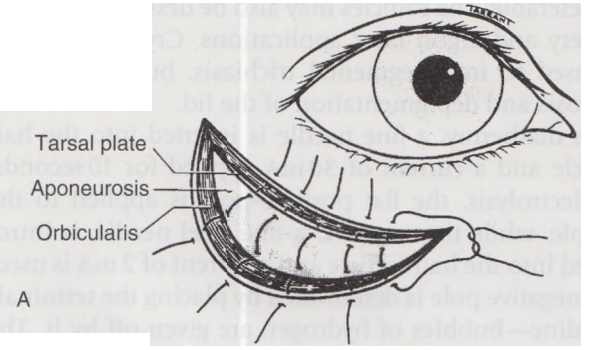
the two wound margins, tied and left long for subsequent fixation to the forehead where it remains in place for 2 or 3 days (Fig. 28.10: 4). The skin margin is closed with interrupted 6-0 silk sutures (Fig. 28.10: 5). At the end of the procedure, the two 4-0 silk sutures are tied firmly to fix the tarsal edge to the lateral canthal tissue. The skin sutures are removed in 4 or 5 days and the 4-0 silk fixation sutures are allowed to remain in position for 10-12 days.

Tucking of inferior lid retractors (Jones, Reeh and Wobig): In cases of severe entropion, tucking of the inferior lid retractors is advisable (Fig. 28.11A and B). An incision is made 5 mm beneath the lid margin from the lateral canthus to the junction of the inner and middle third. The pre-tarsal part of the orbicularis is severed from the pre-septal part and the lower border of the tarsus is identified.

The orbital septum is stripped from the tarsus at its point of attachment to the lower border to open the pre-aponeurotic space. The attachment of the pre-septal muscle to the fascia is freed by blunt dissection over an area of about 10 mm, and excess pre-septal skin and orbicularis muscle may be resected.

A 4-0 silk suture is then brought through the pre-septal skin at the level of the middle and the lateral third of the lower lid. The suture is carried through the inferior lid retractors or aponeurosis about 8 mm inferior to the tarsus with a small bite. The needle is then passed through the retractors at the level of the lower border of the tarsus before penetrating the inferior tarsal margin. The needle penetrates the upper skin margin and is tied in a slip knot.

Ideally, the lower lid should move down 3 mm when the patient gazes downwards. This may require modification of the placement of the lower bite through the aponeurosis. When the central stitch is satisfactory 3 or 4 similar sutures are applied. The sutures are kept in place for 6-10 days.



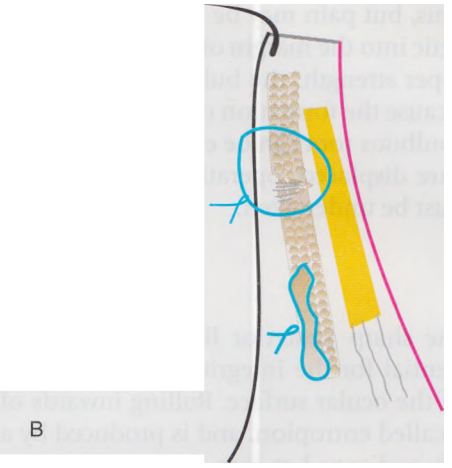


Fig. 28.11 (A) Tucking of inferior lid retractors (Jones, Reeh and Wobig). (B) Cut section of lid showing (I) formation of a fibrous ridge and (II) tucking of inferior lid retractors.

Cicatricial entropion

This is caused by cicatricial contraction of the palpebral conjunctiva, resulting in a relative shortening of the inner tarsoconjunctival lamina of the lid and an inversion of the lid margin. Its most severe form is found in trachoma, where the tarsal plate is also bent and distorted, due to atrophic or hyperplastic changes (Fig. 28.12). Other causes of a cicatricial entropion are trauma, chemical burns, Stevens-Johnson syndrome and ocular cicatricial pemphigoid.

Treatment: Many plastic operations have been devised for the relief of cicatricial entropion, but only the more simple will be described here. The principles governing the various operations are (i) lengthening of the posterior lid lamina to restore the normal direction of the lashes; and (ii) tarsal rotation. A local submuscular pretarsal injection of 2% lignocaine or a general anaesthetic is indicated, but the former method does not obviate all pain, especially if the tarsus is cut.

Mild-to-moderate entropion in the presence of a thickened tarsus is best treated by wedge resection of the

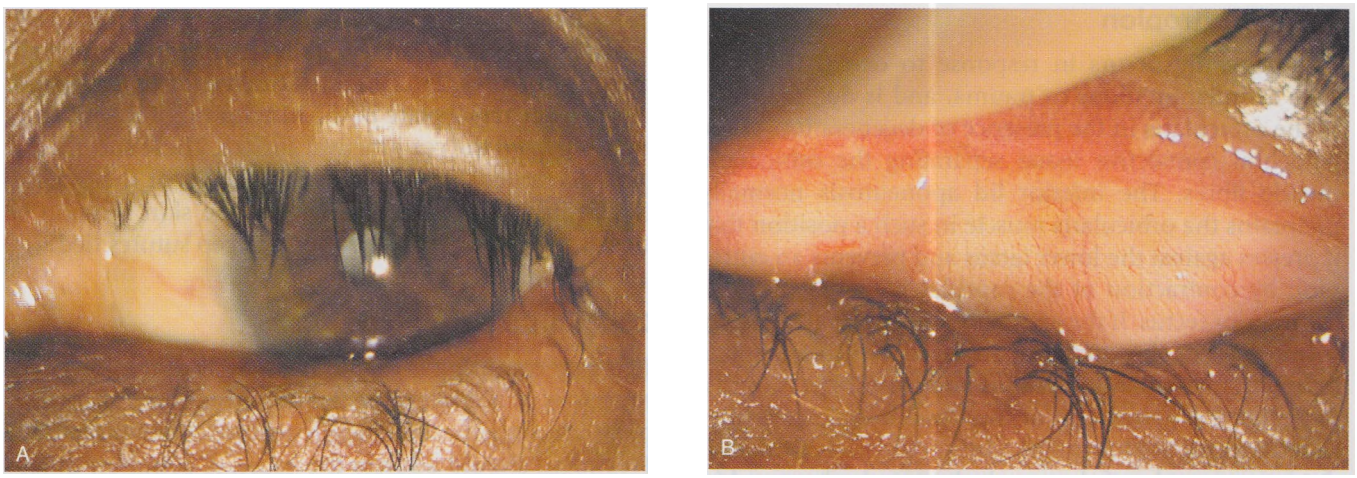


Fig. 28.12 Cicatricial entropion due to trachoma. (A) Thickened tarsus with trichiasis; (B) extensive cicatrization of the conjunctiva. The meibomian glands have been dragged conjunctivally.

tarsus using Fox's modification of the Streatfield-Snellen procedure (Fig. 28.13A and B). A skin incision is made 3 mm from the lash line and a wedge of tarsus approximately 3 mm in height is pared off to a depth of more than three-fourths of the tarsus. Double-armed sutures are passed through the two edges and then between the tarsus and the orbicularis to a point just above the lashes, to evert the lashes. Any excess skin may be excised.

The simplest procedure for a more severe entropion, or one where the tarsus is not thickened, is a modification of *Burrow operation*, or *tarsal fracture* (Fig. 28.13C and D). The lid is everted over the end of a metal lid spatula. A horizontal incision through the conjunctiva and passing completely through the tarsal plate, but not through the skin, is made along the whole length of the lid in the sulcus subtarsalis, about 2-3 mm above the posterior border of the intermarginal strip. The temporal end of the strip may then be divided by a vertical incision through the free edge of the lid, including the whole thickness. The edge of the lid is thus left attached only by skin, and when cicatrization has occurred the edge is turned slightly outwards, so that the lashes are directed away from the eye. The edge of the lid may be kept everted during the process of healing by means of suitably applied sutures.

In an alternative operation, the incision is made as before, but the tarsal plate is pared down to a chiseledge along the whole length and mattress sutures passed through the plate and lid margin, emerging through the grey line. The sutures are tied over a rubber tubing, thus bending the lid margin forwards and upwards.

Very extensive scarring may necessitate the replacement of the conjunctiva by a mucous membrane graft and a distorted tarsal plate by cartilage or chondromucosal grafts.

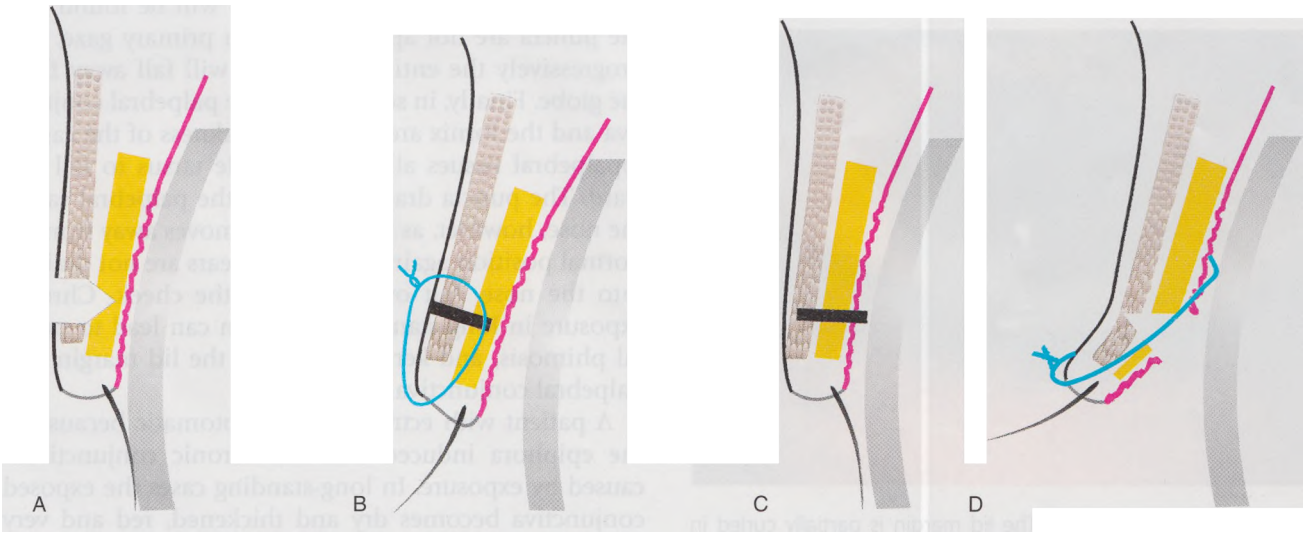


Fig. 28.13 Surgery for cicatricial entropion. (A and B) Wedge resection; (C and D) tarsal fracture.

Spastic entropion

This generally occurs in response to ocular irritation such as inflammations or trauma, and is due to spasm of the orbicularis in the presence of degeneration of the palpebral connective tissue separating the orbicularis muscle fibres. The inferior lid aponeurosis normally maintains the orbicularis muscle in such a position that it presses against the lower tarsus and prevents an entropion by contraction of the capsular palpebral head of the inferior rectus. If the aponeurosis degenerates, strong contraction of the circularly arranged orbicularis tends to approximate the lid margins and turn them inwards. Age-related degeneration of the tarsal muscle of Muller (a retractor of the lower lid) additionally fails to anchor the lower margin of the tarsal plate to the bony orbit. This allows the orbicularis to ride up in front of the tarsal plate towards the lid margin, rolling it in. There is also a horizontal lid laxity present in such cases. These conditions are found particularly in old people who are therefore liable to spastic entropion. It may be caused by tight bandaging, as after a surgical operation, and is favoured by narrowness of the palpebral aperture (blepharophimosis). Spastic entropion is almost invariably restricted to the lower lid (Fig. 28.14).

Treatment: The precipitating reason for the spastic entropion needs to be identified and treated. Lubricants take care of surface disorders and antibiotics of conjunctival or lid inflammations. If the condition is due to bandaging, it is often cured by simply removing the bandage. In spastic entropion of the elderly, temporary relief may be obtained after everting the lid, by pulling it out with a strip of adhesive plaster. If the entropion persists, botulinum toxin may be injected into the pre-tarsal orbicularis to help weaken it and prevent overriding.

Surgery is aimed at producing a ridge of fibrous tissue in the orbicularis muscle and thus preventing the fibres from sliding in a vertical direction. A horizontal incision is made 4 mm below the lid margin through all the lid structures. Two double-armed sutures are placed through the tarsal plate in the inferior lip of the wound, entering from the conjunctival surface. These sutures are inserted under the skin of the upper lip of the wound to exit just below the lid margin. The skin incision is closed, the clamp released and the deep sutures tied.

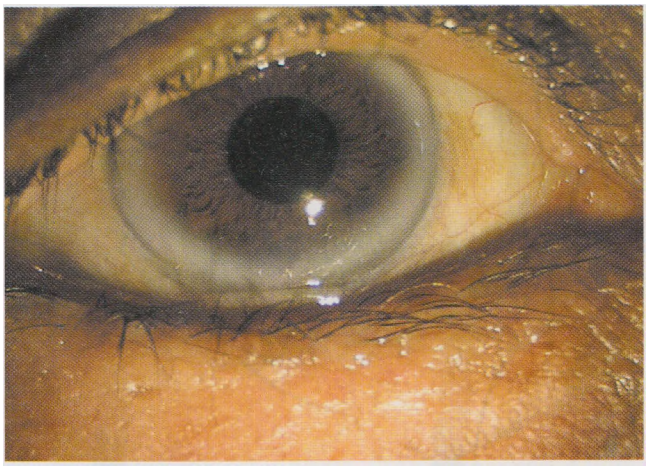


Fig. 28.14 Spastic entropion. The lid margin is partially curled in and the lashes sweep the cornea.

Congenital entropion

This rare condition is due to dysgenesis of the lower lid retractors or a developmental abnormality of the tarsal plate, causing the lid margin to turn onto the globe. Treatment should address the cause. A common differential diagnosis is an epiblepharon where an anomalous skin fold pushes the lashes onto the eyeball.

Ectropion

Eversion of the lid margin and eyelashes away from the globe is known as ectropion. It occurs in several forms, but the main types are as follows:

1. *Acquired,* which may be further subdivided into
   (i) involutional or senile
   (ii) cicatricial
   (iii) paralytic
   (iv) mechanical
2. *CongenitaJ*

The functions of the lower eyelid are protection of the eye and working of the lacrimal pump. Age and gravity cause a slow relaxation of the lid structures, especially the canthal ligaments and the orbicularis, which form the suspensory system of the lid. In very mild cases, asking the patient to look up will show that the puncta are not apposed to the globe. Over time, as the ectropion progresses to the moderate stage, it will be found that the puncta are not apposed even in primary gaze, and progressively the entire lid margin will fall away from the globe. Finally, in severe cases, the palpebral conjunctiva and the fornix are exposed. Weakness of the capsulopalpebral tissues allows the whole tarsus to fall forward. The puncta drain tears from the palpebral sac to the nose; however, as the punctum moves away from its normal position against the globe, tears are not drained into the nose, but overflow onto the cheek. Chronic exposure in long-standing ectropion can lead to punctal phimosis, and keratinization of the lid margin and palpebral conjunctiva.

A patient with ectropion is symptomatic because of the epiphora induced and the chronic conjunctivitis caused by exposure. In long-standing cases the exposed conjunctiva becomes dry and thickened, red and very unsightly and, in severe cases, the cornea may suffer from

the imperfect closure of the lids. Abnormal lid laxity is diagnosed if the lid can be drawn away from the globe by more than 6-7 mm and does not 'snap' back into position when released. If pulling the lower lid laterally and medially causes a displacement of the canthi by more than 2 mm, laxity of the canthal ligaments is diagnosed.

Mild forms of ectropion can be treated with artificial tears and protection from drying of the eyes. Patients should be instructed to wipe their eyes in an upward direction towards the nose.

Senile ectropion: Involutional ectropion usually develops as a result of laxity of the suspensory system of the lower eyelid, and the medial and lateral canthal ligaments, allowing the lid to fall away from the globe. This laxity is accompanied by a horizontal lengthening of the lid.

Surgical treatment: In mild-to-moderate entropion a horizontal spindle of conjunctiva 7-8 mm long, 4 mm high and at least 5 mm below the punctum is excised and sutured to its margins. This allows the puncta to be replaced in their normal position.

If the ectropion is most pronounced in the mid-section of the lower lid, full-thickness lid shortening is recommended in that area. However, this should not be done closer than 5 mm to the punctum. An inverted house-shaped incision of tissue is made and then repaired. If the degree of ectropion is severe and marked over the lateral half of the lower lid, with little laxity of the lateral canthal ligament, a Kuhnt-Szymanowski procedure as modified by Bryon Smith is recommended (Fig. 28.15). A line is drawn 3 mm inferior to the lid margin following the contour of the lower lid. The line is drawn slightly past the lateral canthus in an upward manner, at which point it is sloped downwards. A skin flap is prepared and a full thickness lid shortening then performed at the lateral canthus as previously described. The excess skin is pulled gently upwards and outward, removed and the skin margins sutured with 7-0 silk. Traction sutures are kept at the point of meeting of the lid margin and are taped to the forehead at the end of the procedure. If there is laxity of the lateral canthal ligament, cantholysis and tarsal excision at its lateral margin permits reattachment of the tarsal plate to the periosteum. Excess skin is excised and the orbicularis resutured. A medial ectropion can be corrected by a modified Lazy T operation, in which a medial vertical pentagon of full-thickness lid is excised 4 mm lateral to the lower punctum as well as an infrapunctal wedge of tarsal conjunctiva and inferior lid retractors. The canaliculi have to be identified and protected during surgery at the medial canthus. In the presence of a complete ectropion, the lower retractors or the capsulopalpebral tissues need to be reattached as well. A $C0_2$ laser makes the surgery bloodless and more precise.

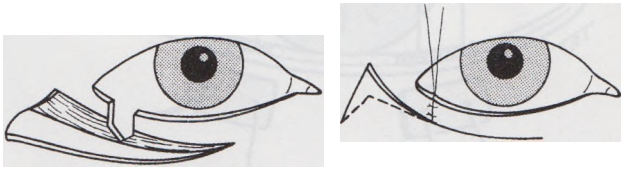


Fig. 28.15 Byron Smith modification of Kuhnt-Szymanowski procedure.

Paralytic ectropion is commonly caused by a paralysis of the facial nerve, in Bell palsy, parotid surgeries, trauma and tumours such as an acoustic neuroma. Initial conservative therapy with taping of the lids and the use of lubricants allows time for recovery of the palsy. As a more permanent solution, *lateral tarsorrhaphy* may be indicated. In this operation the palpebral aperture is shortened by uniting the lids at the outer canthus. The edges of the upper and lower lids are freshened for the requisite distance, the lashes excised, and then sutured together as in central tarsorrhaphy. In long-standing paralysis associated with laxity, shortening of the lid and reattachment of the lateral cut edge to Whitnall ligament may be necessary as described in the therapy of involutional ectropion. Associated lagophthalmos caused by weakness of the superior orbicularis may need taping of the lids at night or a gold weight placed pretarsally.

Cicatricial ectropion is commonly the result of burns, trauma and chronic inflammations of the skin which shorten the anterior lamina of the eyelid, i.e. the skin-muscle layers. This pulls the eyelid away from the globe (Fig. 28.16).

Treatment of cicatricial ectropion requires release and relaxation of the scarred tissues, and an elongation of the skin muscle lamina by some form of *blepharoplasty.* Localized areas of scarring can be released by Z or V-Y plasty. Larger scars have to be excised and the surrounding skin released from any underlying adhesions before the application of a skin graft. Whole or split-skin grafts, or flaps of skin are taken from the upper lid, behind the ear or the inner upper arm. Each case must be treated on its own merits and will often exercise the ingenuity of the surgeon. A superior traction suture prevents early contraction of the graft.



Fig. 28.16 Cicatricial ectropion. (By courtesy of Sanjiv Gupta)

Symblepharon

This is a condition where adhesion of the lid to the globe takes place. Any cause which produces raw surfaces on two opposed areas of the palpebral and bulbar conjunctiva will lead to adhesion if the areas are allowed to remain in contact during the process of healing, e.g. burns from heat or chemical injury, Stevens-Johnson syndrome, ulcers, diphtheria, operations, etc. Bands of fibrous tissue are thus formed, stretching between the lid and the globe, involving the cornea if this has also been injured. The bands may be narrow, but are more frequently broad, and may extend into the fornix so that the lid is completely adherent to the eyeball over a considerable area (*symblepharon posterior).* Bands limited to the anterior parts not involving the fornix are called *symblepharon anterior.* However, *total symblepharon.* in which the lids are completely adherent to the globe, is rare.

Pronounced adhesions cause impairment of mobility of the eye resulting in diplopia. The adhesion may be so intimate that it is impossible to close the lids efficiently resulting in lagophthalmos with its baneful consequences. There is often extensive disfigurement.

Treatment: The prevention of symblepharon by the early and frequent use of a glass rod or therapeutic bandage contact lens is of the utmost importance. When it is already established, it is necessary to operate, though this may be difficult, especially when the bands are broad or if there is symblepharon posterior. There may be no guide as to the limitations of the sclera and tarsus, and great care has to be exercised lest the globe be punctured. The attachments are released and the raw areas covered with conjunctival, buccal mucous membrane or amniotic membrane grafts. The prevention of the re-formation of adhesions is much more difficult, a therapeutic contact lens may be used to separate the raw surfaces.

Ankyloblepharon

This is adhesion of the margins of the two lids. It may be either a congenital condition or due to burns, etc. It may be partial or complete, and is often combined with symblepharon. The treatment depends upon the amount of symblepharon. If it is very extensive, operation may be contraindicated. In other cases the lids are separated and kept apart during the healing process. If the adhesion extends to the angle of the lids, the latter must be covered with an epithelial graft to avoid recurrence.

Blepharophimosis

This is the condition in which the palpebral fissure appears to be smaller than normal. In acquired blepharophimosis the outer angle is often normal, but is obscured by a vertical fold of skin formed by eczematous contraction of the skin following prolonged epiphora and blepharospasm (*epicanthus lateralis).* Mere narrowing of the palpebral aperture is often called blepharophimosis and may be congenital. The condition may require no treatment, disappearing spontaneously after the inflammation has subsided. In other cases canthoplasty is indicated.

Lagophthalmos

This is a condition in which there is incomplete closure of the palpebral aperture when an attempt is made to shut the eyes. It may be due to contraction of the lids from cicatrization or a congenital deformity, ectropion, paralysis of the orbicularis, proptosis due to exophthalmic goitre, orbital tumour, etc. or to laxity of the tissues and absence of reflex blinking in people who are extremely ill or moribund. Owing to exposure, the cornea becomes keratinized and frequently keratitis sets in. The treatment is that of exposure keratopathy, the frequent use of tear substitutes and, in severe cases, a tarsorrhaphy (Fig. 28.17). Apposing areas ofthe intermarginal strip are freshened and two double-armed suture placed to allow the raw edges to adhere and cover the cornea.

Ptosis

This is drooping of the upper lid to a level that covers more than 2 mm of the superior cornea.

Elevation of the upper lid is largely a function of the levator palpebrae superioris, assisted by the frontalis and Muller muscle. Ptosis is the term given to a drooping of the upper lid, usually due to paralysis or defective development of the levator palpebrae superioris. A purely mechanical ptosis may also occur due to deformity and increased weight of the lid brought about by trachoma or tumour. An apparent drooping of the lid—pseudoptosis—may occur due to lack of support as in

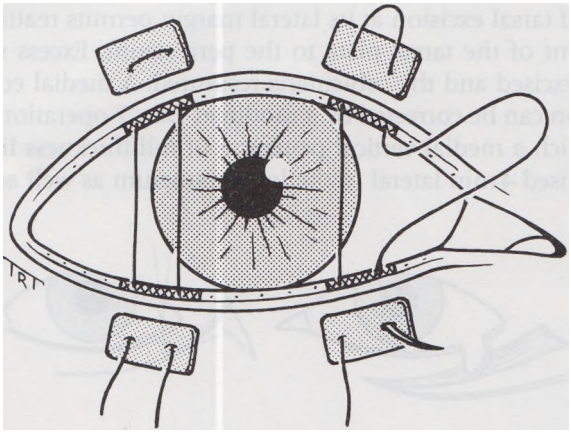


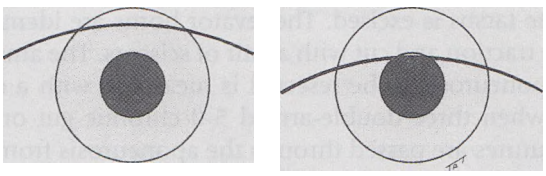
Fig. 28.17 Tarsorrhaphy for lagophthalmos.

phthisis bulbi or anophthalmos. Ptosis may be classified as follows:

1. *Congenital*
   - (i) simple
   - (ii) complicated—associated with ocular motor anomalies, blepharophimosis syndrome and Marcus Gunn ptosis
2. *Acquired*
   - (i) neurogenic
   - (ii) myogenic
   - (iii) aponeurotic
   - (iv) mechanical

The condition may be unilateral or bilateral, partial or complete. In the normal eye the upper lid margin rests midway between the upper border of the pupil and the limbus. A simple diagram in the notes is sufficient for purposes of keeping a record (Fig. 28.18). Ptosis may be measured as a difference between the height of the palpebral aperture in the two eyes, or by measuring the distance between the lid margin and the corneal light reflex. Margin reflex distance (MRD) is measured from the corneal light reflex to the central portion of the upper eyelid, with the eye in the primary position. The difference in the MRD between the normal and ptotic eyelid determines the amount of ptosis. The normal MRD is 4.0 mm, with a variation of 1mm. A ptosis of less than 2 mm is considered mild, 3 mm moderate and 4 mm or more severe. In the more severe degrees, the lid hangs down, covering the pupil more or less completely and interfering with vision. An attempt is made to counteract the effect by overaction of the frontalis and by throwing back the head, the eyes being rotated downwards at the same time. A very characteristic attitude is thus adopted, the forced contraction of the frontalis causes the eyebrows to be raised and throws the skin of the forehead into wrinkles (Fig. 28.19). Partial ptosis, masked by this means, may become manifest if the patient is asked to look up while the eyebrows are fixed by firm pressure with the fingers against the frontal bone.

The amount of levator function must be assessed. The examiner places the thumb of one hand horizontally over the patient's brow. The patient is directed to look down without moving his head. With his other hand, the examiner places a millimetre rule just in front of the upper lid and notes the reading on the ruler opposite the



Fig, 28.18 How to record the position of the upper iid.



Fig. 28.19 Congenital ptosis, more marked on the right side. Note the wrinkling of the forehead in an attempt to open the eyes. (By courtesy of Kamel)

lid margin. The thumb is now pressed firmly on the brow fixing the frontalis. The patient is asked to look up as far as possible without moving his head. The difference in the two readings is a practical measurement of levator function. Infants respond better to this test if an assistant provides a fixation light. The excursion of the lid is recorded as the action of the levator palpebrae superioris in millimetres. An excursion of 8 mm or more is good levator action, 5-7 mm fair and 4 mm or less, poor, lliff found that in children below 1 year of age, if the eyelid is everted, it reverts on its own in a normal lid. If the lid remains in that position while the eyes are elevated, it is an indication of an extreme weakness of levator function. One of the objectives of surgery on unilateral ptosis is to produce a close match of the contralateral upper lid fold. To do this it is important to record whether there is a fold in the unoperated lid with a sketch and description of its contour, its depth and any change in depth produced on elevation of the lid. The presence of more than one fold and the distance of the fold from the lid margin must also be registered and copied.

Bell phenomenon, the upward roll of the eyes on attempted closure, needs to be assessed pre-operatively, because after surgery a poor Bell phenomenon could result in exposure keratitis during sleep. Corneal sensation is evaluated as there will be some exposure post-operatively, and the eye should be aware of any foreign bodies, etc. The observer should also look for possible causes of a pseudoptosis such as enophthalmos, hypotropia of the eye, dermatochalasis and contralateral lid retraction.

Congenital ptosis

This is the commonest form of this affliction. The presence of congenital ptosis should be confirmed by photographs taken during childhood. It is usually, but not invariably, bilateral, and is due in most cases to defective development of the muscles. The condition is not infrequently hereditary. Simple congenital ptosis is an isolated abnormality, but congenital ptosis is called complicated



Fig. 28.20 Marcus Gunn ptosis. The right upper lid is elevated on moving the jaw to the left.

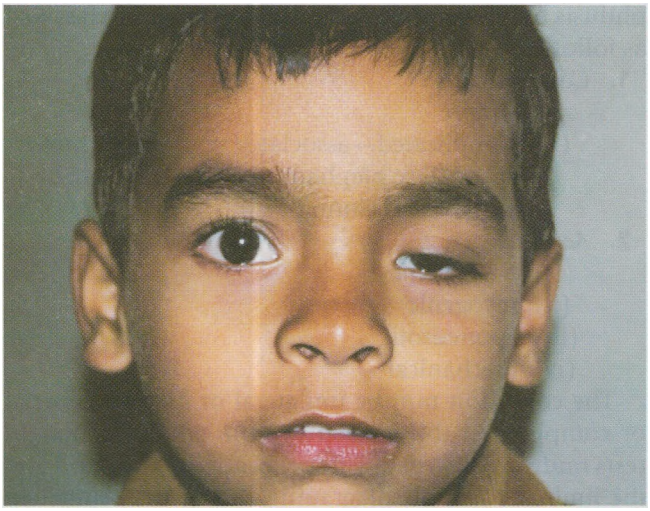


Fig. 28.21 Severe congenital partial ptosis.

when there is an associated maldevelopment of the surrounding structures. There may be a defect in the upward movement of the eyes, due to absence of the posterior insertion of the levator into the fornix, and sometimes to coincident maldevelopment or defective innervation of the superior rectus. Defective upward movement of the eyes is the commonest congenital defect of the bilaterally associated extrinsic muscles. Abnormal synkineses (Fig. 28.20) such as the jaw winking phenomenon or Marcus Gunn ptosis may be seen, in which lid retraction is observed on opening the mouth or moving the jaw to the opposite side. It is important to examine young people with ptosis for other congenital anomalies, disturbances of binocular vision and motility, refractive error and corneal insensitivity. Dystrophy of the levator may also be recognized by looking at the palpebral aperture in down gaze, where the ptotic eye will have a wider aperture as compared to the opposite normal one. This occurs because a dystrophic muscle can neither contract normally, nor relax. In the blepharophimosis syndrome the patient has ptosis, horizontal shortening of the palpebral aperture, epicanthus inversus, telecanthus and lateral ectropion of the lower lids.

Surgery is the *treatment of choice* and is carried out between 3 and 5 years of age if the ptosis is partial, but if the visual axis is covered at least a temporary procedure should be carried out as soon as possible to avoid sensory deprivation amblyopia (Fig. 28.21). The type of surgery performed is determined by the amount of ptosis, the levator action and associated anomalies such as a Marcus Gunn phenomenon.

The Fasanella-Servat operation is indicated for cases of minimal ptosis of 1.5-2 mm with good function of the levator and a good lid fold. The lid is everted and two curved haemostats are placed grasping the conjunctiva, tarsus, levator and Muller muscle. The haemostats are pulled up, the upper tarsus is excised by double the amount of ptosis, i.e. 4-5 mm. A running suture is carefully placed and the knot is buried by bringing both ends of the suture out through a skin wound made in the outer part of the lid fold.

In moderate to severe ptosis with a moderate levator action, levator resection can be carried out by a conjunctival approach or anterior technique. A 10 mm resection is minimal for congenital ptosis and maximal for senile ptosis. A mild congenital ptosis with 8 mm or more of levator function and an intact aponeurosis maybe corrected with 10-12 mm of resection; a patient with 4 or 5 mm of ptosis with 5 or 6 mm of levator function and a thin aponeurosis may need 18-24 mm of resection to produce an acceptable result if the levator function is feeble and the ptosis severe (Table 28.1). Plication of the superior levator aponeurosis is currently being evaluated in moderate ptosis for a better functional result.

Conjunctival approach levator resection: In the Blaskovics operation the upper lid is doubly everted over a Desmarre lid retractor. The conjunctiva above the tarsus is ballooned with saline. An incision is then made through the conjunctiva near the tarsal border and dissected back to the fornix (Fig. 28.22). Abutton-hole incision is made on the temporal side and the scissors passed across, just above the aponeurosis, to the nasal side. A ptosis clamp is inserted, one blade being above and the other below the aponeurosis of the levator which is cut free and drawn downwards; 1 or 2 mm of the upper border of the tarsus is excised. The levator horns are identified with traction and cut with a pair of scissors. The amount of aponeurosis to be resected is measured with a calliper when three double-armed 5-0 chromic gut or vicryl sutures are passed through the aponeurosis from the anterior surface at this point and tied with three knots. The excess aponeurosis is excised and these sutures are

Table 28.1 Surgical treatment of various types of ptosis

Ptosis surgery	Requisite levator action	Amount of ptosis that can be treated	Indications
Fasanella–Servat	Good	<2 mm	Horner syndrome
Levator resection —anterior approach	Moderate	Any	Larger resections in congenital or acquired ptosis
Levator resection — conjunctival approach	Moderate	Any	Moderate congenital or acquired ptosis
Levator resection with aponeurotic reinsertion	Moderate	Any	Acquired ptosis
Frontalis suspension	Poor	>2 mm	Congenital—especially Marcus Gunn ptosis or for temporary relief

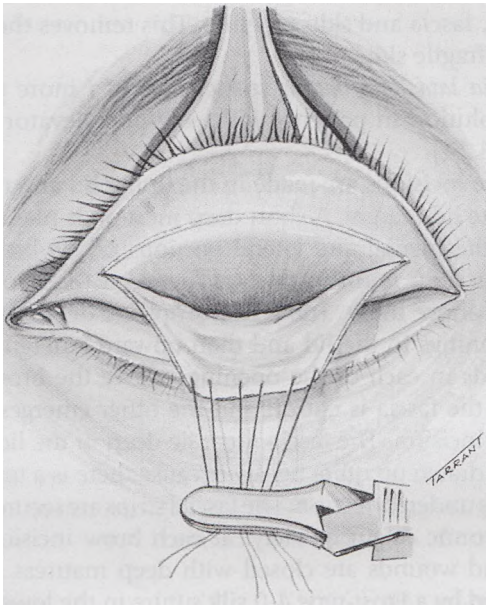


Fig. 28.22 Conjunctival approach levator resection. The upper eyelid is maintained in a position of double eversion to expose the conjunctival surface of the lid and the region of the superior fornix, and this is achieved by the use of Desmarre eyelid retractor which presses on the skin surface of the eyelid. The palpebral conjunctiva is incised in the region of the upper border of the tarsal plate and three double-ended silk sutures (with the loop of each suture on the inner surface of the conjunctiva) are inserted into the upper edge of the incised conjunctiva so that this portion of the conjunctiva is retracted into the region of the superior fornix with exposure of the underlying superior palpebral muscle and levator tendon. [Reproduced from Eyes. In: Miller SJH (ed). *Rob and Smith's Operative Surgery,* 3rd edn, 1976. By courtesy of the publishers, Butterworths, London],

passed completely through the upper edge of the tarsus starting at the posterior edge. They are then carried along the anterior surface to emerge through the muscle and skin in a line which will produce the lid fold. The three mattress sutures are drawn up and tied over a wisp of cotton wool. The conjunctiva is closed with a continuous 6-0 absorbable suture such as chromic catgut or vicryl. A Frost suture is then inserted in the lower lid and afirm dressing applied.

Anterior approach levator resection: The anterior approach is recommended in patients who require larger resections. In the Everbusch technique the line of incision is in the future lid fold. The skin should be drawn up before the markings are made. Excess skin to be removed later should be *taken* from the upper lip of the wound. The skin of the lid is held taut, the incision made with a razor blade, and the dissection carried upwards and downwards under the obicularis muscle to expose the orbital septum. A vertical incision is made through the septum with a knife and spread open with a small pair of scissors. Pressure on the globe usually causes the preaponeurotic fat to appear in the wound. The glistening aponeurosis of the levator tendon lies directly beneath the fat. The aponeurosis should be carefully identified, the lid everted and the conjunctiva above the tarsal border ballooned with saline. A small buttonhole incision is made through the conjunctiva on the temporal side and blunt scissors passed across, watching the blades through the thin conjunctiva. This separates the conjunctiva from Muller muscle and the aponeurosis. A second buttonhole incision is made on the nasal side. A ptosis clamp is passed as the scissors are withdrawn with one blade under the conjunctiva and the other on top of the aponeurosis. With the aponeurosis in the ptosis clamp and all tissues freed from both surfaces, the horns should be carefully incised so as not to damage the superior oblique tendon or the lacrimal gland. The amount of aponeurosis to be excised is measured with a calliper. Three double-armed 6-0 chromic gut sutures are passed through the aponeurosis from below upwards and tied securely with three knots. The excess aponeurosis is removed. One needle from each of the double-armed sutures is passed through the outer layer of the tarsus parallel to the lid border and approximately 4 mm from the lid margin. These sutures are tied. Three or more additional interrupted 6-0 chromic gut sutures are added to ensure firm fixation of the entire aponeurosis.

A good fold is produced with a 6-0 silk suture for adults and vicryl or chromic catgut for children. To produce a firm scar each suture should pass through the depth of the wound about 1.5 mm back and through the outer layer of the aponeurosis. When the suture is drawn up and tied, the skin is firmly anchored to the aponeurosis producing a permanent fold. A 4-0 silk Frost-type suture is inserted below the lash line for at least 10 mm and brought up to be passed through the skin just below the brow. A firm dressing is applied.

Levator plication: In cases of mild to moderate ptosis, the levator instead of being resected can be simply double-breasted over itself to produce a good result. *Advantages* include less time, simpler technique and no extensive dissection to isolate the levator before resection. Disadvantages of this technique are that there is much more lid lag and lagophthalmos as compared to resection and poor results in moderate to severe ptosis. It should be remembered that levator plication can give good results only if the levator function is good/fair. The procedure involves isolating the levator muscle and putting three mattress sutures through the upper border of the tarsus and at appropriate vertical height of the levator. The first suture is the central one, in line with the pupil level starting from upper border of tarsus passing the levator then again through the tarsus 3-4 mm from the original entry, thus completing the mattress suture. Once the proper lift is obtained then one suture is passed medially and one laterally to give a proper lid contour.

Frontalis suspension: When the levator muscle is intact but the function is poor (3 mm or less), strengthening by resection of the levator is not recommended and the lid is then suspended from the frontalis. This may be carried out by the use of sutures, fascia lata sling or silicon bands.

The operation is useful for young children as a temporary measure until they are able to cooperate better as they grow older. It is also useful in elderly and infirm patients. If a levator resection has produced a mild undercorrection a Supramid suture may be used. The suture may be removed at any time.

A 4-0 Supramid extra suture with swedged-on needles facilitates easy passage through the outer layers of the tarsus. After attachment to the tarsus, the needles are removed and the two sutures are carried upwards through the deeper layers of the lid with a one-half curved cutting needle to emerge through the wound made above the brow (Fig. 28.23). These sutures are deep enough to prevent visible suture marks.

Infection of the suture bed is an annoying complication and the suture should be guarded carefully, kept away from the skin and lashes during surgery and the wound in the brow should be carefully closed. A broad-spectrum antibiotic post-operatively for 4 or 5 days is important. To reduce the scar on the forehead, a deeply

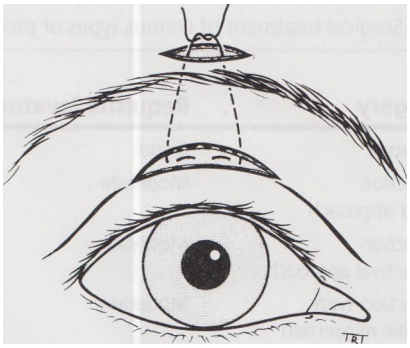


Fig. 28,23 Frontalis suspension.

placed mattress suture of 6-0 silk or Mersilene brings the muscle, fascia and skin together. This removes the strain on the fragile skin.

Fascia lata for frontalis suspension is a more permanent solution in patients with very poor levator action (Fig. 28.24).

Three incisions are made in the upper lid about 4 mm from the lid margin. A short deep incision is made 5 mm above the medial and lateral portions of the brow. The third incision is made midway between the two, some 16 mm above them. The fascial strips are drawn through the openings in the lid and then upward emerging with two ends in each of the openings above the brow. One end of the fascia is cut off and the other emerges at the central incision. The fascia must lie deep in the lid tissue and be drawn up quite tightly because there is a tendency towards undercorrection. The fascial strips are secured with 5-0 chromic catgut or vicryl at each brow incision. The forehead wounds are closed with deep mattress sutures followed by a Frost-type 4-0 silk suture in the lower lid. A broad-spectrum antibiotic should be given for 5 days.

If after these operations it is found that when the eyeball is raised, the skin of the upper lid falls in an unsightly fold over the lashes, a horizontal strip of skin of suitable

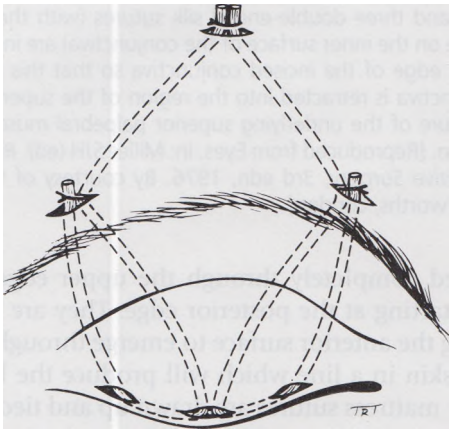


Fig. 28.24 Fascia lata lid suspension.

width is removed from the upper lid, the position of the lower skin incision corresponding roughly to that of the upper edge of the tarsal plate. The sutures which join the edges of the skin incision are carried through the deep tissues in such a way as to stretch the skin over the tarsus and to produce a fold in the skin of the eyelid in the normal position.

Acquired ptosis

Acquired ptosis is usually unilateral and its cause needs to be identified so that appropriate therapy can be instituted.

Neurogenic ptosis: It may be part of the symptom-complex involving the entire third nerve at any point in its path, or rarely it may be due to affection of the branch supplying the levator. Isolated ptosis without other signs of oculomotor paralysis may result from disease of the supranuclear pathways (*see* Chapter 31). Horner syndrome is a common cause of neurogenic ptosis and is accompanied by miosis and anhidrosis, as sympathetic innervation is reduced. It may also be due to direct injury of the muscle or its nerve supply, as by wounds or fractures. In cases of paralysis, treatment must be directed at first to the cause. In all neurogenic ptosis, the patient should be reviewed periodically on conservative management to allow for any spontaneous recovery and for the deficit to stabilize. In complete paralysis of the third nerve, surgery is usually contraindicated till strabismus has been corrected, since if the lid is raised in these cases diplopia becomes manifest. Crutch spectacles may be used in the presence of levator paralysis. Surgery for neurogenic ptosis seldom gives perfect results. Two techniques may be applied: (i) if the levator is not completely paralysed this muscle may be resected as described above and (ii) if the levator is paralysed, the action of the frontalis muscle may be utilized in raising the lid.

Myogenic: Myogenic ptosis develops gradually over years. Bilateral, symmetrical ptosis may occur in myotonic dystrophy and chronic progressive exophthalmoplegia asymmetry is more often seen in myasthenia gravis. Treatment of the primary disorder should be undertaken first, followed by crutch spectacles to help lift the lid.

Myasthenia gravis is a disease characterized by generalized muscular weakness and rapidly developing fatigue of the muscles due to an auto-immune disorder in which damage of the acetylcholine receptors takes place at the post-synaptic membrane. Anti-acetylcholine receptor antibodies are found in approximately 80% of patients with myasthenia, the levels correlating with the severity of the disease. Attempts can be made to modify the defective immune mechanism with corticosteroids, immunosuppressives, plasmapheresis and thymectomy. The symptoms fluctuate and, after a short rest, recovery follows rapidly in the early stages. Ptosis and failure of convergence are early and prominent features. The ptosis is nearly always bilateral and is increased by prolonged fixation or attempts to look upwards; effective compensation by overaction of the frontales is impossible. Ophthalmoplegia externa, partial or complete, occurs in 50% of the cases, but the intrinsic muscles are not affected. Nystagmoid jerks are not uncommon. Remarkable temporary improvement in the action of the muscles is obtained by injections of prostigmin or edrophonium (Fig. 28.25) intravenously. The latter is a rapidly acting and quickly hydrolysed anticholinesterase. Thus, acetylcholine briefly accumulates in greater than normal amounts in the ganglia, post-ganglionic sympathetic nerve endings and in neuromuscular junctions in all types of muscle. The resultant increase in acetylcholine available at the receptor sites leads to an improvement in the muscular function, confirming the diagnosis.



Fig. 28.25 Myasthenia gravis, before and after edrophonium. (By courtesy of Cogan)

Aponeurotic ptosis is involutional, and is due to a weakness or disinsertion of the levator palpebrae superioris aponeurosis from the anterior surface of the tarsus. The diagnostic feature of this form of ptosis is the presence of a high lid fold with good levator action. Sometimes the fold may be absent. The lid is thinned. Surgery consists of re-insertion of the levator aponeurosis to the anterior surface of the tarsus and appropriate resection of the levator.

Mechanical ptosis occurs when tumours or inflammations weigh down the lid and cause it to droop. Treatment is that of the cause.

TUMOURS OF THE LIDS AND ALLIED CONDITIONS

Benign growths

These include xanthelasma, molluscum, warts, naevus, angioma and other tumours *common* to the skin and cutaneous glands.

Small clear *cysts* frequently *occur* among the lashes in old people, due to the retention of secretion of Moll glands. They disappear if the anterior wall is snipped off.

Xanthelasma or *xanthoma* are slightly raised yellow plaques, most commonly found in the upper and lower lids near the inner canthus, and often symmetrical in the two lids and on both sides. They are often seen in elderly women, and are sometimes associated with diabetes and hypercholesterolaemia. They grow slowly, and require treatment only on account of the disfigurement. They may be excised.

Naevus or *mole:* Usually pigmented, this may occur on the lids, generally affects the *margin* and involves both the skin and conjunctiva. Two may be symmetrically situated on the lids of the same eye, indicating their origin at a time when the lids were still united. The microscopic appearance is characteristic, consisting of naevus cells, often arranged in an alveolar manner. They may grow at puberty but very rarely take on malignant proliferation. They may be removed by complete and extensive excision.

Haemangioma: This occurs in two forms—capillary haemangioma or telangiectases and *cavernous* haemangiomata (Fig. 28.26). The former are bright red or port-wine coloured spots composed of dilated capillaries. The latter consist of dilated and anastomosing vascular spaces lying in the subcutaneous tissue having all the characteristics of erectile tissue, and are not infrequently strictly localized as if partially encapsulated. They appear bluish when seen through the skin and form swellings, which become bigger and increase in size on venous congestion as on crying or lowering the head. Cavernous haemangiomata are rarely seen in adults, partly owing to the fact that they are generally treated in early life, but possibly due to spontaneous atrophy of the growth and thickening of the skin.



Fig. 28.26 Cavernous haemangioma of the lid and eyebrow. (By courtesy of JF Talbot)



Fig. 28.27 Sturge–Weber syndrome.

Haemangioma often follows the distribution of the first and second divisions of the trigeminal nerve. In the *Sturge-Weber syndrome* capillary haemangioma of the face (Fig. 28.27) is associated with haemangioma of the choroid and glaucoma, and also with haemangioma of the leptomeninges, causing homonymous hemianopia or epilepsy. The intracranial lesion may be diagnosed radiographically since there are often calcareous deposits underlying the cerebral cortex.

Telangiectases and small haemangiomata usually disappear by the age of 5-6 years, and may well be left alone. If they increase in size, cause amblyopia or strabismus, treatment is indicated. If the mass does not interfere with vision, cosmetic surgery can be undertaken after the child is 3-5 years of age. A local injection of 40 mg triamcinolone and 6 mg betamethasone sodium phosphate into the tumour may lead to involution in some cases. Large diffuse tumours may be treated with alternate-day administration of large doses of systemic steroids for several months under the direction of a paediatrician. Superficial radiotherapy (80-120kV) may be given in doses of 100-200 rad monthly for 6 months, with a total dose not exceeding 500-600 rad. Injection of sclerosing solutions is discouraged because of residual scarring.

Neurofibromatosis

Neurofibromatosis is also known as elephantiasis neuromatodes, plexiform neuroma and von Recklinghausen disease. The lids and orbit may be affected. In typical cases the temporal region is also affected (Fig. 28.28). The swollen lid and temporal region form a characteristic picture in plexiform neurofibromatosis. The hypertrophied nerves can be felt through the skin as hard cords or knobs. The nerve fibres are little changed, the hyperplasia affecting the endo- and perineurium. In several cases the ciliary nerves have been found to be affected; both in the orbit, associated with a true glioma

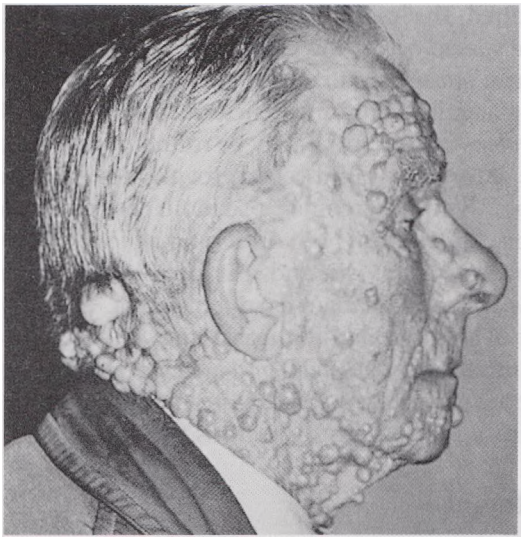


Fig. 28.28 Neurofibromatosis. Multiple facial neurofibromas.



Fig. 28.29 Basal cell carcinoma. (By courtesy of Sanjiv Gupta)

of the optic nerve, and inside the globe, which in many cases is buphthalmic. Operative measures are seldom satisfactory. The choroid and ciliary body may be greatly thickened by layers of dense fibrous-like tissue probably derived from the cells of the sheaths of Schwann.

Malignant tumours

These include carcinomata, sarcomata and malignant melanomata, the first being much the more common (Table 28.2). Any of the glands of the lid may in rare instances undergo carcinomatous proliferation.

The commonest malignant epithelial growth in Caucasians is *basal cell carcinoma* (rodent ulcer), which shows a predilection for the inner canthus (Fig. 28.29). It commences as a small pimple which ulcerates and if the scab is removed it is found that the edges are raised and indurated. The ulcer spreads very slowly, the epithelial growth extending under the skin in all directions and penetrating deeply. The surrounding structures are gradually destroyed, and the lids, orbit and bones are invaded. The growth is only locally malignant and probably originates in the accessory epithelial structures of the skin—hair follicles and glands—but the lymphatic nodes are not affected. Rodent ulcers rarely occur before 40 years of age, and the rate of growth is usually measured in years.

Squamous cell carcinomata shows a preference for sites where the character of the epithelium changes; they therefore commence generally at the edges of the lids (Fig. 28.30). The patients are elderly, the pre-auricular lymph nodes may be enlarged or, if the growth is near the inner canthus, the submaxillary nodes.

Table 28.2 Common malignant tumours of the eyelid

Type	Common location	Clinical features	Spread	Therapy
Basal cell carcinoma	Medial canthus/ lower lid	Nodule, central ulceration with pearly surface, telangiectasia	Local	Resection, radiation
Squamous cell carcinoma	Lower lid, from previous actinic keratosis	–Ulcer with thickened margins, keratosis –Papillomatous	Local, lymph nodes	Resection, radiation, cryotherapy
Sebaceous cell carcinoma	Upper lid	Nodule resembling chalazion, multifocal, females >males, recurrences common	Local, intraepithelial, lymph nodes	Resection, cryotherapy, exenteration
Malignant melanoma	Previous nevi	>6 mm size pigmented lesion, vascularization, inflammation	Local, vascular, lymph nodes	Resection, exenteration



Fig, 28.30 Squamous cell carcinoma.





Fig. 28.31 (A) Early sebaceous cell carcinoma with loss of lashes (By courtesy of Sanjiv Gupta); (B) large sebaceous cell carcinoma.

Sebaceous cell carcinomata commonly affects the upper lid and often present as a hard nodule or recurrent chalazia (Fig. 28.31). Females are more often affected than males. It is more common in Asians. A high index of suspicion in unilateral blepharitis and recurrent chalazia in the elderly is required. The lesion is locally invasive initially, but once orbital spread occurs the prognosis is poor.

Kaposi sarcoma occurs frequently in the lids of patients having acquired immune deficiency syndrome (AIDS).

Sarcoma is rare, and it may be round or spindle-celled *Reticular tumours,* round-celled growths described as lymphoma, lymphosarcoma, pseudoleukaemic tumours, etc. sometimes affect both orbits and all four lids causing symmetrical proptosis, and may occasionally be associated with blood changes as in leukaemia. The growth is slow but continuous and the eyes may be endangered by lagophthalmos. *Malignant melanomata* are rare, as also is a more generalized pigmentation developing in adult life which may become cancerous (*melanosis*).

Treatment

A rodent ulcer is sensitive to radiation, but is best excised, if small, with 3-5 mm of surrounding normal tissue. Involvement of the fornix, extraocular muscles or sclera warrants exenteration. If so large as not to be amenable to operative treatment without sacrificing a good eye or if recurrent, it may be satisfactorily treated with radiotherapy, provided there is no involvement of the bones. Occasionally, however, the results of radiational treatment may be misleading, for the skin surface may show a firm scar while the growth continues to spread beneath the surface, hence, in every case, a careful watch must be kept for any recurrence. Most reticular tumours are radiosensitive just as melanosis is in its precancerous but not always in its cancerous phase.

INJURIES OF THE LIDS

Injuries of the lids—contusions, wounds, burns, etc.—are very common. They must be treated according to general principles but special attention must be directed to associated injuries of the bones of the orbit and the eyeball.

Contusions

These are often more alarming in appearance than in actual morbidity (the 'black eye'). There is great swelling and ecchymosis both in the lids and conjunctiva. In all cases a guarded prognosis should be given, for it may be impossible to determine the full extent of the injury to the orbit or eye.

Wounds

Wounds in the direction of the fibres of the orbicularis gape little and heal without conspicuous scarring, hence surgical wounds should be made in this direction as far as possible. Vertical wounds gape, causing disfiguring

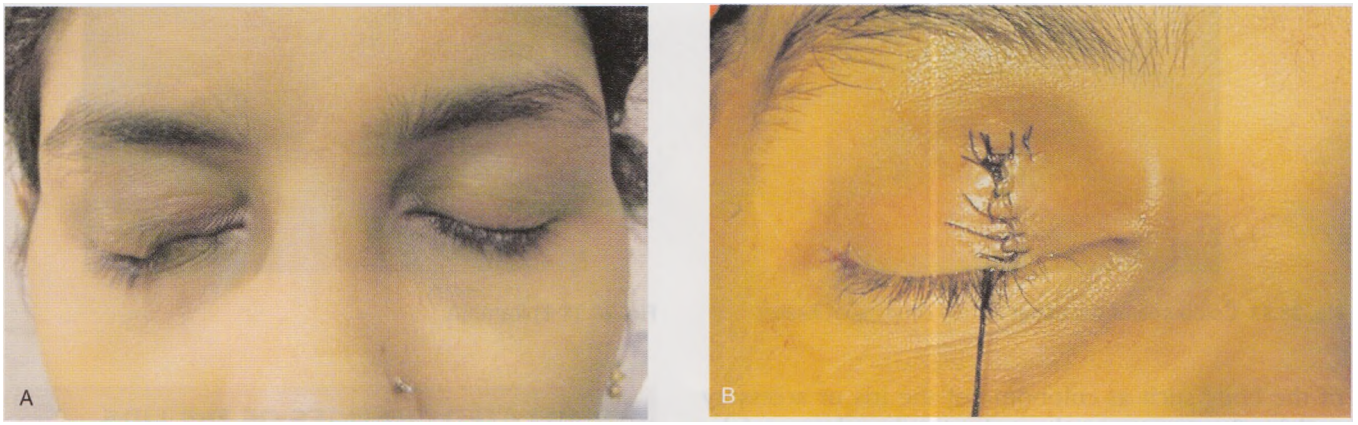


Fig. 28.32 Coloboma repaired by direct closure. (A) Lid coloboma; (B) repair by direct closure.

cicatrices and often lead to ectropion or other distortion, especially if there is adhesion to the subjacent bone. The worst wounds are those which sever the lid vertically in its whole thickness. If they do not unite by first intention, a notch (traumatic coloboma) is left in the lid margin, and disfigurement, lagophthalmos and epiphora result.

Treatment: Simple contusions with ecchymosis require only conservative treatment with cold compresses. Wounds must be thoroughly cleansed and brought together by sutures. On account of the rich blood supply it is not necessary to make a wide excision of the edges, and only obviously contused and devitalized tissue should be excised. Administration of an intramuscular injection of tetanus toxoid may be necessary. Dog bites in children often affect the region of the eyelids and antirabies prophylaxis includes local infiltration and intramuscular injection of antirabies serum in addition to a complete course of antirabies vaccination. Lacerated wounds must be treated by plastic operation as they are likely to leave ugly scars and deformities. If suppuration occurs the abscess must be opened and treated on general surgical principles. Vertical wounds severing the canaliculus require special care to resuture the canaliculus over a silicone tube.

If a wound of the eyelid involving the lid margins is not repaired properly in time it will lead to a lid coloboma which can then be repaired by direct closure if the defect is not too wide, i.e. less than one-third of the lid length (Fig. 28.32).

Burns

It is important to diagnose the degree of a burn. First-degree burns require cleansing and the application of sterile saline and penicillin packs every 3 hours during the day. Second-degree burns should be cleansed, any vesicles opened and dead epithelium removed; subsequent treatment is similar. Third-degree burns should be cleaned and immediately covered by whole or split-skin grafts, a temporary tarsorrhaphy being performed and allowed to remain until the risk of cicatricial ectropion has passed. The great danger from burns of the lids is that they easily lead to a severe exposure keratitis with permanent impairment or even loss of vision, therefore coagulants (tannic acid, etc.) should never be applied. The best prophylactic is grafting before scar tissue has formed; if the initial graft does not take well it can be repeated at leisure. If scarring has developed cicatricial deformities resulting from burns are corrected by plastic operation.

CONGENITAL ABNORMALITIES OF THE LIDS

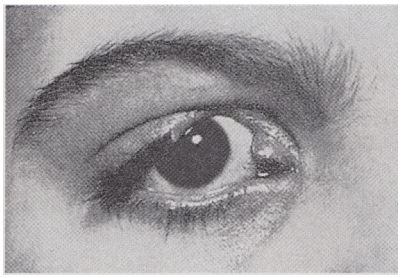
Symblepharon, ankyloblepharon, ectropion, entropion and trichiasis occur occasionally as congenital malformations. Ptosis is a fairly common congenital defect.

Distichiasis

This is a rare condition in which there is an extra posterior row of cilia, occasionally in all four lids. The posterior row occupies the position of the meibomian glands which are reduced to ordinary sebaceous glands performing the normal function of lubricating the hair; these lashes may irritate the cornea. Management is by lid splitting with cryotherapy to the base of the hair follicles.

Coloboma of the lid

This is a notch in the edge of the lid (Fig. 28.33). The gap is usually situated to the inner side of the midline, generally affecting the upper lid, but two or more defects may occur in the same lid. Sometimes a bridge of skin links the coloboma to the globe, or there is a dermoid astride the limbus at the site of the coloboma. There are often other congenital defects of the eye or other parts



Fig, 28.33 Coloboma of the upper lid. (By courtesy of Reese)

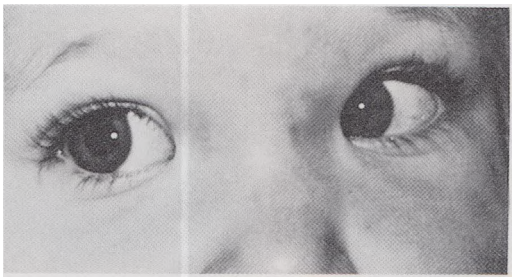


Fig. 28.34 Epicanthus.

of the body such as coloboma of the iris or accessory auricles. Some cases are due to incomplete closure of the embryonic facial cleft, others probably to the pressure of amniotic bands. Occasionally there is a notch at the outer part of the lower lid, associated with maldevelopment of the first visceral arch *(mandibulofacial dysostosis, Goldenhar syndrome).*

Cryptophthalmos

This is a very rare condition in which the skin passes continuously from the brow over the eye to the cheek. It is associated with abnormalities of the eye and often of the orbit.

Microblepharon

This is the condition in which the lids are abnormally small; they may be absent or virtually so—*ablepharon.* These conditions usually occur only in cases of microphthalmos or congenitally small eyes. Microphthalmos may be associated with a congenital *orbitopalpebral cyst,* causing a swelling of the lower lid. The cyst is connected with the eyeball, contains retinal tissue in its lining, and is due to defective closure of the embryonic fissure—an extreme case of ectatic coloboma of the choroid. The eyeball may be apparently absent (*congenital anophthalmos),* but there are always microscopic vestiges of ocular tissues.

Epicanthus

This is a semilunar fold of skin, situated above and sometimes covering the inner canthus (Fig. 28.34). It is usually bilateral and gives the appearance that the eyes are far apart and have a convergent squint and the bridge of the nose is flat. It may disappear as the nose develops. It is normal in Mongolian races, and deformity can be remedied by plastic surgery.

AGE-RELATED CHANGES OF THE LIDS

With advancing age, the eyelids often show early signs of the ageing process. The eyelids may show a number of changes such as wrinkles, large skin folds and a visible fullness or 'bags' of both upper and lower lids. Symmetrical soft swellings above the inner canthus are sometimes seen in elderly people. They are due to *prolapse of the orbital* fat through an aperture in the orbital septum. *Dermatochalasis* is the presence of loose folds of skin and muscle due to weakening of connective and elastic tissue with age.

Blepharoplasty removes excess skin and fat in the eyelids. A fine incision is made in the crease of the upper lid, and beneath the eyelashes in the lower lid. Through these incisions, excess skin and fat is then removed and the incisions are closed with fine sutures. The droopy eyelid is corrected, the pouches and bags removed and the excess skin smoothed and tightened. Because the incisions are made in the eyes' natural contours, they are barely visible and fade over time.

A laser blepharoplasty entails the use of the carbon dioxide laser to make a nearly bloodless incision allowing the fat pads under the eyes to be removed by laser dissection. Next, the erbium: YAG laser can be used to resurface the lower lid skin. Erbium laser treatment also stimulates the production of collagen, creating a tightening and smoothening of the skin.

SUMMARY

The eyelids serve to protect the eye, reconstitute the tear film and cover the eye during sleep. For normal lid function healthy lids with normal height and contour, with apposed margins, normal muscle tone and lid movement are important.

Blepharitis, chalazion, stye, entropion, ectropion, ptosis and lid tumours are common conditions that can affect the eyelids.

29

Diseases of the Lacrimal Apparatus

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ANATOMY AND PHYSIOLOGY

The lacrimal apparatus consists of the lacrimal glands and the lacrimal passages (Fig. 29.1).

The *lacrimal glands* of each eye have a superior or orbital gland, the inferior or palpebral gland, and the accessory lacrimal or Krause glands. All these are serous acinous glands, scarcely distinguishable microscopically from serous salivary glands with which they are morphologically identical. The orbital gland, about the size of a small almond, is situated in the lacrimal fossa at the outer part of the orbital plate of the frontal bone; 10 or 12 lacrimal ducts pass from it to open upon the surface of the conjunctiva at the outer edge of the upper fornix. The palpebral gland consists of only one or two lobules situated on the course of the ducts of the superior portion. It can be seen when the upper lid has been everted and the eye looks downwards and inwards. The accessory or Krause glands are microscopic groups of acini, lying below the surface of the conjunctiva between the fornix and the edge of the tarsus *(see* Fig. 28.1). There are about 42 in the upper fornix and 6-8 in the lower fornix. The ducts of numerous acini unite to form a larger duct, which opens into the fornix.

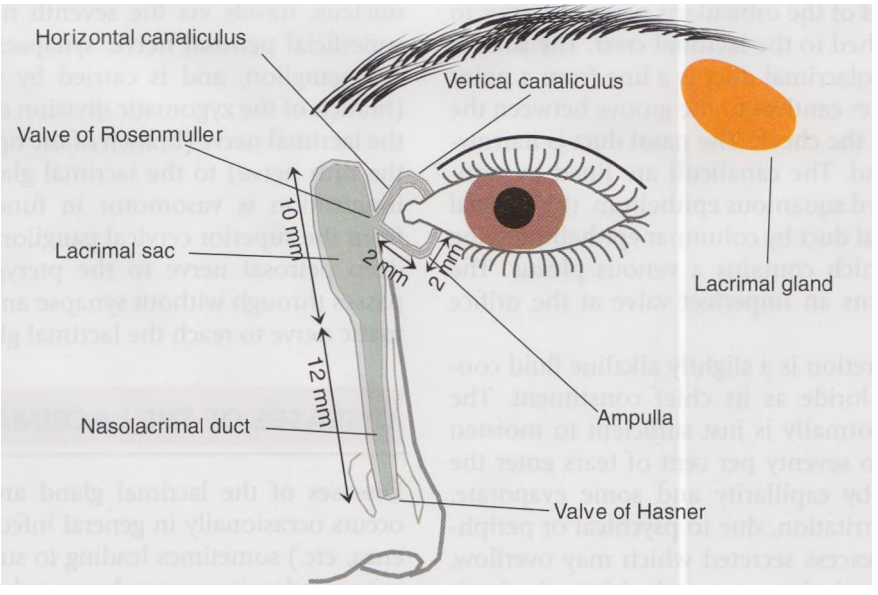


Fig. 29.1 Lacrimal apparatus.

The *lacrimal passages* consist of the lacrimal puncta, the canaliculi, the lacrimal sac and the nasolacrimal duct. The lacrimal *puncta* lie near the posterior border of the free margin of the lid about 6 mm from the inner canthus, where the lashes end. The punctum is relatively avascular and is situated upon a slight elevation, larger in elderly people, the lacrimal papilla. As already mentioned, this is visible in normal circumstances only when the lid is slightly everted. The canaliculus passes from the punctum to the lacrimal sac; it is first directed vertically for about 1-2 mm, then turns at right angles at the ampulla and runs horizontally for 6-7 mm. The upper and lower *canaliculi* usually join together to form a common canaliculus which opens immediately into the outer wall of the lacrimal sac. A fold of mucosa at this point forms the *valve of Rosenmuller,* preventing reflux of tears. The lacrimal sac lies in the lacrimal fossa formed by the lacrimal bone; when distended it is about 15 mm long vertically and 5-6 mm wide. The upper portion or fundus extends slightly above the level of the medial palpebral ligament and the sac itself is surrounded by fibres of the orbicularis muscle. The lower end narrows as it opens into the *nasolacrimal duct* (a tube which is 12-24 mm long, 3 mm in diameter), which is bounded by the superior maxilla and inferior turbinate, and passes downwards and slightly outwards and backwards, to open at the anterior part of the outer wall of the inferior meatus of the nose. Another flap of mucosa forms the *valve of Hasner,* closing this opening when necessary (Fig. 29.1). The lacrimal sac is lined by pseudostratified columnar epithelium and the walls contain elastic and lymphoid tissues. The periorbita splits to form the lacrimal fascia that covers the anterior and posterior surfaces of the sac. The deep heads of the orbicularis are attached posterior to the sac, with some fibres being attached to it. The superficial head of the orbicularis passes anterior to the sac and is attached to the lacrimal crest. The surface marking of the nasolacrimal duct is a line from a point just outside the inner canthus to the groove between the ala of the nose and the cheek. The nasal duct is narrowest at the upper end. The canaliculi are lined by non-keratinized, stratified squamous epithelium, the *lacrimal sac* and nasolacrimal duct by columnar epithelium lying upon a corium which contains a venous plexus. The mucous lining forms an imperfect valve at the orifice into the nose.

The lacrimal secretion is a slightly alkaline fluid containing sodium chloride as its chief constituent. The amount secreted normally is just sufficient to moisten the eyeball. Sixty to seventy per cent of tears enter the lower canaliculus by capillarity and some evaporate. Only under reflex irritation, due to psychical or peripheral stimuli, is an excess secreted which may overflow. Tears in the conjunctival sac are sucked into the lacrimal sac and forced through the nasal duct into the nose during the act of blinking, when the fibres of the orbicularis contract around the sac (*the lacrimal pump).* Closure of the eyelids occurs from lateral to medial, bringing fluid in the conjunctival sac medially. Blinking causes the attachment of the preseptal orbicularis muscle to the lacrimal sac to contract, widening the sac and producing a negative pressure which sucks the tears into the sac. On opening the eye this pressure is relieved and the tears are then emptied into the nose by gravity and contraction of the orbicularis.

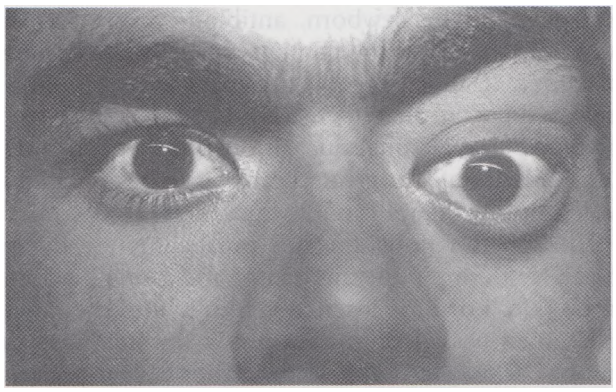
Tears are formed by secretory glands around the eye. The tear film lubricates the ocular surface; it facilitates lid movements and creates a smooth surface for the passage of light. It provides nutrition to the cornea, and also protects the ocular surfaces from injury and infection. The tear film has three layers—oil, water and mucus. The posterior mucus layer is formed by the conjunctival glands, is closely attached to the corneal epithelium and helps the tear film to spread evenly and adhere to the eye. The largest, serous, middle layer is secreted by the lacrimal gland. This washes away any particles or irritants in the palpebral sac. The superficial oily layer is secreted by the meibomian glands. It smoothens the tear surface and prevents evaporation. The tears have some bacteriostatic properties owing to the presence of an enzyme, lysozyme.

Xerosis or dryness of the conjunctiva does not result from extirpation of the superior and inferior lacrimal glands, as the moistening of the conjunctiva by Krause glands and its own mucous cells are sufficient to prevent it.

The nerve supply to the lacrimal gland is from the autonomous nervous system by parasympathetic and sympathetic fibres which travel along the cranial nerves to reach the gland. The parasympathetic innervation is secretomotor and originates from the superior salivatory nucleus, travels via the seventh nerve and the greater superficial petrosal nerve, synapses in the pterygopalatine ganglion, and is carried by the zygomatic nerve (branch of the zygomatic division of the fifth nerve) and the lacrimal nerve (branch of the ophthalmic division of the fifth nerve) to the lacrimal gland. The sympathetic innervation is vasomotor in function and originates from the superior cervical ganglion, then travels via the deep petrosal nerve to the pterygopalatine ganglion, passes through without synapse and travels in the zygomatic nerve to reach the lacrimal gland.

DISEASES OF THE LACRIMAL GLAND

Diseases of the lacrimal gland are rare. *Dacryoadenitis* occurs occasionally in general infections (mumps, influenza, etc.) sometimes leading to suppuration. Infectious mononucleosis may produce a red, painful swelling with redness of the outer third of the upper eyelid. This may



Fig, 29,2 Pleomorphic adenoma of the lacrimal gland.

be associated with a follicular conjunctivitis, periorbital oedema, uveitis and sometimes optic neuritis. Occasionally, the central nervous system is involved, but fortunately the disease is usually self-limiting. A permanent fistula may result from the bursting of an abscess in the gland.

Dacryops is a cystic swelling in the upper fornix due to retention of secretion following blockage of one of the lacrimal ducts. It can only be distinguished from retention cysts of Krause glands by its position.

Mikulicz syndrome is characterized by symmetrical enlargement of the lacrimal and salivary glands. The aetiology varies but the swelling is usually of a lymphomatous nature. Both parotid and lacrimal glands are enlarged in a uveoparotid inflammation.

Tumours of the lacrimal gland show a very marked resemblance to those of the parotid. Much the commonest is a pleomorphic adenocarcinoma, frequently characterized histologically by myxomatous material (the so-called 'mixed tumour'). Benign mixed lacrimal gland tumours present in middle life as slowly progressive painless swellings in the upper lid and later proptosis. The bone is not usually invaded. Benign tumours should be removed in their pseudocapsule. Malignant tumours present in the elderly with a short history and pain. A painful tumour or one with bone invasion or calcification should be a biopsied through a trans-septal incision. If malignant, radical surgical removal is necessary.

All conditions which cause swelling of the gland may lead to impairment of eye movements. The globe is pushed downwards and inwards (Fig. 29.2). Ocular movement outwards, and especially outwards and upwards, is limited. There may be some proptosis.

DRY EYE

A dry eye is a disease of the ocular surface (*see* p. 184) caused by disturbances of the natural function and protection of the external eye leading to an unstable tear film when the eye is open. This is among the commonest ocular disorders, especially among the elderly.

A dry eye produces discomfort and reduces vision when the tear film becomes chronically unstable and repeatedly breaks up into dry spots between blinks, exposing the corneal and conjunctival epithelium to evaporation. Tear film instability may be the result of several diseases.

Tests for dry eye

Features which help in the diagnosis of a moderately dry eye are the presence of particulate matter in the tear film generally due to mucus, which is stainable with Alcian blue. The tear film stained with sodium fluorescein 1% is observed with a slit-lamp and the time noted after instructing the patient to blink. The time taken for the first appearance of a 'dark' dry spot is recorded as the 'tear-film break-up time' or TBUT. A tear film break-up time of less than 10 seconds is suggestive of a dry eye with deficiency of mucin. Other vital dye staining tests for dry eye include staining the ocular surface with rose Bengal 1% or lissamine green which stains devitalized, desiccated corneal and conjunctival epithelium red or green. A teardysozyme ratio between 0.9 and 0.6 or a Schirmer test producing wetting of less than 6 mm support the diagnosis.

The Schirmer test is performed by folding 5 mm at the top end of a special Schirmer test filter paper strip and placing it in the lower conjunctival sac of the open eye. It is placed at the junction of the outer one-third and medial two-thirds of the lower lid, left in place for 5 minutes or until 30 mm of the strip becomes wet. If tear fluid fails to diffuse over the lid margin along the strip within 2 minutes, it is removed to another site within the sac for another 5 minutes. Such a method obviates false-positive results. The strip is removed from the eye after 5 minutes and the wet portion measured. Wetting of less than 10 mm is indicative of an aqueous tear deficiency.

Symptoms arising from a dry eye may be mimicked by chronic blepharoconjunctivitis due to the staphylococcus, rosacea keratoconjunctivitis or allergic conjunctivitis. These diagnoses should first be eliminated.

The concentration of tear lysozyme is measured in units per microlitre. The result is divided by the value of the critical lower limit to express the concentration as the tear lysozyme ratio.

Treatment

Frequent application of tear substitutes is effective. The most suitable preparations for a dry eye are preservative-free. If this does not suffice, a slow-release artificial tear supplement, a pellet of a cellulose compound, without preservatives, can be inserted below the tarsus of the lower lid where it dissolves slowly providing a continuous source of tears. If obstruction of the canaliculi with gelatin plugs gives relief it is worth considering permanent obstruction of the lower puncta. Excess mucus may

be treated by 5% acetyl cysteine drops buffered to a pH of 8.4 with sodium bicarbonate.

DISEASES OF THE LACRIMAL PASSAGES

Dacryocystitis

Inflammation of the lacrimal sac is known as dacryocystitis. It generally affects two age groups, infants and adult females over 40 years of age. Congenital dacryocystitis is almost always chronic, while acquired dacryocystitis may be acute or chronic.

Chronic dacryocystitis

It is more common. The essential symptom is epiphora, aggravated by such conditions as exposure to wind. There may be a swelling at the site of the sac (a mucocele) and the caruncle and neighbouring parts of the conjunctiva are frequently inflamed. On pressure over the sac, mucopus or pus regurgitates through the puncta, or more rarely passes down into the nose. Chronic dacryocystitis is commonly attributed to the effects of stricture of the nasal duct arising from chronic inflammation, usually of nasal origin. Obstruction to the lower end of the nasal duct may also be caused by the pressure of nasal polypi, a hypertrophied inferior turbinate bone or extreme deviation of the septum. This accumulation of secretions and tears within the lacrimal sac is easily infected. Ethmoidal infections are frequently associated with dacryocystitis.

Bacteriological examination of the fluid demonstrates the presence of an extraordinary number of bacteria—staphylococci, pneumococci, streptococci—reflecting the conjunctival flora. This fact is of considerable importance since it explains the frequency with which a hypopyon ulcer arises in these cases and the danger of panophthalmitis if any intraocular operation is undertaken. Dacryocystitis is a constant menace to the eye since minute abrasions of the cornea are of almost daily occurrence and such an abrasion is liable to become infected and give rise to an ulcer.

Untreated chronic dacryocystitis never undergoes spontaneous resolution. The condition tends to progress and the walls of the sac ultimately become atonic, the contents never being evacuated except by external pressure. An acute inflammation may arise at any time leading to the formation of a lacrimal abscess.

Congenital dacryocystitis is due to incomplete canalization of the lacrimal system, most often the valve of Hasner. Hydrostatic pressure is applied by massaging downwards and medially with a clean thumb behind the lacrimal crest. Congenital dacryocystitis needs aggressive therapy as the infection can spread to become an orbital cellulitis, leading further to even meningitis. Common organisms cultured in children are *Staphylococcus aureus, Haemophilus influenzae,* beta-haemolytic streptococci and pneumococci.

Treatment: In the newborn, antibiotic drops and frequent expression of the contents of the sac cure most infections. If, however, 1 year elapses without marked improvement, an anaesthetic should be given and probing of the nasolacrimal duct through the upper canaliculus carried out. The greatest care has to be exercised to avoid injuring the walls of the duct.

The superior punctum and canaliculus are dilated with a Nettleship punctum dilator and a small lacrimal probe (No. 1 or 2) is inserted vertically into the canaliculus, then passed gently but firmly inwards until the point is felt against the lacrimal bone. The probe is then rotated downwards and towards the midline, and pushed down the nasal duct until it touches the floor of the nose; it should be remembered that the duct is short in the newborn. Little force is required if applied correctly in the line of the duct. The passage of a probe once will cure most congenital cases. A balloon dilatation of the duct or placement of a silicone tube may be used as a secondary procedure.

In adults, antibiotic drops and repeated syringing of the nasolacrimal duct may first be attempted, particularly in recent cases with a view to reducing the swelling of the inflamed mucosa and restoring patency. The conjunctival sac is anaesthetized, the punctum dilated and the sac syringed out with a lacrimal syringe. The point of the cannula is inserted into the canaliculus, and two or three syringefuls of an antibiotic solution are passed; probably all the fluid will regurgitate through the upper canaliculus. The operation should be repeated daily and in many cases the fluid will pass freely down into the nose in a few days. When this occurs syringing should be repeated at increasing intervals. A number of cases can be cured in this manner, particularly if the patient is told to squeeze out the contents of the sac frequently in the intervals between syringing.

If the case is still recalcitrant, the condition of the lacrimal passages is assessed by syringing or Jones test, and may also be visualized radiologically after injecting lipiodol with a lacrimal syringe into the puncta and the upper part of the sac, and the site of an obstruction thus located. Anatomical assessment of the lacrimal drainage apparatus is more precise using digital subtraction macrodacryocystography with canalicular catheterization (Fig. 29.3). The functional efficiency of lacrimal drainage may be assessed by a technique using a radioactive tracer instilled into the conjunctival sac and visualized with an Anger gamma camera. The tracer employed is usually a sulphur colloid, or technetium (Fig. 29.4A and B).

Obstruction at the junction of the nasolacrimal duct and sac is commonly found, for which permanent drainage into the nose by dacryocystorhinostomy must be performed. In this operation an opening is made in the nasal bone connecting the lacrimal sac to the middle



Fig. 29.3 Bilateral subtraction macrodacryocystography. Normal right lacrimal duct system. On the left side there is a block at the proximal end of the common canaliculus. (By courtesy of Glyn Lloyd)

meatus and if properly performed, removes the obstruction and retains the function of drainage.

Acute dacryocystitis

A lacrimal abscess may be due to acute inflammation of the sac or to suppuration starting in the pericystic tissues (Fig. 29.5). The skin over the sac becomes red and swollen. The redness and swelling rapidly extend to the lower lid and upper part of the cheek, so that the condition may be easily mistaken for erysipelas. There is severe pain, and often slight fever. The abscess usually points below and to the outer side of the sac owing to gravitation of the pus to the margin of the orbit. If it bursts spontaneously, pus continues to be discharged for some time, and a permanent fistula is likely to result.

General treatment by oral and topical antibiotic drugs should be instituted at once. If seen at the beginning of the process, an attempt may be made to draw the contents of the sac into the nose by inserting a tampon soaked in adrenaline (1 in 100 000) and procaine over the opening of the nasolacrimal duct. In some early cases the mucopus can then be coaxed down the nasal duct.



Fig. 29.5 Bilateral chronic dacryocystitis. Right: operated dacryocystectomy; left: acute exacerbation of the infection. (By courtesy of MS Bajaj)

Hot fomentation should be carried out and the abscess should not be opened unless it is pointing under the skin, in which case a small incision should be given, the pus gently squeezed out, a piece of rubber glove drain inserted and an antibiotic dressing applied.

If a chronic discharge continues and nasolacrimal obstruction is present, a dacryocystorhinostomy is indicated.

Epiphora

The commonest symptom of lacrimal disorders is *epiphora.* Tearing from the eye can be due to either an increased production or a decreased outflow of tears. Increased production is seen in conjunctival irritation or psychogenic stimuli such as a tragedy. Epiphora is the term reserved for an overflow of tears from the eye because of an obstruction, stenosis, punctal malposition or functional disorder of the lacrimal passages. The patient complains of a constant flow of tears, exacerbated by exposure to wind and prolonged near work. Constant wetting of the lid may lead to excoriation and wiping of the eyes downwards may exacerbate the degree of ectropion of the lower lid.

Evaluation of a patient complaining of epiphora must be thorough so that the cause can be identified and treated. First, lid-globe apposition should be assessed,

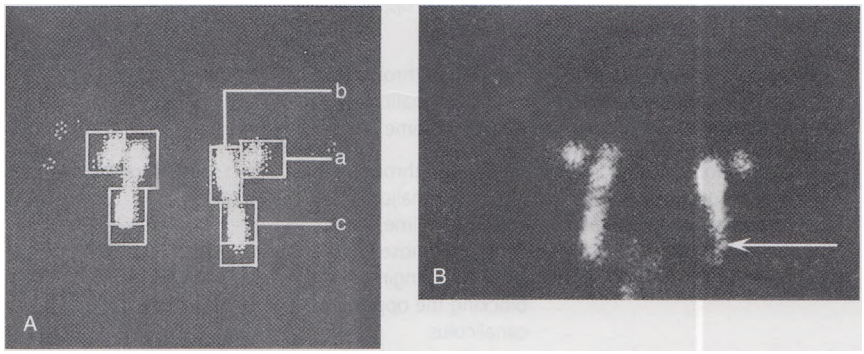


Fig. 29.4 (A) Regions of interest within the lacrimal excretory system: a, inner canthus; b, lacrimal sac; c, lacrimal duct ending in the inferior meatal entrance of the lacrimal duct (By courtesy of Hurtwitz). (B) gamma camera image demonstrates hold-up of tracer in the left lacrimal sac (By courtesy of Hurtwitz).



Fig. 29.6 Eversion of the punctum in a case of senile ectropion.

and asking the patient to look upwards may reveal an everted punctum, unmasking a mild lower lid ectropion (Fig. 29.6). The lacus lacrimalis at the medial canthus appears full and the marginal tear strip high.

Lacrimal syringing is performed after dilatation of the punctum with a punctum dilator. A cannula is then inserted into the punctum and vertical canaliculus. Pulling the lower lid temporally straightens the ampulla allowing entry into the horizontal canaliculus. Sterile saline is injected slowly, looking for regurgitation through the same or opposite punctum and also asking the patient for any flow into the nose. The interpretation of the outcome is detailed in Table 29.1. Passing a blunt-tipped probe medially through the punctum, canaliculus and sac till the probe comes to a stop, enables the observer to feel a 'hard' stop if the lacrimal bone is felt or a 'soft' stop if there is an obstruction which does not allow the probe to pass through into the sac. A soft stop 5-8 mm from the punctum implies a canalicular obstruction. If present more than 8 mm from the punctum, the obstruction is probably at the common canaliculus. As a therapeutic measure, in children over the age of 6 months with a congenital nasolacrimal duct blockage, the probe is rotated to a vertical position after coming to a stop. It should slide down into the lacrimal duct. Any minor obstruction can be broken, but force should not be used at any time in the procedure. Jones dye tests distinguish functional disorders of the lacrimal passages, such as a malfunction of the lacrimal pump, from organic blockage. In Jones test 1, a drop of fluorescein is instilled into the palpebral sac and flow into the nose is detected by positioning an anaesthetic-soaked cotton bud in the inferior meatus. If fluorescein is seen on the bud, the passages are patent, and Jones test 1 is positive. If Jones test 1 is negative but syringing allows detection of fluorescein in the nose, Jones test 2 is considered positive and the epiphora is due to a functional problem, not obstruction. Dacryocystography is performed by injecting radio opaque dyes or radioactive tracers and looking for pooling of the dye in the nose. If there is a block, the dye can be seen to be retained within the lacrimal passages. The commonest location of such a block is the junction between the

Table 29.1 Obstructive lesions of the lacrimal passages

Site of obstruction	Clinical features	Syringing	Jones test	Treatment
Single canaliculus	Pouting or narrowing of punctum, 'soft stop' on probing	Regurgitation through the same canaliculus	Test 1: may be positive if other canaliculus normal	Astringent drops
Both canaliculi	'Soft stop' on probing	Regurgitation through the same canaliculus	Tests 1 and 2: negative	Conjunctivodacryo-cystorhinostomy with Jones tube
Common canaliculus	'Soft stop' on probing	Immediate regurgitation through the opposite canaliculus	Tests 1 and 2: negative	Canaliculodacryocysto-rhinostomy
Complete nasolacrimal duct	Regurgitation on pressure over the lacrimal sac, 'hard stop' on probing	Regurgitation through the opposite canaliculus after some time	Tests 1 and 2: negative	Dacryocystorhinostomy: transcutaneous or endonasal
Partial nasolacrimal duct	Regurgitation on pressure over the lacrimal sac, 'hard stop' on probing	Regurgitation through the opposite canaliculus after some time, some fluid in the nose with pressure syringing after blocking the opposite canaliculus	Test 1: some fluorescein in nose	Pressure syringing with antibiotics
'Functional' nasolacrimal duct or lacrimal pump failure	No regurgitation	Patent	Test 1: negative Test 2: positive	Astringent drops

sac and nasolacrimal duct, which is at the level of the inferior orbital rim on an X-ray.

Some common causes of epiphora are discussed below.

Eversion of the lower punctum

This occurs from laxity of the lids in old age, from chronic conjunctivitis or blepharitis, or any cause leading to ectropion. If on clinical examination the punctum is visible when the lower lid apposes the globe it may be considered to be everted. This causes epiphora which, in turn, aggravates the condition.

Treatment: The simplest method of treating a punctual phimosis or mild malposition of the punctum is the so-called three-snip operation. The conjunctival sac is anaesthetized and local anaesthetic injected into the tissues around the canaliculus. The punctum is dilated with a Nettleship dilator, which is introduced vertically and then pushed inwards along the canaliculus. A canaliculus knife is then taken and the probe-point is passed into the punctum in the same manner, downwards and then inwards, the back of the knife being directed forwards and slightly downwards. As the knife is pushed inwards, the posterior wall of the canaliculus is incised. While this manoeuvre is being performed the lid is kept stretched outwards, so that the wall of the duct is taut against the edge of the knife. The triangular flap of the posterior wall formed between the vertical and horizontal parts of the canaliculus is then snipped off with scissors. A probe should be passed on the day following the operation, and occasionally on the successive days, so as to prevent closure of the incision.

In mild cases, especially in old people, the eversion may be sufficiently counteracted by punctal excision of a tarsoconjunctival segment 2 mm below the punctum. It must be spindle-shaped and 8 mm in length. It is closed with 6-0 catgut/vicryl, burying the knots to avoid abrading the cornea. As the cicatricial tissue contracts the punctum is pulled inwards towards the eye.

In cases of marked eversion of the lower punctum, a more radical operation for ectropion may be necessary *(see* p. 448).

Occlusion of the puncta

This rarely occurs as an isolated disorder, and maybe congenital or cicatricial. The epiphora caused in both cases is very difficult to treat. Before treatment commences, the patency of the lacrimal passages should be ensured by syringing through the other (upper) punctum.

An endeavour should be made to slit the occluded punctum—not the whole canaliculus. On inspection no trace of the punctum may be visible, but on minute examination of the normal site with the slit-lamp, a dimple or avascular point may be identified. The point of the dilator is inserted at this site, and may succeed in opening up the punctum sufficiently to admit the probe-point of the canaliculus knife.

Occlusion of the canaliculus

This may be due to a scar or a foreign body (Table 29.1). It may follow the prolonged use of idoxuridine drops. An eyelash is the commonest obstructive foreign body, a 'concretion' less frequent. An eyelash usually projects somewhat from the punctum and is easily removed with a pair of forceps. Concretions are masses of the mycelium of a fungus, usually *Actinomyces,* and are removed by dilating the canaliculus, slitting it, curetting it and injecting a solution of penicillin.

Congenital anomalies of the puncta and canaliculi

These are occasionally seen. The puncta may be absent or constricted; there may be two puncta in a lid, both generally opening into the same canaliculus. Sometimes a groove is found instead of a canaliculus.

Lacrimal obstruction

Obstructions commonly occur at the junction of the lacrimal sac and nasolacrimal duct (Table 29.1). Chronic inflammation leading to fibrosis and strictures is the commonest reason for the block.

Retention of mucoid secretions and tears within the sac leads to frequent, recurrent inflammation and infections—dacryocystitis. Generally a distention of the sac may occur, known as a *mucocele* (Fig. 29.7) Pressure over the sac leads to regurgitation of mucoid material. On syringing of the lacrimal passages there is a reflux, first of mucoid material and then clear fluid through the opposite punctum. Jones tests will be negative. In some cases a rounded mass may be visible below the medial canthus. This may be a mucocele and behave as already described, with regurgitation of the sac contents on pressure over it or there may be no regurgitation. In the latter case, there is an additional mucosal stenosis in the sac wall or stricture at the common canaliculus, and this is called an *encysted mucocele.* A space-occupying lesion such as a fungal or neoplastic growth must be ruled out; if a mass is palpable dacryocystography should be performed.

Functional blockage of the lacrimal passages is diagnosed when there is epiphora in the absence of an obstruction to the outflow of tears. This could be due to punctal phimosis, stenosis at any point or a failure of the lacrimal pump. Functional blockage is identified by scintigraphy or by a positive Jones test 2 in the presence of a negative Jones test 1.

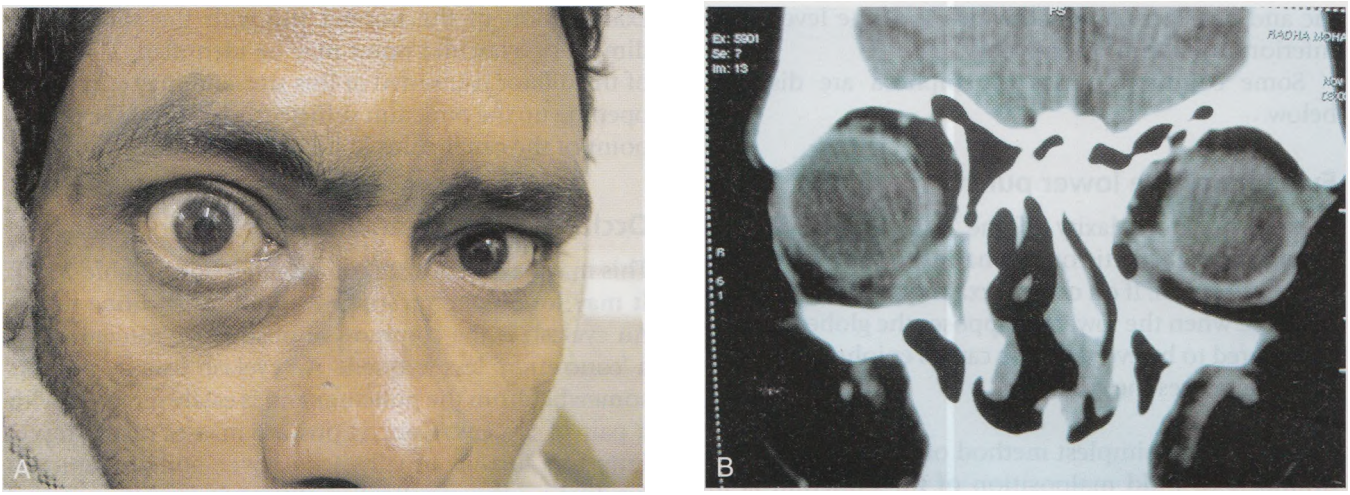


Fig. 29.7 Lacrimal mucocele. (A) shows a cystic swelling visible in the region of the lacrimal sac; (B) shows the appearance on CT scan.

Epiphora with pain and nasal discharge, especially with intermittent nasal bleeding, must always raise the suspicion of a neoplasm of the antrum or ethmoid.

Treatment

In infants with congenital nasolacrimal duct blockage, conservative treatment with antibiotics and massage of the contents of the sac downwards may relieve the block. If the block persists till the age of 6 months, a probing is performed under general anaesthesia and can be repeated a couple of times if required. Chronic epiphora beyond the age of 3 years would necessitate a dacryocystorhinostomy. A dacryocystorhinostomy should not be performed earlier as the bones are not adequately developed till then.

Dacryocystorhinostomy can be undertaken under general or local anaesthesia. The ipsilateral nasal fossa is sprayed with local anaesthetic and adrenaline, and packed with a ribbon gauze soaked in the same drugs. The canaliculi are then dilated, and the lacrimal sac irrigated with warm saline. With the skin stretched by moderate traction at the outer canthus, a curved incision can be made, beginning 2 mm above the medial palpebral ligament and 3 mm to the nasal side of the inner canthus; it is carried vertically downwards for 4 mm, and then outwards along the line of the anterior lacrimal crest to a spot 2 mm below the inferior orbital margin. A straight incision 11 mm medial to the medial canthus can also be used. The skin of the temporal edge of the incision is undermined for 2 or 3 mm, but not that of the nasal edge owing to the risk of wounding the angular vein or its branches. The orbicularis is split in the line of the incision, and a lacrimal retractor inserted so as to retract it with the skin. The periosteum over the lacrimal crest is incised and separated from the lacrimal fossa to expose the lacrimal bone. The bony crest is removed with a gouge and punch and when the nasal mucosa is reached, the gap in the bone is enlarged to make the anastomosis of sac and nasal mucosa possible. The sac is opened through the periosteum and its nasal wall and the entrance of the common canaliculus inspected and tested for patency. Two flaps are dissected in the nasal mucosa that is seen through the bony window and these are sutured to the anterior and posterior walls of the sac. Silicon tubing is passed through both puncta, down the sac to the nose where the ends are attached together. All the anterior structures are replaced and sutured in layers. The tubing is removed after 4-6 months. *Endoscopic transnasal dacryocystorhinostomy* does not cause facial scarring and is indicated if there is an associated nasal disorder.

A *Lester-Jones tube* is placed in the presence of persistent epiphora in a patient with less than 8 mm of the lateral part of the canaliculus remaining. In this procedure, called a *conjunctivodacryocystorhinostomy*, the initial steps are those of a dacryocystorhinostomy. When the posterior mucosal flaps have been sutured, attention is directed to the caruncle which is excised. A needle is then inserted in a slightly downward direction from a point about 2 mm behind the medial commissure to merge just behind the anterior mucosal flap. It should lie anterior to the body of the ethmoid and middle turbinate. This track is then enlarged using a Graefe knife and a polythene tube is inserted. This tube is about 18 mm long and its medial end is trimmed short of the nasal septum and its expanded lateral end sutured at the inner canthus. The dacryocystorhinostomy is then completed and a few days later this tube is replaced by a 2 mm glass capillary tube about 10-16 mm in length (Fig. 29.8). The lateral end of this tube has a cuff 3-4 mm in diameter and its medial end is expanded to 2.5 mm. Six months after the tube is inserted it may become blocked with inspissated mucus and its removal is necessary for adequate cleaning. Replacement of the tube is difficult and



Fig. 29.8 Jones tube in position.

has to be carried out under local anaesthesia. Lester-Jones tubes are not recommended for children.

If there is epiphora with the canaliculus being blocked more than 8 mm medially, a *canaliculodacryocystorhinostomy* is performed. The operation of canaliculodacryocystorhinostomy consists of dissecting out the common canaliculus, and a little of both the upper and lower canaliculi, removing any strangulating fibrosis in the region of the medial palpebral ligament, anastomosing the common canaliculus with the sac and completing the procedure with a dacryocystorhinostomy. Intubation of the canaliculi, using lacrimal stents and silicone tubing through to the nasal cavity is mandatory, and should be maintained for about 6 months.

SUMMARY

The lacrimal system includes the lacrimal gland, accessory lacrimal glands and the lacrimal drainage system. A healthy precorneal tear film is important for clear vision and general health of the ocular surface. Abnormalities of the drainage system can lead to epiphora. A systematic approach in investigating the problem, with judicious use of tests like syringing and use of dyes can help in proper management of such cases.

30

Diseases of the Orbit

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The orbit houses the eyeball and subserves the major functions of protection of the eye and facilitation of the extreme degree of motility possible by the eye.

ANATOMY

It is important to understand the relations of the orbit and its neighbouring structures. These include the nasal cavities and their accessory sinuses, and the communications with the interior of the cranial cavity by way of the optic foramen and sphenoid fissure. The dural sheath of the optic nerve is adherent to the walls of the optic foramen, and the intraorbital and intracranial circulation are inter-connected. The optic foramen allows passage of the optic nerve, ophthalmic artery and its sympathetic plexus (Fig. 30.1A). The superior orbital fissure is bounded by the greater and lesser wings of the sphenoid bone and transmits the superior and inferior divisions of the oculomotor nerve, nasociliary nerve and abducens nerve through the annulus of Zinn, a common tendinous ring from which the recti muscles originate (Fig. 30.1A). The eye is slung in position in the orbit by fascia, one sheet of which, the Tenon capsule, forms a socket in which the globe moves. The extraocular muscles of the eye do not perforate this capsule, but invaginate it, the fascia being reflected from their surfaces.

From the surgical point of view there are thus four spaces which are relatively self-contained, within each of which inflammatory processes are contained for a considerable time, and each of which must, if necessary, be opened separately (Fig. 30.IB): (i) the *subperiosteal space* between the bones of the orbital wall and the periorbita; (ii) the *peripheral orbital space* between the periorbita and the extraocular muscles which are joined by fascial connections making a more or less continuous circular septum; (iii) the *central space*, a cone-shaped area enclosed by the muscles (the 'muscle cone'); and (iv) *Tenon space* around the globe.

COMMON SIGNS AND SYMPTOMS OF ORBITAL DISEASES

The normal position of the eye is such that a straight edge applied vertically to the middle of the upper and lower

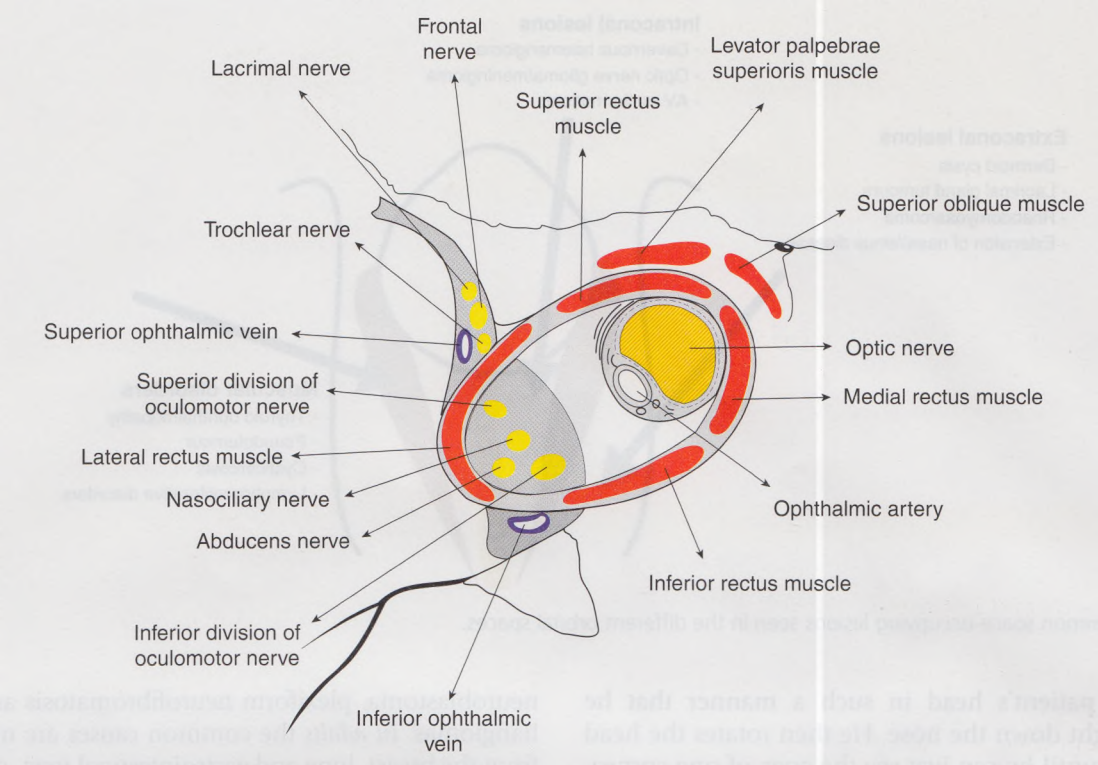


Fig. 30.1 (A) Diagrammatic representation of the orbital apex.

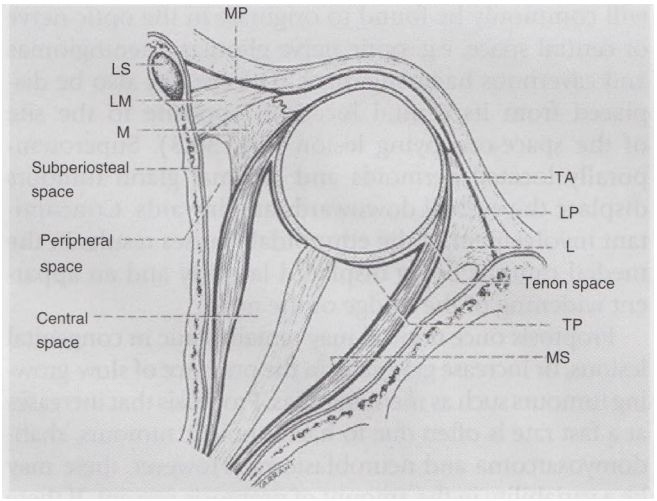


Fig. 30.1 (B) Horizontal section through the orbit. L, lateral check ligament; LM, lacrimal portion of orbicularis muscle; LP, lateral palpebral ligament; LS, lacrimal sac; M, medial check ligament; MP, medial palpebral ligament dividing into a superficial and a deep band; MS, muscle sheaths; TA, anterior part of Tenon capsule; TP, posterior part of Tenon capsule.

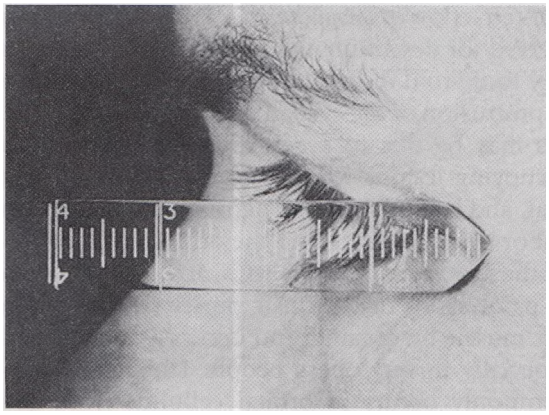


Fig. 30.2 A simple exophthalmometer. The instrument is made of a transparent plastic with a groove which fits into the outer bony margin of the orbit. The scale is engraved on both sides of the solid bar of plastic and the observing eye is aligned to read off the level of the apex of the cornea so that the scales on either side of the bar and the apex of the cornea are in one straight line. In the illustration, the two scales at 3 cm are seen out of alignment, and at 4cm this tendency is increased.

margins of the orbit just touches the closed lids over the apex of the cornea. There are individual variations, which are of no pathological importance when symmetrical, and in all cases of doubt the two sides should be compared. Accurate estimates of the amount can be obtained only by special mechanical devices called exophthalmometers; a simple one is illustrated in Fig. 30.2. A subjective assessment of proptosis can be made by the following test which is convenient. The patient is seated, the surgeon standing behind him. The surgeon

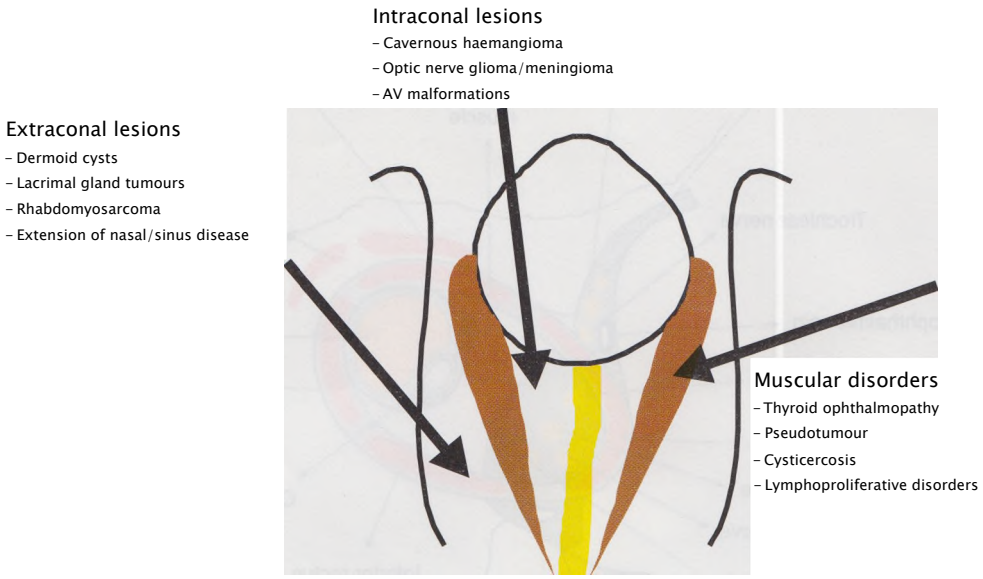


Fig. 30.3 Common space-occupying lesions seen in the different orbital spaces.

holds the patient's head in such a manner that he looks straight down the nose. He then rotates the head backwards until he can just see the apex of one cornea. If he can see more of one cornea than the other that eye is relatively proptosed.

An abnormal protrusion of the globe is called *exophthalmos* or *proptosis.* It is much commoner than abnormal retraction or *enophthalmos.* Exophthalmos is a term reserved for describing the prominence of the eyes secondary to thyroid disease, while proptosis is used to signify a protrusion of the eyeball due to all other causes. Proptosis may be due to many causes, among which space-occupying lesions within the orbit are the most important, and less frequent are herniation or extension of cranial or sinus contents into the orbit. Slight prominence of the eyes, or a *pseudoproptosis,* accompanies high myopia, paralysis of the extrinsic muscles, stimulation of Muller muscle by cocaine, and occurs as an idiosyncrasy, especially in very obese people. Unilateral proptosis commonly occurs in orbital cellulitis from any cause, idiopathic orbital inflammatory disease, thrombosis of the orbital veins with or without implication of the cavernous sinus, arteriovenous aneurysm, tumours of the orbit and its contents, and orbital haemorrhage or emphysema. Bilateral exophthalmos occurs almost always in endocrine exophthalmos, but bilateral proptosis is seen in the later stages of thrombosis of the cavernous sinus, empyema of the accessory sinuses of the nose, symmetrical orbital tumours (lymphoma, pseudoleukaemia), and as a result of diminished orbital volume in oxycephaly or 'tower-skull' and leontiasis ossea.

Proptosis in children is usually caused by dermoid and epidermoid cysts, capillary haemangiomas, optic nerve glioma, rhabdomyosarcoma, leukaemias, metastatic neuroblastoma, plexiform neurofibromatosis and lymphangiomas. *In adults* the common causes are metastases from the breast, lung and gastrointestinal tract, cavernous haemangiomas, mucoceles, lacrimal gland tumours, lymphoid tumours and meningiomas.

The proptosis can be *axial,* with the eye being pushed directly forwards. In such patients the causative lesion will commonly be found to originate in the optic nerve or central space, e.g. optic nerve gliomas, meningiomas and cavernous haemangiomas. The eye can also be displaced from its central location, opposite to the site of the space-occupying lesion (Fig. 30.3). Superotemporally located dermoids and lacrimal gland tumours displace the eyeball downwards and inwards. Concomitant involvement of the ethmoidal sinuses results in the medial canthus being displaced laterally and an apparent widening of the bridge of the nose.

Proptosis once noticed may remain static in congenital lesions, or increase gradually in the presence of slow-growing tumours such as meningiomas. Proptosis that increases at a fast rate is often due to haemopoietic tumours, rhabdomyosarcoma and neuroblastoma. However, there may be a variability in the amount of proptosis present. If there is a regular pulsatility of the proptosis the cause could be a carotid-cavernous fistula or transmitted pulsations from the cranium, as seen with the loss of bone in neurofibromatosis. Proptosis that increases on the Valsalva manoeuvre or on bending forwards is probably caused by a vascular lesion such as varicosities of the orbital veins.

The mobility of the eyeball is impaired in the direction towards the position of the tumour; diplopia is therefore common, while papilloedema may be present, especially with optic nerve tumours. Optic atrophy from pressure on the nerve occurs in the other forms.

Enophthalmos is generally due to severe injury in which the bones of the floor of the orbit are fractured and soft tissues herniate into the maxillary sinus. It may also be the result of a resolved orbital cellulitis, which is followed by fibrosis and mechanical retraction. Metastasis to the orbit, e.g. scirrhous breast carcinoma, may also cause this.

Careful examination of neighbouring parts—nose, antrum, mouth and especially the nasopharynx—must be made to determine whether the invasion of the orbit is secondary or whether the growth is primarily orbital.

INVESTIGATION OF ORBITAL LESIONS

The investigation of orbital disease may be considered in three stages: (i) imaging of bony structures by plain X-ray; (ii) imaging of soft tissues principally by computerized tomography (CT) and ultrasonography, aided in some patients by magnetic resonance imaging (MRI) and (iii) demonstration of the orbital vasculature by orbital venography, carotid angiography, digital subtraction angiography or MR angiography.

Plain X-rays

Plain X-rays of the orbit highlight bony disorders which contribute to a proptosis or other orbital disease. Different X-ray views have to be ordered, keeping the possible differential diagnosis in mind. Posteroanterior views of the orbit allow the visualization of calcification or hyperostosis due to meningiomas, while lateral X-rays are more useful for intracranial lesions. Water's view is specifically asked for in blow-out fractures of the orbit as it delineates the floor of the orbit and the sinuses. Special views are required for imaging of the optic foramen and superior orbital fissure. With the advent of CT and MRI scans, the importance of plain X-rays has considerably reduced. Plain X-ray examination in a patient presenting with proptosis should be backed by CT which helps to reveal the majority of causes of unilateral exophthalmos.

Ultrasonography

Ultrasonography has been described in detail in Chapter 12. Orbital ultrasonography requires a probe functioning at lower speeds to allow greater penetration into the depths of the orbit, generally 5-10 mHz. There is extremely clear delineation of soft tissues, so that the size and position of space-occupying lesions can be documented and easily reviewed. With real-time ultrasonography vascular pulsatile changes can also be documented.

Computerized tomography in orbital lesions

Fat, a tissue of low density, in the intraconal space acts as a natural contrast medium. Its presence has made CT an accurate method of orbital diagnosis when soft tissues are involved. This also provides the clinician with information as to the anatomical extent of any space-occupying lesion, especially when it also involves the paranasal sinuses, or extends into the cranium. The advantage of using a body scanner for orbital diagnosis lies in its ability to take scans in planes other than the axial (CAT) one. Coronal (CCT), oblique and sagittal sections of the orbit are feasible because of the large aperture of the body scanner. It allows the ophthalmologist to determine the type of tissue affected, the position, origin and shape of a space-occupying lesion. This is important in both the diagnosis and in planning therapy for such patients.

Magnetic resonance imaging

MRI generates high-resolution images of any portion of the human body without the use of ionizing radiation. The physical basis of MRI is the interaction of nuclear particles of selectively stimulated atoms, mainly protons within the body, with an external static magnetic field and an applied radiofrequency stimulus. It is capable of imaging soft tissues, not only within the orbit but within the globe itself, allowing better tissue diagnosis of an orbital lesion.

Computerized tomographic scans are preferred for viewing bony lesions and identifying calcification, while MRI is better for soft tissues, although it is contraindicated if the presence of a magnetic foreign body is suspected.

Angiography techniques are only required in a minority of patients, principally those with vascular anomalies in the orbit or within the cranium. In the rectus muscle cone and apex of the orbit, a high proportion of obstruction in the intraconal course of the superior ophthalmic vein is due to an inflammatory process, e.g. the Tolosa-Hunt syndrome wherein obstruction may be shown in the venous system due to granulation tissue. Carotid arteriography should only be carried out in selected patients, particularly those who are clinically suspected of having an arteriovenous shunt or other intracranial vascular anomalies. Other patients requiring carotid angiography are those with a vascular tumour in the orbit where it is important to identify the feeding vessel before surgery. Digital subtraction angiography and MR angiography are three-dimensional and provide very detailed information, especially about vascular malformations in the orbit.

ORBITAL INFLAMMATION

Periostitis

This is rare but particularly affects the orbital margin. It is most often due to injuries, extension of inflammation from neighbouring parts, tuberculosis or syphilis.

In traumatic cases, it is the margin that is naturally most affected, but a traumatic element is often an exciting cause in the other cases, so that in them also the margin suffers most frequently.

Periostitis of the deeper parts of the orbit causes less definite signs. There is more pain of a deep-seated nature. There may be proptosis with deviation of the direction of the eye. If the apex of the orbit is implicated, various ocular motor palsies may develop together with trigeminal anaesthesia and neuralgia, and occasionally amaurosis due to involvement of the optic nerve (*the orbital apex syndrome).*

In most cases general treatment by antibiotic drugs to which the infecting organism is susceptible has a dramatic effect. If suppuration supervenes, the abscess is opened and any carious bone removed.

In deep-seated periostitis an exploratory operation may be necessary and should not be too delayed.

Orbital cellulitis

This is a purulent inflammation of the cellular tissue of the orbit. It is due most frequently to extension of inflammation from the neighbouring parts, especially the nasal sinuses; other less common causes are deep injuries, especially those with a retained foreign body, septic operations, posterior extension of suppurative infections of the eyelids or the eyeball such as panophthalmitis, facial erysipelas, or metastases in pyaemia.

There are two recognized types of orbital cellulitis with differing presentations, therapy and prognosis. *Pre-septal orbital cellulitis* involves structures anterior to the orbital septum that is largely the lids. *Orbital cellulitis* is a term reserved for infections behind the orbital septum, which may or may not spill over to the lids.

Pre-septal cellulitis commonly presents as a swelling of the lids, with erythema and chemosis (Fig. 30.4). There is often a conjunctival discharge associated, but no proptosis or restriction of ocular movements or visual function is present. Pre-septal cellulitis is treated with appropriate oral antibiotics, depending on the source of the infection, and non-steroidal anti-inflammatory drugs. The resolution is generally quick and complete.



Fig. 30.4 Pre-septal cellulitis.

In *orbital cellulitis* there is extensive swelling of the lids with chemosis (Fig. 30.5). The eye is proptosed and its mobility impaired with resulting diplopia. Pain is severe, increased by movement of the eye or pressure. Fever is present and cerebral symptoms may arise. Vision may be reduced owing to retrobulbar neuritis or compression of the optic nerve or its blood supply at the apex of the orbit, due to raised tissue pressure caused by inflammatory oedema of the extraocular muscles, orbital fat and

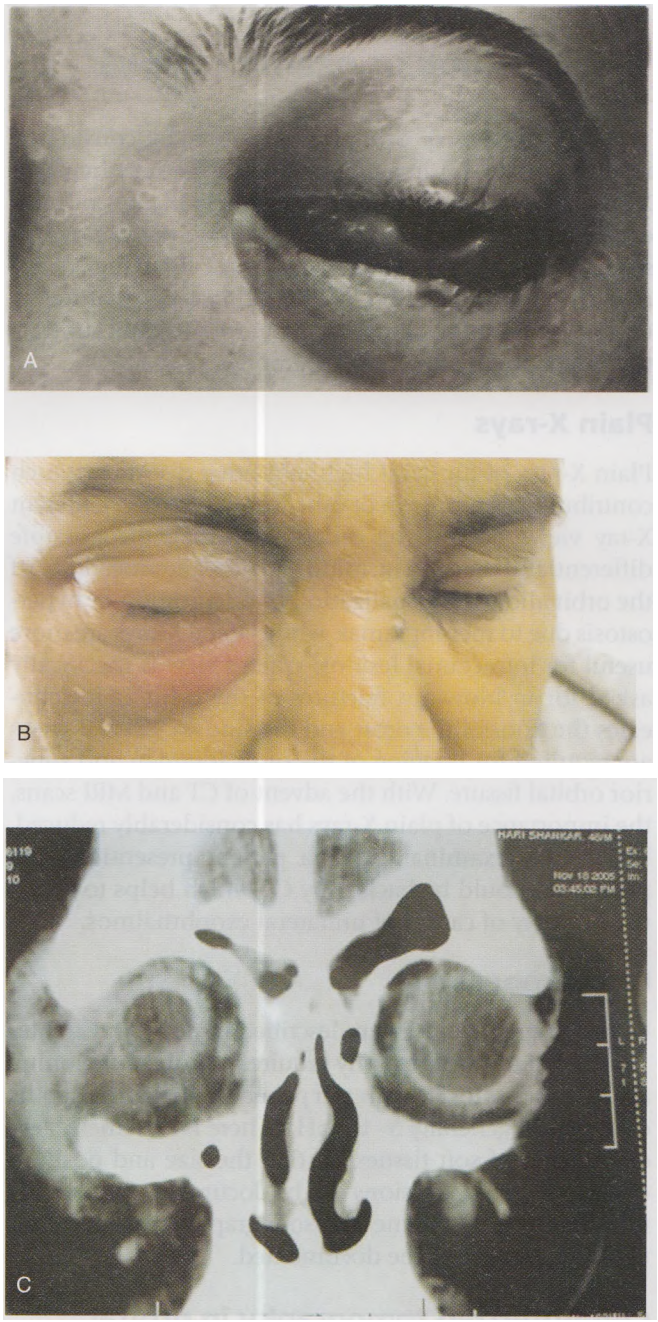


Fig. 30.5 (A) Orbital cellulitis. Tense, erythematous and swollen lids with proptosis (By courtesy of Jarrett). (B) Severe orbital cellulitis in a diabetic patient whose CT scan (C) shows soft tissue swelling of the orbit.

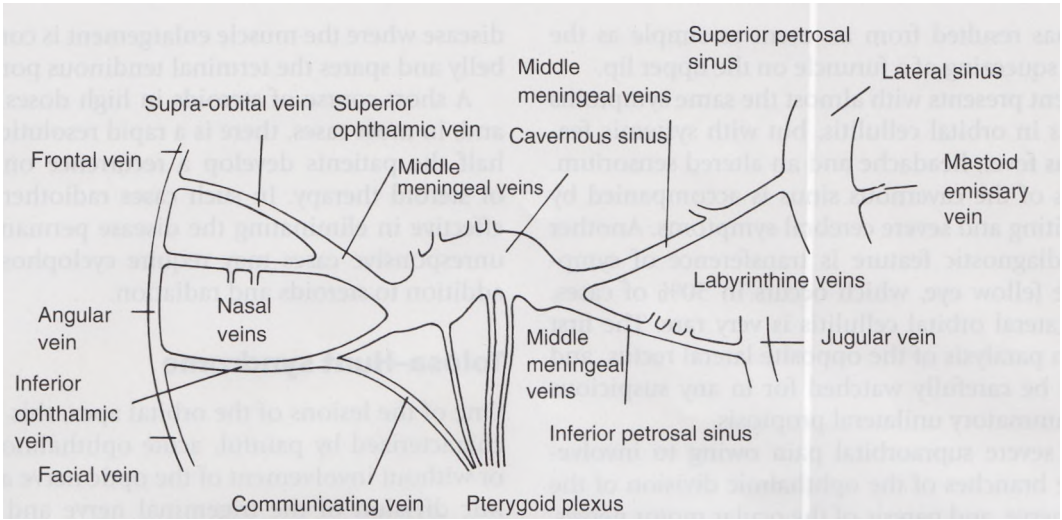


Fig. 30.6 Tributaries of the cavernous sinus (lateral view).

congested veins. The fundus is difficult to examine; it may be normal or show engorgement of the veins and optic neuritis, developing later into optic atrophy. An abscess is formed which usually points somewhere in the skin of the lids near the orbital margin or may empty into the conjunctival fornix. Panophthalmitis may supervene and there is grave danger of extension to the meninges and brain as purulent meningitis, a cerebral abscess or thrombosis of the cavernous sinus. In diabetics a particularly fulminant infection with *Mucor* or *Aspergillus* is possible.

Treatment: After taking blood samples for culture, intravenous treatment with broad-spectrum antibiotics and anti-inflammatory drugs should be instituted immediately, and if instituted reasonably early, resolution may rapidly follow. The presence of a localized abscess may necessitate prolonged therapy or drainage of the pus.

Thrombosis of the cavernous sinus

This may be due to extension of thrombosis from various sources.

There are many venous channels which communicate with the cavernous sinus (Figs 30.6 and 30.7). The superior and inferior ophthalmic veins enter it from the front and the superior and inferior petrosal sinuses leave it from behind. It communicates directly with the pterygoid plexus through the middle meningeal veins and the veins of Vesalius, and indirectly through a communicating vein from the inferior ophthalmic to the pterygoid plexus. The anastomoses of the ophthalmic veins with the frontal and angular veins opens up a communication with the face. Labyrinthine veins opening into the inferior petrosal sinus afford a communication with the middle ear. Numerous tributaries throw it into direct or indirect communication with most parts of the cerebrum. The mastoid emissary

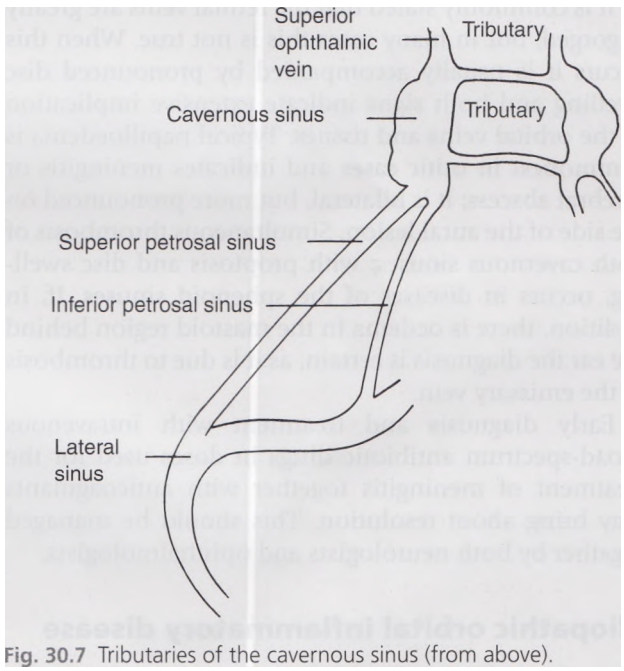


Fig. 30.7 Tributaries of the cavernous sinus (from above).

vein places the sinus in communication with the subcutaneous tissues behind the ear, through the lateral sinus and superior petrosal sinus, and is of great diagnostic importance, since a swelling behind the ear may decide the question of thrombosis in each direction along these sinuses. The sinus of one side communicates with that of the other by two (or sometimes three) transverse sinuses, which surround the pituitary body.

Infection may occur via the orbital veins, as in erysipelas, septic lesions of the face, orbital cellulitis, and infective conditions of the mouth, pharynx, ear, nose and accessory sinuses, or as a metastasis in infectious diseases or septic conditions. On more than one occasion bilateral

blindness has resulted from an event as simple as the injudicious squeezing of a furuncle on the upper lip.

The patient presents with almost the same symptoms and signs as in orbital cellulitis, but with systemic features such as fever, headache and an altered sensorium. Thrombosis of the cavernous sinus is accompanied by rigors, vomiting and severe cerebral symptoms. Another important diagnostic feature is transference of symptoms to the fellow eye, which occurs in 50% of cases, whereas bilateral orbital cellulitis is very rare. The first sign is often paralysis of the opposite lateral rectus, and this should be carefully watched for in any suspicious case of inflammatory unilateral proptosis.

There is severe supraorbital pain owing to involvement of the branches of the ophthalmic division of the trigeminal nerve, and paresis of the ocular motor nerves. In the later stages the eye is immobile, the pupil dilated, and the cornea anaesthetic. Proptosis occurs in nearly all cases, but is of late onset in those of otitic origin.

It is commonly stated that the retinal veins are greatly engorged, but in many cases this is not true. When this occurs it is usually accompanied by pronounced disc swelling and both signs indicate extensive implication of the orbital veins and tissues. Typical papilloedema is commonest in otitic cases and indicates meningitis or cerebral abscess; it is bilateral, but more pronounced on the side of the aural lesion. Simultaneous thrombosis of both cavernous sinuses, with proptosis and disc swelling, occurs in diseases of the sphenoid sinuses. If, in addition, there is oedema in the mastoid region behind the ear the diagnosis is certain, as it is due to thrombosis of the emissary vein.

Early diagnosis and treatment with intravenous broad-spectrum antibiotic drugs in doses used for the treatment of meningitis together with anticoagulants may bring about resolution. This should be managed together by both neurologists and ophthalmologists.

Idiopathic orbital inflammatory disease

Idiopathic orbital inflammatory disease, also known as non-specific orbital inflammatory disease or pseudotumour, is of uncertain aetiology. It produces proptosis due to a non-neoplastic mass in the orbit. It is a diagnosis of exclusion, when all other causes of inflammatory masses have been discounted. The condition mimics thyroid ophthalmopathy clinically. It can occur at any age but is commonest between 40 and 60 years and slightly commoner in men. The symptoms are proptosis, pain, diplopia, lid swelling and redness. It is usually unilateral but occasionally bilateral. Ultrasonography of the orbit shows a diffuse infiltration of heterogeneous consistency. CT scan shows diffuse thickening of the extraocular muscles including their tendinous insertion, which is useful in differentiating this from thyroid eye disease where the muscle enlargement is confined to the belly and spares the terminal tendinous portion.

A short course of steroids in high doses is indicated and, in most cases, there is a rapid resolution, although half the patients develop a recurrence on withdrawal of steroid therapy. In such cases radiotherapy is often effective in eliminating the disease permanently. A few unresponsive cases may require cyclophosphamide in addition to steroids and radiation.

Tolosa-Hunt syndrome

One of the lesions of the orbital apex, this syndrome is characterized by painful, acute ophthalmoplegia, with or without involvement of the optic nerve and ophthalmic division of the trigeminal nerve and it responds promptly to steroid treatment. Tolosa described a case in which a mass of granulation material was found around the carotid artery in the cavernous sinus; this syndrome is now referred to as the Tolosa-Hunt syndrome. The patient should be fully investigated to eliminate diagnoses such as infraclinoid aneurysm, carotid-cavernous fistula, pituitary tumour, meningioma and orbital tumour.

Steroids usually relieve the pain within a period of 24-48 hours, as well as any signs of compression. Other lesions may be responsive to steroids but neither is the remission complete nor does it occur so rapidly after the onset of treatment. The Tolosa-Hunt syndrome is not a pathological diagnosis and should not be made without arteriography and venography, or when there are atypical features (clinically, radiologically, or in response to treatment).

Parasitic infestations of the orbit

Trichinosis

This is an infestation of the striated muscles by the larva of the nematode *Trichinella spiralis*. The encysted larvae are ingested in undercooked pork and develop in the intestine into mature adults. Infection occurs worldwide, but is most common in areas where raw or undercooked pork, such as ham or sausage, is eaten. Eggs develop and hatch in the female nematode and the larvae enter the general circulation.

Nausea, diarrhoea, vomiting, fatigue, fever and abdominal discomfort are the first symptoms of trichinosis. Headache, fever with chills, cough, eye swelling, joint and muscle pain, itchy skin, diarrhoea or constipation follow the initial symptoms. There may be muscle weakness and pain, remittent fever and oedema localized to the orbit, particularly the upper lid. There is pain on movement of the eyes.

The extraocular muscles themselves are tender and there is an associated eosinophilia. If tissue invasion

does occur, the aim of therapy is to decrease subsequent muscle damage.

The most effective treatment modalities are bedrest and salicylates. Antihelminthic therapy has no proven role at this stage, though albendazole appears to be marginally more effective as compared to mebendazole. A trial of albendazole is thus justified in severe or prolonged infections. Prednisone (50 mg/day) can be used in severe infections, especially if there is haemodynamic instability or involvement of the central nervous, cardiac or respiratory systems. Steroids may decrease inflammation, but may also hinder the eradication of the adult worm, resulting in the continued production of larvae.

Cysticercosis

Cysticercosis is an infestation caused by the pork tapeworm *Taenia solium,* and occurs when the tapeworm larvae enter the body and form cysticerci. The tapeworm that causes cysticercosis is found worldwide, but the infestation is found most often in rural areas of developing countries with poor hygiene and where pigs are allowed to roam freely and eat food contaminated with human faeces. This allows the tapeworm infection to be completed and the cycle to continue. Tapeworm eggs are passed in the bowel movement of a person who is infected, and are spread through food, water or surfaces contaminated with faeces. Once inside the stomach, the tapeworm egg hatches, penetrates the intestine, travels through the bloodstream and may develop into cysticerci in the muscles, brain or eyes. Radiological and serological tests are usually required for diagnosis. Orbital ultrasonography is an extremely useful diagnostic tool. Demonstration of a cystic lesion with a central hyperechoic highly reflective scolex is diagnostic. Since the cysts are small, CT scans, if required, should be performed with 1 mm sections. Asymptomatic subcutaneous or intramuscular cysticerci do not require treatment. Cysticidal therapy with praziquantel (50 mg/kg/day thrice daily orally for 14 days) or albendazole (15 mg/kg orally twice or thrice daily for 8-15 days) with simultaneous administration of steroids accelerates the radiological disappearance of viable cysticerci. Corticosteroids counter the severe inflammatory response of the local tissues to the toxins released by the dying cyst. A dilated fundus examination to rule out intraocular and intracranial cysticercosis is mandatory before starting cysticidal therapy. If an intraocular cyst is present, the cyst must be surgically removed to avoid loss of the eye from severe toxic uveitis following death of the cyst from medical therapy.

Hydatid disease

Hydatid cysts in the orbit are the result of infestation by the larvae of tapeworms. Animals such as dogs, cats and jackals get infected by eating infected sheep and pass the infestation to humans when petted or by contaminating drinking water or food. This is commonly seen where animals and people are liable to ingest contaminated water and vegetables grown in soil mixed with human and animal faeces.

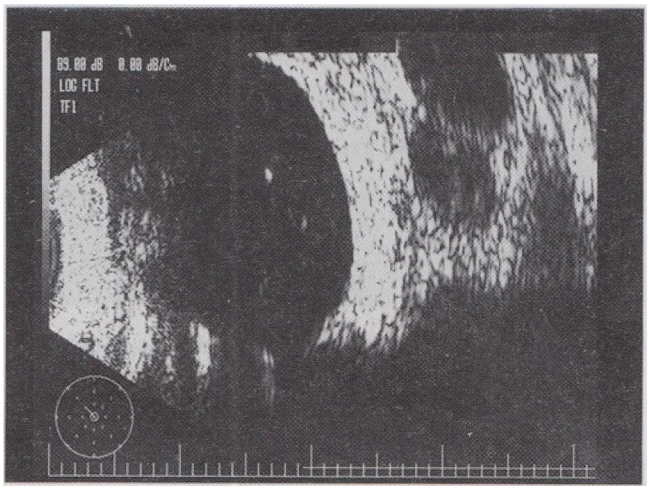


Fig. 30.8 Orbital hydatid cyst.

A hydatid cyst can grow to a large size (Fig. 30.8) and surgical removal is the treatment of choice. Care should be taken to remove the cyst *in toto.*

DISTENSION OF THE PARANASAL SINUSES

The paranasal sinuses - frontal, ethmoid and sphenoid and the antrum of the superior maxilla - are separated from the orbit only by thin plates of bone. The orifices which form the communication between these cavities and the nose are liable to become occluded by catarrh, polypi or neoplasms, so that the normal seromucus discharge is unable to drain into the nose; the cavities, therefore, become distended with fluid. Such mucus cysts are called mucoceles. A dual expansion and inflammation results in erosion and remodelling of adjacent bone. If the mucocele becomes infected, it is called a mucopyocele. The frontal sinus is affected most commonly, but the ethmoid and sphenoid sinuses are also often involved.

Distension or empyema of the frontal sinus causes bulging at the upper and inner part of the orbit (Fig. 30.9). There may be some proptosis and displacement of the eyeball downwards and outwards, together with oedema of the upper lid or slight ptosis. There is considerable pain and tenderness with severe headache.

Distension of the ethmoid cells by polypi, new growths or inflammatory products may also cause bulging into the orbit, lateral displacement of the medial canthus and protrusion of the globe. Diplopia, chemosis, venous engorgement and ptosis may result.



Fig, 30.9 Fronto-ethmoidocele. (By courtesy of MM Kulvin)

In all cases, there is often discharge from the nostril of the same side, or manifest disease of the nasal cavities. Owing to erosion of the walls of the sinus the fluid may extend under the periorbita causing bulging into the posterior part of the orbit or orbital cellulitis. Occasionally retrobulbar neuritis may occur, a complication most likely with inflammation and distension of the sphenoid cells, which lie in close proximity to the optic nerve.

In doubtful cases, an X-ray of the paranasal sinuses would help confirm the diagnosis.

Treatment: Broad-spectrum antibiotic therapy is instituted, and the cavity is opened and drained into the nose.

Wegener granulomatosis

This is a rare, chronic disease affecting the upper respiratory tract, lungs and kidneys and characterized by widespread distribution of necrotizing angiitis with surrounding granuloma formation.

The most common sign of Wegener granulomatosis is involvement of the upper respiratory tract, which occurs in nearly all patients. Symptoms include pain in the paranasal sinuses, discoloured or bloody nasal discharge and, occasionally, nasal ulcerations. A common manifestation of the disease is persistent rhinorrhoea ('runny nose') or other symptoms of cold that do not respond to standard treatment or that become progressively worse. Ocular manifestations occur secondary to an adjacent granulomatous sinusitis or as a result of focal vasculitis. The nasolacrimal duct may be obstructed and there may be episcleritis, scleritis, proptosis and extraocular muscle or optic nerve involvement.

Standard therapy consists of a combination of a corticosteroid that reduces inflammation and a cytotoxic drug that interferes with the abnormal growth of cells. Cytotoxic agents are required for the control of this systemic inflammatory disease. Cyclophosphamide is the preferred cytotoxic drug when used in low dosage with careful monitoring of the white blood cell count. A daily oral dose of 1-2 mg/kg of body weight should be administered. Conjunctivitis and episcleritis are treated with topical corticosteroids 3-4 times daily, together with cycloplegics. Scleritis needs to be treated with oral corticosteroids.

TUMOURS OF THE ORBIT

Orbital tumours are rare, and can occur at all stages in life. Common orbital tumours in children and adults are listed in Table 30.1.

Benign growths

These include dermoid cyst, dermolipoma angioma, osteoma (Fig. 30.10), plexiform neuroma, meningioma and meningoencephalocele. *Dermoid cysts* appear as swellings under the lid, usually at the upper and outer

Table 30.1 Common orbital space-occupying lesions

Origin	Children	Adults
Congenital	Dermoid cyst	
	Teratoma	
Vascular	Capillary haemangioma	Cavernous haemangioma
	Lymphangioma	Haemangiopericytoma
		Orbital varices
Neural	Optic nerve glioma	Optic nerve meningioma
	Plexiform neurofibroma	Schwannoma
		Neurofibroma
Mesenchymal	Rhabdomyosarcoma	Fibrous histiocytoma
Haemopoietic	Acute myeloid leukaemia Histiocytosis	Lymphomas
Metastatic	Neuroblastoma	Breast, lung, prostate carcinoma
	Wilm tumour	
	Ewing sarcoma	

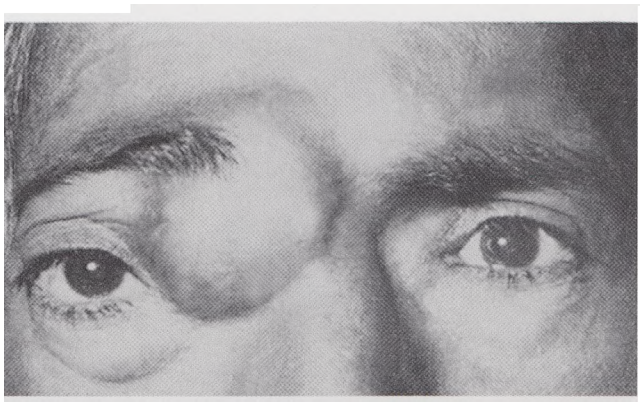


Fig. 30.10 Ethmoidal osteoma. (By courtesy of Mortada)

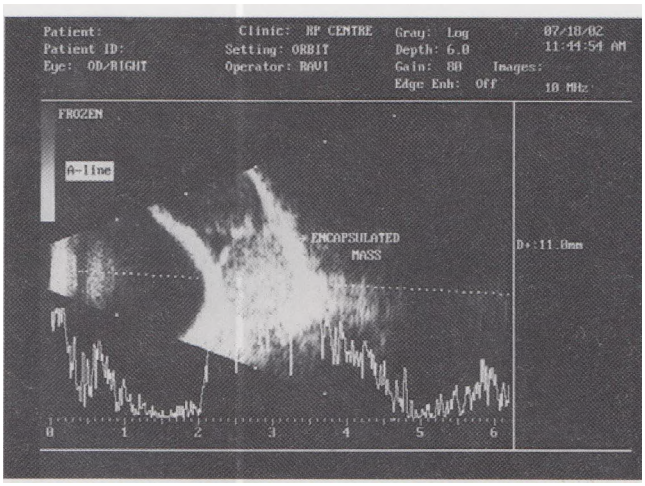


Fig. 30.12 Ultrasound of the orbit showing a well-encapsulated mass with medium-to-high amplitude spikes suggestive of a haemangioma.

angle; they contain sebaceous material derived from sebaceous glands in the walls, which are lined with epithelium and possess hair follicles; they sometimes contain remnants of foetal tissue (teratoid cysts).

Clinically they may be mistaken for *meningoencephaloceles* (protrusions of the cerebral contents), which usually occur at the upper and inner angle where there are the most sutures between the bones. In the latter
(i) the tumour is immovably attached to the bones;
(ii) the hole in the bone may be palpable; (iii) pulsations, synchronous with respiration and the pulse, increasing in amplitude on straining, can be seen; (iv) pressure may cause diminution in size due to fluid being pressed back into the cranium and (v) exploratory puncture (which should only be undertaken with full aseptic precautions) produces clear fluid with the characteristics of cerebrospinal fluid.

Orbital haemangiomas

These are commonly capillary in the younger age group and cavernous haemangiomata in the elderly

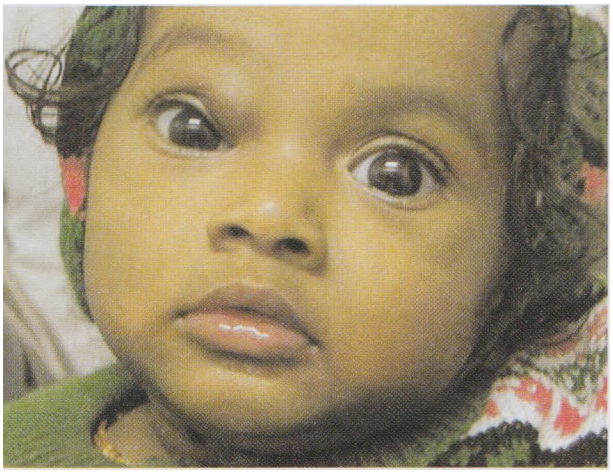


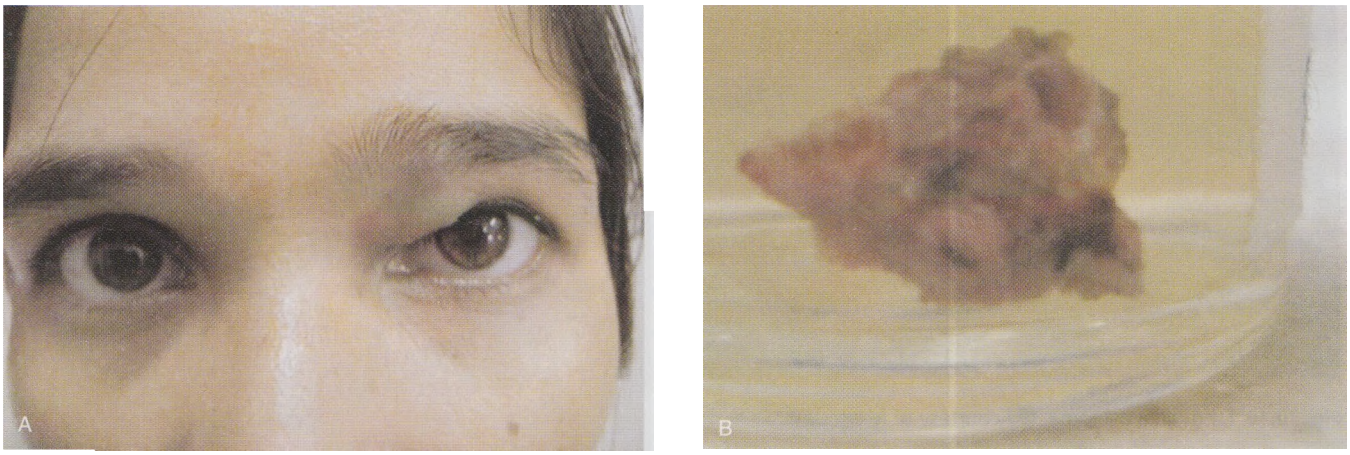
Fig. 30.11 Capillary haemangioma.

(Fig. 30.11). Capillary haemangiomas usually go through a phase of growth followed by involution within 1-5 years of onset. Diagnosis is confirmed by orbital ultrasonography which demonstrates a poorly outlined lesion, with an irregular shape, high internal reflectivity and an irregular acoustic structure with variable sound attenuation (Fig. 30.12). They are benign and can be treated by simple observation if there is no threat to vision. If vision is threatened in young children, treatment may be with oral, intravenous or intratumoral corticosteroids. When localized and causing visual dysfunction or marked proptosis these tumours can be surgically excised.

Cavernous haemangiomas usually present in adults during mid-life and are associated with proptosis or distortion of vision. These lesions vary in size, have smooth contours and are non-invasive. The lesions are well-defined with internal spaces giving rise to a characteristic picture on ultrasound of a well-circumscribed, round-to-oval lesion with high internal reflectivity, a regular acoustic structure with poor vascular flow. A similar picture is seen in contrast-enhanced CT. Cavernous haemangiomas are situated within the muscle cone, often in association with a muscle. When interfering with visual function or causing marked proptosis, a complete surgical excision is carried out.

Orbital varices

Orbital varices are due to an engorgement of the orbital veins. They present as a soft tissue compressible swelling sometimes with a 'bag of worms'. The venous stasis can lead to formation of a phlebolith. Surgical excision is required for laser tumours producing a cosmetic blemish or functional dehiscence.



Fig, 30.13 (A) Case with orbital varices. (B) Phlebolith removed from the lesion after surgery.

Haemopoietic tumours

These may occur as various types of reticular tumours (lymphoma, lymphosarcoma, reticulosarcoma, Hodgkin disease, etc.) and chloroma. Ocular changes in lymphomatous tumours include painless infiltration of the lids and a characteristic subconjunctival involvement with a smooth surface. Proptosis may occur due to deposits in the orbit itself or the lacrimal gland (Fig. 30.13). In cases of suspected lymphoma a biopsy is indicated and a search should be made for an abnormal lymph node, which may clinch the diagnosis. Most of the tumours are sensitive to radiation. The histological appearance of orbital biopsy material can be that of lymphoid hyperplasia, which is benign and may require no treatment, or an unequivocal malignant lymphoma which should be substantiated by a peripheral blood picture, bone marrow aspiration and trephine, chest X-ray, lymphatic angiogram and, if possible, a whole-body CT scan. If evidence of dissemination is found, treatment is by chemotherapy. In children, primary orbital lymphoma is rare and dissemination is likely so the initial treatment should be chemotherapy. In adults, dissemination occurs in half the cases and radiotherapy alone is probably the best initial treatment. A tumour dose of 4000 rads in 4 weeks is given for histiocytic lymphoma. Cytotoxic therapy should be held in reserve for those cases which later show evidence of dissemination. In those cases which are of an indeterminate lymphocytic character treatment is by radiotherapy.

Tumours originating from the optic nerve and its sheaths

These may be conveniently divided into two groups:

1. ectodermal tumours of the nerve—gliomas; and
2. mesodermal tumours of the sheath of the nerve—meningiomas.

Simple glial tumours derived from astrocytes and oligodendroglial cells of the optic nerve are either a solitary manifestation or a component of von Recklinghausen neurofibromatosis. These gliomas are generally non-neoplastic and self-limiting with a good prognosis for life. They are more prevalent in childhood and probably congenital, the peak incidence being 2-5 years. They present with gradual diminution of vision and increasing axial proptosis. Signs include a relative afferent pupillary defect and optic atrophy, though sometimes they may present with disc oedema. They grow slowly over a large number of years and are treated conservatively. If they can be removed and are confined to the optic nerve the prognosis for life is good. The neoplasm advances by extension along the nerve in a centripetal direction (Fig. 30.14). Once it reaches the chiasm the prognosis is poor. Enlargement of the optic canal is practically always present (Fig. 30.15). It is not, however, a reliable

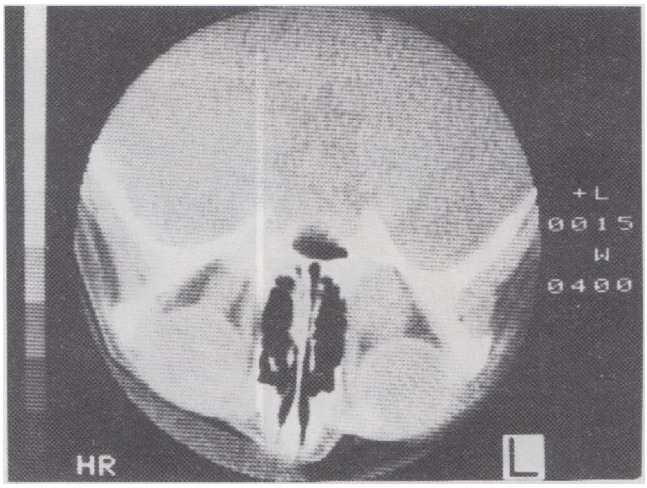


Fig. 30.14 Axial CT scan showing a left optic nerve glioma. (By courtesy of Wrigh)

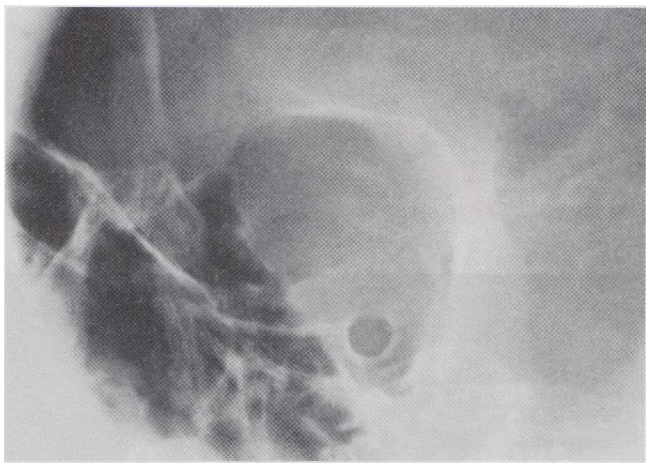


Fig. 30,15 Oblique radiograph of skull showing a rounded enlargement of the optic canal typical of optic nerve glioma. (By courtesy of Wright)

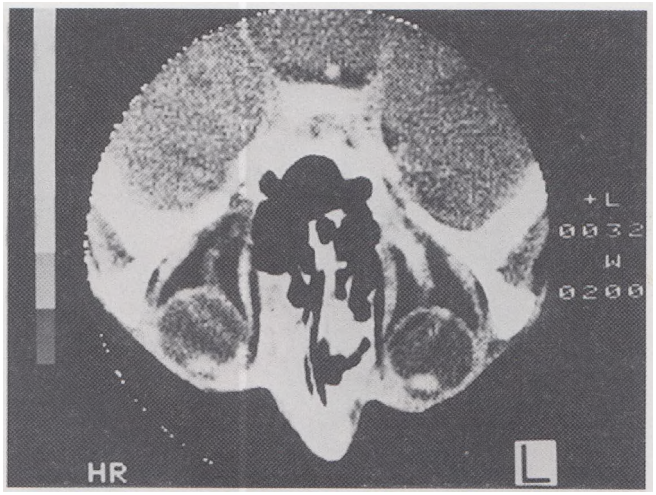


Fig. 30,16 Axial CT scan showing an enlarged left optic nerve caused by secondary meningioma. (By courtesy of Wright)

indicator of the posterior extent of the tumour. There may be a place for radical surgery for a minority of patients in whom there is progressive growth without evidence of chiasmal involvement.

MRI is superior to tomography in evaluating the intracanalicular, chiasmal and post-chiasmal extension of tumour growth, and is unimpeded by artifacts produced by surrounding bone, as encountered in CT. It is also more sensitive in delineating subtle differences in fat content and hydration of the neural tissues.

Orbital *optic nerve meningiomas* arise from the cap cells of the arachnoid around the intraorbital portion of the optic nerve. Rarely, meningiomatous tissue may extend from adjacent structures into the orbit in the subdural space of the optic nerve. CT scan can show the orbital structures in both the axial and coronal planes and provide pictures which confirm the origin of the tumour (Figs 30.14 and 30.16).

The predominant feature of optic nerve sheath meningiomas is early visual loss. Proptosis of a small degree occurs later. Tumours arising outside the dural sheath may cause considerable proptosis before compressing the optic nerve; the exception is an extradural tumour at the apex of the orbit.

Optic nerve meningiomas occur predominantly in middle-aged women. Patients present with swollen or atrophic optic discs when first examined and, in many cases, opticociliary shunt vessels are present, particularly if the meningioma of the optic nerve lies immediately behind the globe. Restriction of movement is common, particularly upwards, when it is associated with a rise in intraocular pressure. Patients with primary optic nerve meningiomas have a good prognosis because the tumours are peripheral, slow growing and isolated from the central nervous system. Patients with relatively good vision are kept under observation until it deteriorates and then the meningioma together with the optic nerve is removed. Biopsy or any surgery which transgresses the dura is to be avoided unless the rate of growth suggests a malignant type of meningioma, when biopsy is indicated. If high-resolution CT scans show a small anterior tumour and useful vision is retained, the orbit may be explored and the lesion removed without endangering vision.

Apart from those originating in association with the optic nerve sheath, meningiomas generally arise in association with the intracranial meninges and invade the orbit secondarily causing a hyperostosis. The most typical are those arising from the lateral portion of the sphenoid ridge—these are slow-growing tumours causing proptosis, a fullness of the temporal fossa and visual failure due to pressure on the optic nerve.

Osteomata

These start from the nasal sinuses, usually from the frontal (Fig. 30.10); they are intensely hard and often large, producing great displacement of the globe.

Malignant tumours

Malignant tumours of the orbit are usually sarcomata, although carcinomata derived from the lacrimal gland or by extension from the nasal mucous membrane also occur. Rhabdomyosarcomata are extremely malignant tumours and occur in the first decade of life (Fig. 30.17). They arise from voluntary muscle and often produce a rapidly increasing proptosis. Extension occurs in all directions. Diagnosis is by biopsy in which cross-striations in the tumour cells are pathognomonic.



Fig. 30.17 Rhabdomyosarcoma.

The *treatment* of rhabdomyosarcoma is a combination of chemotherapy and radiotherapy. Two injections of vincristine, cyclophosphamide and actinomycin D are given at weekly intervals before radiotherapy. Radiotherapy is given in a dose of 5000 rads for 5 weeks during which vincristine and cyclophosphamide are administered weekly. After radiotherapy, a combination of vincristine, cyclophosphamide and doxorubicin is given three times weekly for a year or longer in those patients in whom metastases were detected.

Secondary orbital tumours

Tumours may also invade the orbit from adjacent structures or by metastasis. In adults metastasis commonly originates from the lung, thyroid, breast and prostate, and nasopharyngeal carcinomas spread into the orbit most frequently. In young children neuroblastomas from the adrenal medulla metastasize to the orbit and retinoblastomas may spread out of the eye to cause orbital infiltration.

Malignant nasopharyngeal tumours

These form 0.4% of all cases of cancer; 38% of cases show ophthalmoneurological symptoms, these being the earliest signs in 16% of cases (Fig. 30.18). The fifth and sixth nerves are most frequently involved; more rarely the third, fourth and the optic nerve. Quadrantic and hemianopic lesions are rare, thus distinguishing these cases from lesions in the neighbourhood of the sella turcica. The presence of abducens paralysis, especially if associated with impairment of vision, Horner syndrome or proptosis or enlargement of the cervical lymph nodes, should suggest a nasopharyngeal growth. Treatment is by radiotherapy.



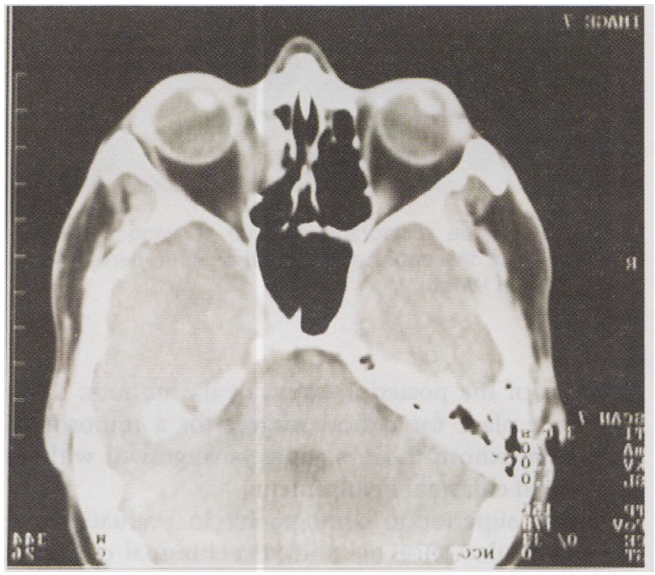


Fig. 30.18 Clinical picture and CT of a nasopharyngeal carcinoma extending into the right orbit.

Lipodystrophies

These may give rise to tumour-like formations resulting from the reaction of the reticuloendothelial system to the deposition of lipids—*diabetic exophthalmic dysostosis* (Hand-Schuller-Christian disease), *xanthomatosis,* etc.

Therapy of orbital tumours

A thorough evaluation of the orbit by ultrasound (Fig. 30.19), CT and MRI allows a good topographical and fair diagnostic assessment to be made of the mass. Anterior masses can be subjected to a fine needle biopsy or, if necessary, an exploratory operation with removal of a portion of the growth for microscopic examination preliminary to radical treatment. It may be feasible to remove dermoid cysts and some other benign tumours without injury to the globe, although its mobility is likely to be impaired in extensive operations. As already mentioned, many malignant orbital growths show little tendency to metastasis, so that their treatment may be more conservative than is usual in other parts of the body. Some tumours (particularly the reticular tumours) respond to radiation therapy and recurrences in the orbit or metastases should be treated by these means.



Fig, 30.19 Orbital lymphoma.

The majority, however, require surgical excision. Many routes of approach with retention of the eye are available: (i) an *anterior orbitotomy,* in which an incision made anteriorly at the orbital margin or through the conjunctival sac provides access to the anterior half of the orbit; (ii) a *lateral orbitotomy,* which provides access to the deeper parts of the orbit and is a valuable exploratory procedure; (iii) medial transconjunctival orbitotomy for anterior and medial tumours within the muscle cone; (iv) inferior orbitotomy through the skin or maxillary antrum approaches for inferior tumours and orbital floor fractures and (vi) transcranial orbitotomy through a coronal flap. In the case of more malignant tumours, their complete removal is imperative at all costs, and the eye, even if normal, may have to be sacrificed. In these cases, as well as in recurrence or in orbital extension of malignant intraocular growths (retinoblastoma, malignant melanoma of the uveal tract), it may be necessary to remove all the contents of the orbit by exenteration.

In *lateral orbitotomy* a curved incision is made in the lateral two-thirds of the eyebrow, concentric with the superior and lateral orbital margin, extending obliquely below the level of the lateral canthus over the zygomatic arch for about 4 cm. The bone is cut through at the upper and lower outer angles of the orbit with a Stryker saw and bone, muscle and skin are reflected backwards in one flap. The part of the orbit immediately posterior to the globe is thus freely exposed.

Exenteration of the orbit is indicated in the presence of a malignant tumour of the orbit, which is not responsive to radiation or amenable to surgery. Exenteration would delay or prevent systemic spread of the disease. It is contraindicated if metastasis is already present. The lids may be retained if they are not implicated in the growth, but the free margins, carrying the cilia, should always be removed. If this is not done the lashes are troublesome when the lids become retracted into the orbit, as invariably follows. If the lids are removed, the incision is carried through the skin at the margin of the orbit in its whole circumference. The orbital contents are separated from the walls by a periosteal elevator, so that they remain attached only at the apex of the orbit. The pedicle is then severed with strong scissors, or preferably by diathermy, thus avoiding haemorrhage. At a later stage it may be advisable to apply split-skin grafts to the walls, since the lids and conjunctiva never afford sufficient epithelial covering, and the extension of the epithelium over such a large surface is a tedious process.

Endocrine exophthalmos

Graves ophthalmopathy (dysthyroid eye disease) is the most common cause of unilateral or bilateral proptosis in adults between the ages of 25 and 50 years. Diagnostic clinical features include proptosis, eyelid retraction, restrictive myopathy and possibly compressive optic neuropathy. Type I and type II orbitopathy have been described. In type I there is a largely symmetric, mild proptosis and lid retraction; in type II there is an extreme exophthalmos, compressive neuropathy and extraocular muscle involvement. The cause of exophthalmos in either type is not yet understood. A mild exophthalmos may be associated with thyrotoxicosis and an extreme exophthalmos in any state of thyroid activity, but usually in hypothyroidism, often after a thyroidectomy.

The retraction of the lid in thyrotoxicosis is due to contraction of Muller muscle owing to the sensitizing action of thyroxine on sympathomimetic receptors. The exophthalmos of exophthalmic ophthalmoplegia is due to oedema, lymphocytic infiltration and fibrosis of the orbital contents, particularly the extraocular muscles. These changes are probably due to a generalized disturbance of the endocrine system, possibly associated with the thyrotrophic hormone secreted by the anterior lobe of the pituitary gland which normally stimulates the thyroid gland into activity.

Graves disease includes in its symptomatology exophthalmos and all the signs of thyrotoxicosis—tachycardia, muscular tremors and a raised basal metabolism. From the ocular point of view, the exophthalmos in the early stages may be unilateral but usually becomes bilateral. A peculiar stare with retraction of the upper eyelid is seen, so that there is an unnatural degree of separation between the margins of the two lids (Dalrymple sign, Fig. 30.20). Normally, when the eye is directed downwards, the upper lid moves concordantly with it; however, in Graves disease the upper lid follows tardily or not at all (von Graefe sign). This symptom is not always present and may occur in other forms of exophthalmos. There is diminished frequency of blinking with deficient closure of the lids (Stellwag sign). There may be a decreased

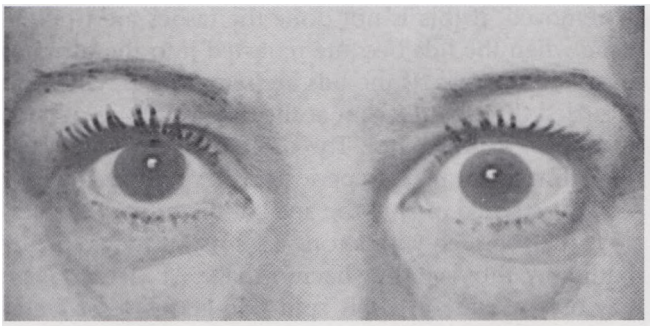


Fig. 30.20 Thyrotoxicosis, showing retraction of the upper lid and proptosis.



Fig. 30.21 Exophthalmic ophthalmoplegia.

power of convergence (Mobius sign), and often the skin of the eyelids shows pigmentation. Ophthalmoscopically, veins and arteries maybe somewhat distended, but specific signs are absent. One or more of the cardinal symptoms may be absent. The common signs of Graves disease are listed in Table 30.2.

Werner classification reflects the severity of the ophthalmopathy and is well known by the acronym of NO SPECS. Each grade is further subdivided as 0-4 and a-c.

Grade 0—No signs or symptoms
Grade 1—Only signs (lid retraction)
Grade 2—Soft tissue involvement (chemosis, grit, etc.)
Grade 3—Proptosis (minimum <23, moderate, marked >28)
Grade 4—Extraocular muscle involvement
Grade 5—Corneal involvement
Grade 6—Loss of sight.

Exophthalmic ophthalmoplegia usually commences in middle age with insidious signs of proptosis and external ophthalmoplegia, typically asymmetrically divided between the two eyes, and preferentially limiting upward movement or abduction. The ocular muscles are enormously swollen, pale, oedematous and infiltrated, giving rise to an irreducible *exophthalmos* which may easily result in the development of an exposure keratitis or even dislocation of the globe (Fig. 30.21). Mechanical compression of the optic nerve and ophthalmic blood vessels can occur, especially if the orbital apex is narrow. The disease runs a self-limited course characterized by intermissions and relapses, more or less unaffected by any kind of treatment, but eventually there is spontaneous resolution which, however, is rarely complete.

Short-term oral steroids (40-60 mg prednisone daily) are effective in reducing the soft tissue inflammatory signs but if they prove unrewarding, radiotherapy (1000 rad from each lateral port) should be employed in association with steroids as long as the inflammation lasts.

From the ophthalmological point of view, protection of the exposed cornea is of paramount importance; in less severe cases this is achieved by tarsorrhaphy, while in more severe cases a decompression of the orbit through its floor by a Caldwell-Luc approach may be necessary, especially if the optic nerve is threatened. Residual muscle palsies may require surgical adjustment. Once the disease stabilizes, myopathy, lid retraction and minor corneal exposure require an elective lateral canthoplasty with release of the upper and lower retractors of the eyelid.

Table 30.2 Common signs of Graves disease

- Lid retraction
- Lid lag (upper and lower)
- Infrequent blinking
- Exophthalmos
- Diplopia
- Lid oedema and chemosis
- Conjunctival injection over insertion of the recti
- Increased intraocular pressure with elevation
- Superior limbic keratopathy

INJURIES OF THE ORBIT

Pulsatile proptosis

This is generally due to an arteriovenous fistula, the communication taking place between the internal carotid artery and the cavernous sinus (caroticocavernous fistula or CCF). The eyeball is proptosed and the blood vessels of the conjunctiva and lids are widely dilated (Fig. 30.22). The angular vein and its branches near the inner canthus are very prominent and can be seen, or more easily felt, to pulsate synchronously with the arterial pulse since, owing to the arteriovenous communication, they are under arterial pressure. The patient complains of continuous rumbling, as of a waterfall, which can be heard on auscultation over the eye or orbit by the surgeon. The proptosis is diminished by steady pressure on the globe, and may be diminished or abolished by pressure on the common carotid artery of the same side or sometimes only by pressure on the carotid of the opposite side as well. Ophthalmoscopically, the veins of

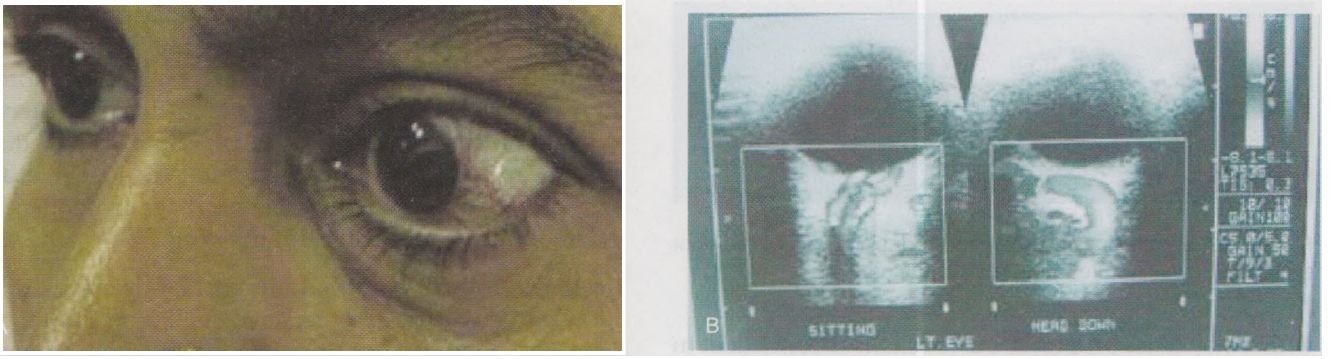


Fig. 30.22 (A) Caroticocavernous fistula (CCF) with proptosis and dilated vessels. (B) Ultrasonogram showing a dilated superior ophthalmic vein due to CCF.

the retina are greatly distended; there may be papilloedema with defective vision, which may amount to complete blindness. There is often considerable pain from stretching of the branches of the trigeminal nerve.

The cause of the arteriovenous fistula is usually a severe blow or fall upon the head, and it is therefore commoner in men, but in most cases the walls of the artery are already degenerated. It may occur from atheromatous or syphilitic disease without discoverable trauma, especially when it occurs in women. The exophthalmos in most cases subsides spontaneously. More commonly it increases, and may end in haemorrhage or death from cerebral causes.

Treatment is conservative. If continuous pressure applied to the carotid artery stops the pulsation, ligation of the carotid artery may affect a cure, but recurrence of pulsation frequently occurs. Embolization during arteriography is presently the treatment of choice. Ligation of both internal and external carotids does not appear to give better results. The opposite carotid artery may also be tied, but should not be done for some weeks after the first operation, owing to the risk of cerebral anaemia.

This procedure also may fail to relieve the condition, and in these cases intracranial ligation proximal and distal to the aneurysm has been practised, but is both difficult and dangerous.

Intermittent proptosis

This occurs infrequently, especially when the head is depressed, enophthalmos being present in the erect position. The proptosis is increased by pressure on the corresponding jugular vein or by performing a Valsalva manoeuvre. It is usually due to varicosity of the orbital veins and has also been found to be caused by intracerebral arteriovenous communication.

Penetrating injuries

Injuries to the soft parts usually arise from penetration by a foreign body which may be retained, frequently involving the lids and eyeball. The signs depend upon the particular structures injured. In most cases there is considerable haemorrhage and, as the blood does not find a ready exit, proptosis may result and extravasation of blood under the conjunctiva into the lids is common. Paralysis of the extrinsic muscles may be due to direct injury or damage to the motor nerves. The optic nerve may be injured or severed with resultant atrophy. Avulsion of the optic nerve head, with the formation of a traumatic 'coloboma' or 'conus' of the disc may occur, even without rupture of the sheath of the nerve. The eyeball may be perforated, contused or dislocated outside the lids. Retained foreign bodies are liable to set up suppuration and orbital cellulitis.

Gunshot wounds of the orbit cause similar penetrating wounds. Even if there is no direct involvement of the eye, such injury frequently produces concussion changes which appear ophthalmoscopically as coarse tracks of white exudate in the retina and choroid, large blot-like haemorrhages and multiple small choroidal tears. These resolve into densely scarred areas fringed with pigment, with finer pigmentary disturbances elsewhere in the fundus. The site may give an indication of the direction of the track of the missile and assist in localizing a retained intracranial foreign body. Both eyes should be examined as the missile may have traversed both orbits.

Non-penetrating injury

A blow in the orbital region without the penetration of a foreign body may lead to an intraorbital haemorrhage; this may occur from pressure with forceps at birth. Forward dislocation of the globe between the lids occurs most often when the blow is directed from the outer side where the orbital margin affords least protection, but does not necessarily result in loss of sight.

Injuries to the bone most commonly affect the margin of the orbit but deep fractures may be caused by penetrating wounds or by severe contusions. Fractures near the orbital rim are easy to diagnose from the unevenness of the margin, sensitivity to pressure, and sometimes crepitation. Deeper fractures may give rise to *emphysema,*



Fig, 30.23 Enophthalmos and downward displacement of the right eyeball due to a fracture of the floor of the orbit.

which may cause proptosis, but is usually most evident in the lids. This is due to communication of the subcutaneous tissues with the nasal air sinuses so that air is forced into the tissues on blowing the nose, sneezing, straining, or coughing. The diagnostic signs are the considerable swelling and the peculiar soft crepitation on palpation.

Blow-out fractures of the orbit are usually due to blunt trauma caused by a large object such as a cricket ball. The object transmits force into the orbit, which is then reflected back. As the orbital opening is blocked by the object the force is directed at the orbital walls, damaging the thinner walls that abut the sinuses. Most commonly the orbital floor 'blows out', but it can also affect the medial wall of the orbit. As the orbital floor fractures, the eye and its surrounding tissues may collapse into the maxillary sinus, causing enophthalmos and entrapment of the inferior rectus muscle.

The patient may present with pain, local tenderness, epistaxis and diplopia. The patient may complain of a prominence of the eye on blowing his nose. On examination there is an initial oedema, ecchymosis or emphysema around the ocular adnexa with a restriction of ocular movements, commonly upwards or outwards. Associated damage to the sinuses may cause orbital crepitus. Infraorbital hypoesthesia may be present because of an entrapment of the infraorbital nerve. After the inflammation resolves, the patient is left with a relative enophthalmos (Fig. 30.23) and restricted ocular motility upwards.

In fractures of the orbital floor, the globe may sink backwards and be depressed with a resultant trouble-some diplopia *(traumatic enophthalmos)* (Fig. 30.23). It is important to accurately diagnose blow-out fractures at an early stage, since correction of the diplopia involves the insertion of a thin layer of silicone rubber between the periosteum and bone of the orbital floor after reducing the herniation of the soft tissues. Such fractures are diagnosed accurately by computerized coronal tomography which enables the entrapment of the inferior rectus to be localized accurately.

Tomography can be used to estimate the size of the fracture. Large fractures (greater than one-half of the orbital floor) need early repair, preferably within 2 weeks after injury, as do fractures producing substantial muscle dysfunction due to entrapment of the tissue.

Fractures of the base of the skull may involve one or both optic foramina, in which case the optic nerve may be injured, or pulsating exophthalmos may ensue. Blindness without ophthalmoscopic signs may be caused in this manner, probably as the result of a shearing force injuring the vessels entering the periphery of the nerve in its course through the optic canal; atrophy of the disc follows in 3-6 weeks. It is important to note that an orbital and subconjunctival haemorrhage is frequently a sign of fracture of the base of the skull.

Treatment: If there is a wound it must be cleaned and, if a foreign body is possibly retained, a CT scan should be done. The wound should not be probed without expert guidance, otherwise more damage may occur. It should be dusted antibiotic powder and a prophylactic course of systemic antibiotic treatment given if indicated. Absorption of extravasated blood is often slow. The treatment of a retained foreign body depends upon its situation and the probability of subsequent infection. If the foreign body cannot be extracted with ease, an X-ray should be taken. If the position is such that serious manipulations would be necessary for its removal, and if there is evidence that the substance is aseptic, expectant treatment may be adopted. If suppuration occurs, the foreign body must be removed and the case treated as one of orbital cellulitis.

SUMMARY

The orbit contains orbital fat, external ocular muscles, nerves, vessels and the lacrimal gland in addition to the eyeball or globe. The walls provide protection superiorly, inferiorly, medially and laterally. Diseases of the orbit include both local conditions such as infections and tumours, but also those resulting secondary to systemic diseases such as dysthyroid ophthalmopathy. The orbital vascular channels are connected with the intracranial system and infectious diseases like orbital cellulitis can spread intracranially and *vice versa.* Intracranial vascular abnormalities like cavernous sinus thrombosis and caroticocavernous fistula can also have profound effects on the orbital contents.

Ultrasonography and other radiological investigations help in the diagnosis and management of orbital lesions. Invasive investigations like fine needle aspiration cytology and orbital biopsy are required in specific situations.

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Section VII

Systemic Ophthalmology

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Diseases of the Nervous System with Ocular Manifestations

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Summary 519

The ocular signs of central nervous system (CNS) disorders often appear complicated and confusing but, in most cases, they are readily explained by the anatomy of that part of the nervous system. More importantly, there are several potentially serious diseases of the nervous system which may first present with ocular manifestations. Even at the risk of some repetition the main ocular symptoms of these diseases will be summarized in this section.

A careful *history* detailed *neuro-ophthalmic evaluation* and judicious use of *neuroimaging* help in arriving at the correct diagnosis. Ocular examination should specifically include visual acuity, visual fields, colour perception, extraocular movements including nystagmus, and funduscopy for papilloedema or optic atrophy.

Modem imaging techniques of ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) and MR angiography, digital subtraction angiography and

conventional angiography all help to identify and localize diseases of the CNS. Plain X-rays now have a limited role which is restricted to detecting radio-opaque foreign bodies, demonstrating sinusitis, visualizing enlarged optic foramina due to optic nerve gliomas, an enlarged sella in sellar tumours of long duration, intracranial calcification in congenital toxoplasmosis, tuberculosis, cysticercosis, certain brain tumours, Sturge-Weber syndrome, bony hyperostosis in meningiomas and lytic lesions in multiple myeloma. Other older invasive methods of positive contrast ventriculography, polytomography and pneumoencephalography have become obsolete.

Scans of the orbit require thin slices (<3mm) and should include axial, coronal and sagittal views. Scanning with 1 mm cuts is required in special situations such as looking for a scolex in suspected cysticercosis. The choice between CT and MRI is guided by the lower cost of CT *vis-a-vis* MRI and balanced by the absence of any ionizing radiation in the latter. MRI is contraindicated in patients with ferromagnetic foreign bodies or implants and cardiac pacemakers. Sedation would be required for MRI in patients with severe claustrophobia or psychotic disorders as the individual is placed in a tunnel-like chamber and hears the sound of the magnet throughout the duration of the scan. Lesions with increased vascularity or those associated with a breakdown of the blood-brain barrier are better visualized by contrast enhancement scans using intravenous injection of an iodinated contrast for CT or a gadolinium-diethylenetriamine chelated compound for MRI.

MRI scans are specifically preferred over CT for better demonstration of demyelinated plaques in the white matter in multiple sclerosis (MS), differentiating an optic nerve glioma from meningioma (using the technique of fat suppression with gadolinium enhancement), study of the sella, chiasma and juxtasellar region and viewing lesions in the posterior fossa. In all other conditions CT scans are equally informative but are specifically preferred over MRI scans in cases with ferromagnetic foreign bodies, visualizing calcification, particularly in retinoblastoma and craniopharyngioma, lesions at the orbital apex especially bone fragments in fractures of the optic canal, haemorrhage of the optic nerve sheath and dysthyroid ophthalmopathy.

A rapidly developing field is that of 'functional imaging' where attempts are made to demonstrate the physiological and metabolic functions of parts of the brain and their change in pathological conditions. Functional MRI, positron emission tomography (PET), and single photon emission computed tomography (SPECL) are some of the techniques being used for this purpose.

For evaluating vascular lesions several choices are available. A non-invasive, well tolerated, relatively inexpensive technique which is effective in rapidly studying orbital and cerebral vasculature is that of Doppler ultrasonography. Intracranial vascular lesions can be viewed by digital subtraction angiography, CT or MR angiography. CT scan is superior to MRI in detecting acute subarachnoid haemorrhage. Though all large intracranial aneurysms can be detected by a combination of MRI and MR angiography, conventional angiography remains the most definitive diagnostic procedure for the imaging of aneurysms (Fig. 31.1).

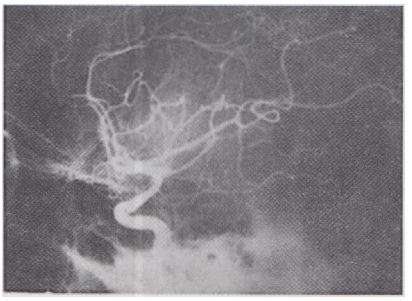


Fig. 31.1 Carotid angiogram showing the internal carotid artery and its branches.

THE VISUAL PATHWAY AND NEUROLOGICAL DISORDERS

The normal visual field related to the visual pathway has been described in Chapter 4. An important feature to be remembered is that the central 120° of the field is seen with both eyes (binocular field) and is bilaterally represented in the occipital cortex. The extreme temporal 30 ° of the field (temporal crescent) is viewed monocularly and is unilaterally represented more anteriorly in the occipital cortex (Fig. 31.2A: 7).

Apart from the disturbances of vision which have been described earlier *(see* Chapter 9) and have their origin in the eye itself, there are others dependent upon lesions in the visual nervous pathways.

Hemianopia

Hemianopia denotes loss of half of the field ofvision. The commonest clinical form is *homonymous hemianopia,* in which the right or left half of the binocular field of vision is lost, owing to loss of the temporal half of one field and the nasal half of the other. This condition is due to a lesion situated in any part of the visual paths from the chiasma to the occipital lobe. A focus of disease in this area causes loss of vision of the corresponding halves of each retina (hence the designation homonymous) and therefore loss of the opposite halves of the visual fields (Fig. 31.2). Right hemianopia is more quickly discovered

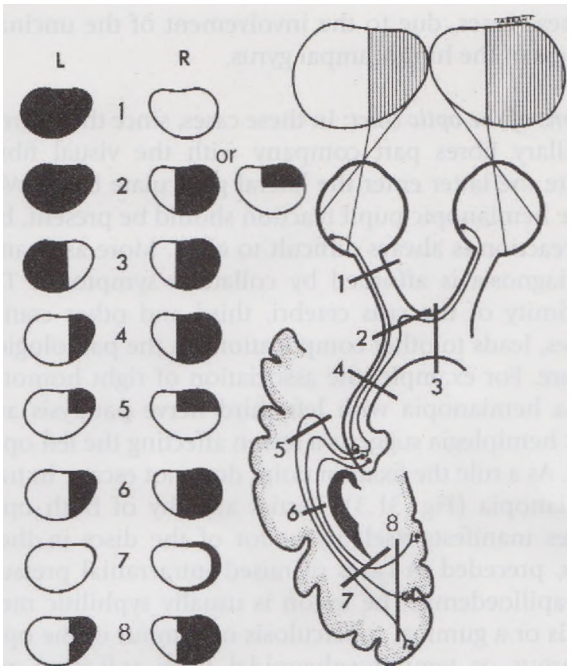
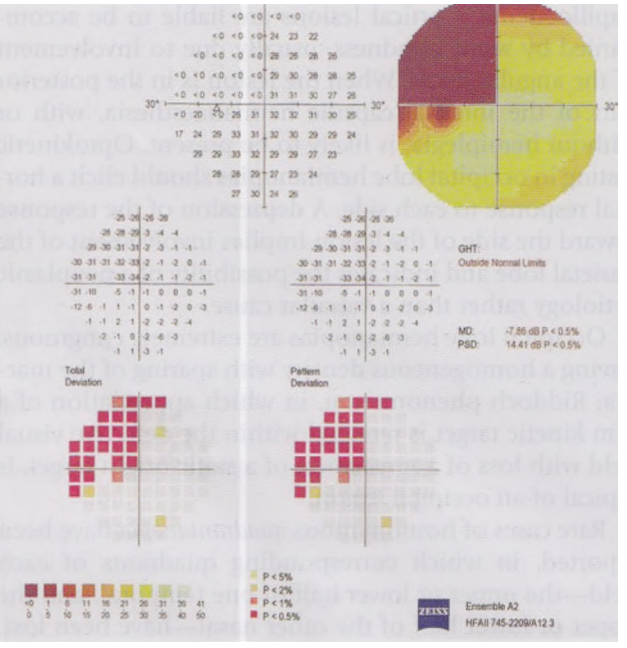


Fig. 31.2 (A) Diagram of the visual paths, showing sites of lesions and the corresponding field defects: 1, lesion through optic nerve—ipsilateral blindness; 2, lesion through proximal part of optic nerve—ipsilateral blindness with contralateral hemianopia or superior quadrantanopia (Traquair junctional scotoma); 3, sagittal lesion of chiasma—bitemporal hemianopia; 4, lesion of optic tract—homonymous hemianopia; 5, lesion of temporal lobe—quadrantic homonymous defect; 6, lesion of optic radiations—homonymous hemianopia (sometimes sparing the macula); 7, lesion more anteriorly in occipital cortex—contralateral temporal crescentic field defect; 8, lesion of occipital lobe—homonymous hemianopia (usually sparing the macula).



Fig, 31.2 (B) Automated perimetry colour printout showing left superior quadrantanopia. The right eye was blind (similar to Fig. 31,2A: 2). Colour coding reflects the density of the scotoma.

than left owing to the fact that reading is impossible; left hemianopia is often discovered when the patient does not see food on the left side of the plate.

In many cases of hemianopia the fixation area in each field escapes, especially if the lesion is near the occipital cortex. This is probably because the macular fibres are spared owing to their widespread but segregated course in the optic radiations and their separate representation in the occipital pole. The immunity of the macula in vascular lesions of the cortex is attributed to the fact that the occipital pole is supplied by the posterior and middle cerebral arteries, both of which are seldom blocked at the same time. The explanation in other cases is not so obvious. In certain cases the sparing of the macula may be only apparent owing to a functional shift of fixation towards the seeing part of the retina, while in other cases a possible explanation may be sought in the integrative powers of the central visual mechanism. In infrageniculate lesions the fixation point is usually bisected.

Lesions of the lateral geniculate body cause homonymous hemianopia (Fig. 31.2); those limited to the pulvinar and superior colliculus do not.

Cortical and subcortical lesions: The majority of cases of hemianopia are due to lesions above the primary visual centres, usually in the occipital lobe or optic radiations (Fig. 31.2A: 6, 8). The chief causes are injury by falls on the back of the head, gunshot wounds, cerebral tumour, or cerebral softening due to disease of the blood vessels. In gunshot wounds both occipital lobes may be injured; there is usually unconsciousness from concussion at first and the hemianopia becomes manifest with recovery. If both lobes are extensively injured there is complete blindness; often, however, some portion of the cortex of one or other calcarine fissure escapes, and in these cases some measure of central vision is regained. In less extensive injury the hemianopic symptoms may gradually improve. The first sign of improvement is the perception of the movement of objects in the affected field without recognition of their nature and details.

The onset of hemianopia due to intrinsic disease of the cortex is more gradual, and careful investigation with the perimeter shows that the colour fields are often lost before the field for white light, although this is always contracted. This *hemiachromatopsia* is itself of gradual onset. In cortical and subcortical lesions the pupillary reactions are normal *(see* Chapter 4), and the fundi reveal no ophthalmoscopic changes, except in the case of tumours which may be associated with bilateral

papilloedema. Cortical lesions are liable to be accompanied by word blindness, usually due to involvement of the angular gyrus. When the lesion is in the posterior part of the internal capsule hemianaesthesia, with or without hemiplegia, is likely to be present. Optokinetic testing in occipital lobe hemianopias should elicit a normal response to each side. A depression of the response toward the side of the lesion implies involvement of the parietal lobe and indicates the possibility of a neoplastic aetiology rather than a vascular cause.

Occipital lobe hemianopias are extremely congruous, having a homogeneous density with sparing of the macula. Riddoch phenomenon, in which appreciation of a dim kinetic target is retained within the defective visual field with loss of appreciation of a static bright target, is typical of an occipital lesion.

Rare cases of homonymous *quadrantanopia* have been reported, in which corresponding quadrants of each field—the upper or lower half of one temporal, and the upper or lower half of the other nasal—have been lost. These may be caused by cortical or subcortical partial lesions of one occipital lobe, destruction of the part above the calcarine fissure leading to loss of the lower quadrants and *vice versa (see* Fig. 4.4). A similar quadrantic defect occurs in lesions of the temporal lobe owing to the fact that a ventral band of the optic radiations passes first forwards and then backwards in the temporal lobe in its course from the lateral geniculate body to the occipital lobe (Fig. 31.2A: 5). Partial hemianopia of a quadrantic type is then commoner than the typical homonymous defect, usually greater on the side of the lesion. Subjective sensations of smell occur in some of these cases, due to the involvement of the uncinate process of the hippocampal gyrus.

Lesions of the optic tract: In these cases, since the afferent pupillary fibres part company with the visual fibres before the latter enter the lateral geniculate body, Wernicke hemianopic pupil reaction should be present, but the reaction is always difficult to elicit. More assistance in diagnosis is afforded by collateral symptoms. The proximity of the crus cerebri, third and other cranial nerves, leads to other complications in the pathological picture. For example, the association of right homonymous hemianopia with left third nerve paralysis and right hemiplegia suggests a lesion affecting the left optic tract. As a rule the fixation point does not escape in tract hemianopia (Fig. 31.3). Partial atrophy of both optic nerves manifests itself by pallor of the discs in these cases, preceded in cases of raised intracranial pressure by papilloedema. The lesion is usually syphilitic meningitis or a gumma, tuberculosis or tumour of the optic thalamus or temporosphenoidal lobe; softening and haemorrhage are rare. It is important that the patient is often subjectively unaware of his visual defect in lesions above the geniculate body, but is conscious of a hemianopic defect from geniculate or infrageniculate causes. Primary lesions of the optic tract are very rare and the tract is usually disturbed by compression. Chordomas, pituitary adenomas, tentorial meningiomas, temporal lobe gliomas or aneurysms of the upper basilar distribution or on the superior cerebellar arteries or posterior cerebral arteries are the common causes. Tract hemianopias are incongruous with a variation in density.

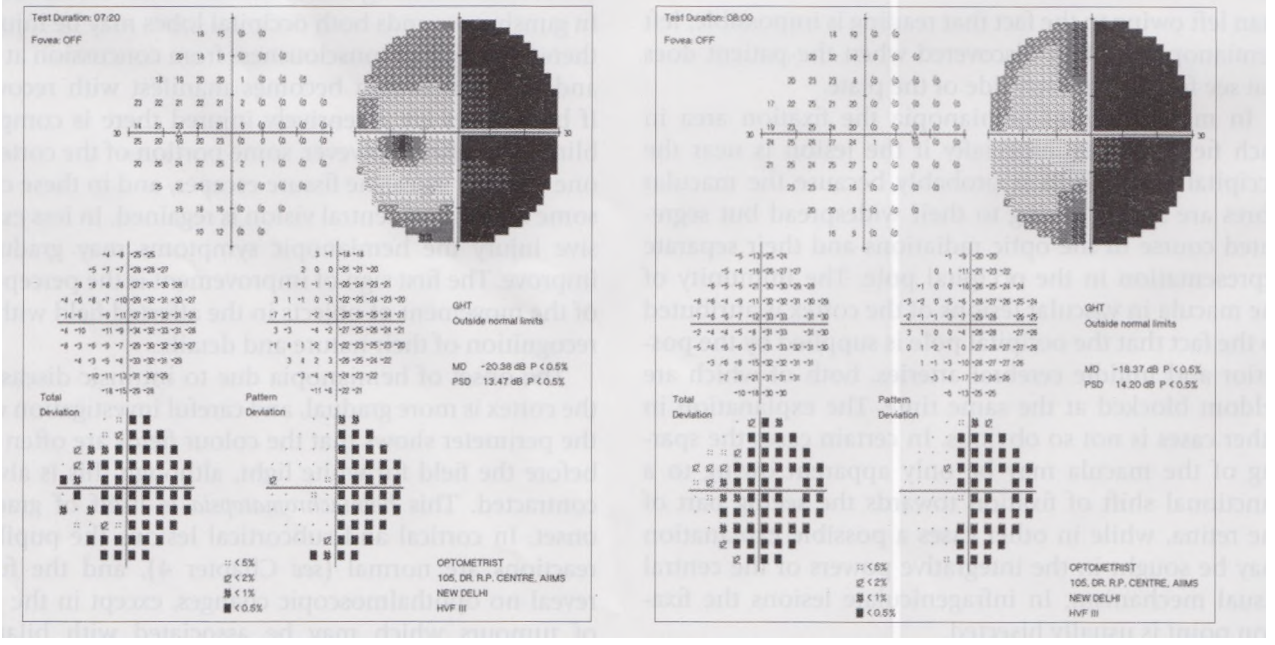


Fig. 31.3 Homonymous hemianopia.

Lesions of the optic chiasma: Bitemporal hemianopia is usually caused by tumours in the region of the sella turcica, pressure by a suprasellar aneurysm or by chronic arachnoiditis; these press upon the chiasma, so that the fibres going to the nasal halves of each retina are destroyed (Fig. 31.2A: 3). Tumours of the pituitary body are most common; but suprasellar tumours, particularly craniopharyngiomata derived from Rathke pharyngeal pouch and suprasellar meningiomata must be considered. Other lesions are gliomas of the third ventricle, ectopic pinealomas, dermoid tumours and third ventricular dilatation due to obstructive hydrocephalus.

Enlargement of the pituitary body, whether from functional hyperplasia, adenoma, or malignant growth, leads to visual defects in about 80% of cases, due to pressure upon the chiasma which lies immediately above it and upon the inner sides of the optic tracts. The earliest visual symptoms may be a unilateral central *scotoma* simulating retrobulbar neuritis, for one side is usually compressed before the other. There may be contralateral superior quadrantanopia due to involvement of von Willebrand knee which consists of fibres from the inferonasal retina of the other side which loop forward slightly into the opposite optic nerve after crossing over in the chiasma (Fig. 31.2A and B). This may be followed by homonymous hemianopia from pressure on one tract, or rarely by *altitudinal hemianopia,* i.e. loss of the upper or, more rarely, the lower halves of the fields from pressure upon the chiasma; early loss in the upper half of the field may be caused by intra- or extra-sellar tumours, early loss in the lower half suggests a suprasellar tumour. More commonly, bitemporal hemiachromatopsia, passing into a bitemporal hemianopia, supervenes. The field does not show the accurate delimitation characteristic of homonymous hemianopia, but gradually contracts from the temporal side inwards and from above downwards, finally involving the nasal field from below upwards and leading to complete blindness. Complete temporal hemianopia in one eye may also be associated with temporal achromatopsia in the other; such a combination emphasizes the importance of charting the colour fields in all cases. Many patients may have a homonymous hemianopia, due to pressure and traction on one optic tract. Variations in the type and progress of the visual defects are thus not uncommon. This often occurs because of variation in the site of pressure and also anatomical variations in the position of the chiasma relative to the sella, i.e. central, pre-fixed or post-fixed.

A chronic *chiasmal arachnoiditis* of obscure origin may also cause bitemporal hemianopia due to compression of the chiasma by fibrous cicatricial bands. The same field defect has also resulted from anteroposterior injury to the chiasma in fracture of the base of the skull.

Binasal hemianopia is very rare. It necessitates two lesions, one on each side of the chiasma, destroying the fibres to the temporal halves of each retina while leaving the nasal fibres intact. It may be due to distension of the third ventricle, causing the optic nerves to be pressed downwards and outwards against the internal carotids, or to atheroma of the carotids or posterior communicating arteries.

Cases have been described in which there has been some loss in the temporal field in one eye and depression of vision progressing to blindness in the other. These are due to a lesion at the point where one optic nerve meets the chiasma so that the crossed fibres from the opposite side are involved as they loop forward into the nerve (Fig. 31.2A and B).

In all cases of chiasmal damage a careful survey of the CNS must be made as well as an enquiry into the function of the pituitary. X-rays may provide valuable information, showing, for example, erosion of the sella, enlargement of the pituitary fossa or vascular calcification; simple radiography should be supplemented by computerized tomography. If, as frequently occurs, vision progressively deteriorates, transfrontal or nasopharyngeal extirpation may be advisable in many cases, particularly of pituitary tumours; the prognosis of operative removal, if undertaken in time, is reasonably good.

THE OCULAR MOTOR SYSTEM AND NEUROLOGICAL DISORDERS

Extraocular muscle paresis

Neurological disorders can affect the control of eye movements by involving the higher cortical centres (supranuclear lesions), the cranial nerve nuclei or the nerve fasciculi within the brainstem (brainstem syndromes), the nerve trunks, the neuromuscular junctions (myasthenia gravis, Eaton-Lamben paraneoplastic syndrome) or the muscles themselves (myopathies). Clinical features of paralytic squints are described in Chapter 27.

Nuclear and fascicular palsies can be due to several causes but are commonly due to trauma or intrinsic tumours in children; trauma, demyelinating disease or tumours in young adults and vascular lesions such as haemorrhage or infarction or tumours in older adults. Lesions of the nerve trunks could be anywhere along the intracranial course or locally in the orbit and could be due to compression, ischaemia or inflammation.

Skew deviation is a hypertropia that is caused neither by a peripheral neuromuscular lesion nor by a local mechanical factor in the orbit. Lesions within the CNS cause skew deviation but scanty evidence for localization suggests a posterior fossa lesion.

Skew deviation is characterized by a maintained deviation of one eye above the other, frequently fixed for all directions of gaze but equally often variable for different directions of gaze. It may simulate palsies of individual

vertically acting muscles and be differentiated from these only through the absence of mid-brain or peripheral nerve disease.

Skew deviation may occur with any lesion of the brainstem or cerebellum but is more common with unilateral than with bilateral lesions. It is characteristically present with unilateral internuclear ophthalmoplegia. The eye on the side of the lesion is usually hypotropic. The fact that a vertical divergence occurs on stimulating the labyrinth or with unilateral labyrinthine disease suggests that the pathogenesis of skew deviation is linked with the vestibulo-ocular pathways. It is found with cerebellar tumours, acoustic neuromas, compressive lesions, platybasia and vascular accidents of the pons and cerebellum (especially thrombosis of the cerebellar and pontine arteries). It is infrequent with demyelinating lesions.

Nystagmus

Nystagmus (to nod) is the term applied to rapid oscillatory movements of the eyes, independent of normal eye movements. The oscillations are involuntary, although in rare cases normal persons can imitate them. They are usually lateral, but vertical, rotatory and mixed (rotatory and lateral or rotatory and vertical) nystagmus occur. The condition is almost always bilateral, although the movements may be much more marked in one eye than the other.

Aetiopathogenesis and classification

Nystagmus occurs because of a disturbance in the sensory-motor apparatus controlling normal binocular position. Nystagmus can be classified into various types (Table 31.1).

Congenital jerky nystagmus is not associated with any recognizable pathological lesion in the eyes. The causative lesion probably lies in the complex nervous mechanisms in the brainstem, which are concerned in the centring and 'steady fixation' of the eyes. Nystagmus may be regarded as an exaggeration of the fine persistent movements of the eyes (microsaccades, slow-motion random drifts, and rapid impulsive saccades which correct the random drifts) which are essential in the maintenance of a clear foveal projection of the retinal image.

Table 31.1 Classifications of nystagmus

Based on aetiology

A. Physiological
- End-gaze
- Optokinetic
- Vestibulo-ocular reflexes

B. Pathological

1. Congenital
   a. Infantile manifest
      - Idiopathic
      - Albinism
      - Aniridia
      - Leber congenital amaurosis
      - Bilateral optic nerve hypoplasia
      - Bilateral congenital cataracts not operated within 6 months of age
      - Rod monochromaticism
   b. Infantile latent
   c. Infantile manifest—latent
   d. Nystagmus blockage syndrome

2. Acquired
   a. Secondary to visual loss
   b. Toxic or metabolic (alcohol, lithium, barbiturates, phenytoin, salicylates, benzodiazepines, phencyclidine, other anticonvulsants or sedatives, Wernicke encephalopathy, thiamine deficiency)
   c. Neurological disorders (tumour, trauma, multiple sclerosis, stroke, thalamic haemorrhage)
   d. Non-physiological, non-organic or 'functional'

Based on pattern of manifestation

A. Manifest
B. Latent
C. Manifest—latent

Based on direction of movement

A. Horizontal
B. Vertical
C. Rotary (rotatory)

Based on pattern of movement

A. Jerky/jerk
B. Pendular

Nystagmus in adults occurs in diseases of the midbrain, cerebellum and vestibular tracts, and of the semicircular canals. It is common in MS wherein the movements are generally horizontal and are elicited in the early stages only in extreme lateral position of the eyes. Cerebellar irritative lesions cause coarse nystagmus towards the side of the lesion and fine nystagmus to the opposite side. Nystagmus may also occur in adults as an 'occupation neurosis,' the commonest form being 'coal-miners' nystagmus

Clinical features

In congenital and early infantile nystagmus the patient is wholly unaware of the movements, since objects do not appear to move. *To-and-fro movement* is noticed by parents or relatives. Vision is usually defective in spite of correction of errors of refraction which generally accompany the defect. Visual symptoms of oscillopsia are usually absent when the onset is less than 8 years of age. In some cases of acquired nystagmus in adults, objects appear to move (oscillopsia). *Oscillopsia* is the perception of the environment appearing to oscillate horizontally, vertically or torsionally. Others may complain of blurred or unstable vision.

On examination, repetitive oscillations of the eye horizontally, vertically or torsionally are looked for. In some cases the movements are very fine and not easily detectable. In such cases it may be necessary to examine the eye very carefully with an ophthalmoscope because the presence of nystagmus can be demonstrated in the magnified ophthalmoscopic image. Unilateral nystagmus does occur, but it is probable that many of the cases described are really bilateral. Generally the eye movements in nystagmus can be slow, fast; fine, coarse; horizontal, vertical, rotatory, mixed; jerky (slow drift in one direction as slow phase followed by an abrupt return to normal position by fast phase, cyclic pattern) or pendular (drift occurs in two phases of equal speed with a smooth back-and-forth movement of the eye).

In *latent nystagmus* no movement is present when both eyes are open but nystagmus is elicited only when either eye is covered. The fast phase of nystagmus beats towards the viewing eye. Latent nystagmus is often associated with *alternating sursumduction* or *dissociated vertical deviation* characterized by either eye slowly elevating with an excyclorotation when the eyes are dissociated. This may occur spontaneously when the patient is tired or day-dreaming or on occlusion of one eye. The deviation is usually bilateral but may be asymmetrical. *Manifest latent nystagmus* occurs in children with strabismus or decreased vision in one eye, in whom the non-fixating or poorly seeing eye behaves as an occluded eye. When either eye is covered, the nystagmus increases.

Nystagmoid jerks—larger rhythmic jerking movements, most pronounced at the extreme limits of the normal movements of the eyes—should be distinguished from true nystagmus. They are not uncommon in normal people in certain conditions such as fatigue. It is a jerk-type nystagmus which is slightly more pronounced in the abducting eye and is poorly sustained. The rapid component is in the direction of gaze. The fundamental cause is probably quite different from that of true nystagmus, although both may occur together.

Optokinetic nystagmus has already been described.

Nystagmus may be *congenital* or *early infantile,* or it may be *acquired.* These two groups of cases should be carefully distinguished on account of their different pathological foundations. Congenital and early infantile nystagmus dating from birth or within a few weeks of birth occurs in congenitally malformed eyes, in albinism, and in eyes with congenital or early acquired opacities of the media (such as leucoma or cataract) or macular disease. The cause in these cases is inability to develop normal fixation. Fixation is normally developed during the first few weeks of life, the eyes being moved aimlessly and independently before it is acquired. Any cause operative at this period seriously diminishing the acuity of macular vision is liable to give rise to nystagmus; if the eye is totally blind, nystagmus does not develop but vague 'searching movements' are seen. Nystagmus is present in most cases of total colour blindness in which vision is carried out by the rods alone, and there is therefore a central scotoma. In some congenital cases it is impossible to discover any cause. In a few such cases ancestors or relations have been albinos.

Nystagmus in infancy may be acquired after the period at which fixation is developed. This form occurs in the first year of life as *spasmus nutans,* in which it is associated with nodding movements of the head. The nodding of the head may be anteroposterior (affirmation), lateral (negation) or rotatory. It develops some weeks before the nystagmus, ceases during sleep, and disappears before the nystagmus. The nystagmus is very fine and rapid, and may be vertical, rotatory or lateral and is generally more marked in one eye. The whole symptom-complex disappears in time—one of the few cases in which nystagmus spontaneously resolves. The nystagmus may disappear in one eye before the other; such cases may be mistaken for true unilateral nystagmus. In rare cases head nodding with nystagmus is congenital and hereditary, a condition which persists throughout life.

Nystagmus blockage syndrome is a specific type of disorder where nystagmus decreases when the fixating eye is in adduction and patients demonstrate esotropia to dampen the nystagmus.

There are some important types of nystagmus with localizing neuroanatomical significance and these are briefly described in the following paragraphs.

See-saw nystagmus: One eye rises and intorts while the other descends and extorts and then the reverse is seen. Also called *see-saw nystagmus of Maddox,* this is a disjunctive pendular type of nystagmus in which the patient's eyes move in opposite directions with an associated torsional component. It is classically considered as a sign of parachiasmal disease and the lesion usually involves the chiasma or third ventricle or both.

Convergence and retraction nystagmus: These are two special forms found with neurological damage localized to the upper mesencephalon. On attempted upgaze, the eyes display convergence-like movements accompanied by retraction of the globe. This occurs most commonly due to a pineal gland tumour or other mid-brain abnormalities involving the aqueduct of Sylvius known as Parinaud syndrome or Sylvian aqueduct syndrome. In young patients, retraction nystagmus should suggest the diagnosis of mid-brain glioma or pinealoma. The characteristic ocular features of the Sylvian aqueduct syndrome consist of

1. retraction (and/or convergence) nystagmus;
2. vertical nystagmus;
3. difficult voluntary vertical gaze (especially upward gaze);
4. better vertical gaze on following or 'doll's-head movements' than on command (with an intact Bell phenomenon);
5. adduction movements with attempted vertical gaze;
6. defective convergence;
7. retraction nystagmus with downgoing optokinetic targets;
8. pupillary abnormalities (light-near dissociation) and
9. pathological lid retraction.

Upbeat nystagmus: The fast phase is upwards. The commonest site of the lesion is the vermis of the cerebellum or the brainstem when nystagmus is present in the primary position. If present only in upgaze, upbeat nystagmus is most likely due to drug toxicity (phenytoin).

Downbeat nystagmus: The fast phase is downwards, and indicates posterior fossa dysfunction often at the foramen magnum level. The lesion is usually at the cervicomedullary junction (Arnold Chiari malformation).

Rebound nystagmus: The fast phase is in the direction of gaze but fatigue occurs with sustained gaze, and the fast phase changes direction. When the gaze is returned to the primary position, the fast phase increases in the direction the eye takes in returning to the primary position. Cerebellar lesions are the most common cause.

Gaze-evoked nystagmus: In gaze-evoked nystagmus there is no movement of the eyes in the primary position and nystagmus appears as the eyes look to the side. As the patient's gaze is gradually diverted in any direction, particularly horizontally, a rather coarse, jerk-like nystagmus develops with its rapid phase in the direction of gaze and increases when looking in the direction of the fast phase. This builds to a maximum intensity in the extremes of conjugate gaze and is well sustained. This appears as the eyes look to the side and is absent in the straight-ahead position. The frequency is slow (3-8beats/second on an electronystagmogram). The common causes include alcohol intoxication, sedatives (barbiturates), cerebellar or brainstem disease.

Gaze-paretic nystagmus: This has a frequency of 1 -2 beats/second and the eye tends to return to the primary position with the slow phase of the nystagmus. This nystagmus disappears completely when total gaze paralysis occurs. It is always seen in association with some degree of conjugate gaze weakness. It is common in brainstem disorders at the pontine level.

Periodic alternating nystagmus: Fast eye movement is in one direction for 60-90 seconds, then the reverse direction for 60-90 seconds. This cycle is repeated continuously. It may be congenital or acquired and it may be caused by blindness, or by lesions at the cervicomedullary junction.

Vestibular or labyrinthine nystagmus: This may be horizontal or horizontal-rotary. It may be accompanied by deafness, vertigo, tinnitus and may be due to disease affecting the vestibular end-organ (inner ear), eighth cranial nerve or nucleus. Destructive lesions produce a fast phase opposite to the affected end organ or nerve. Irritative lesions produce fast phase in the same direction. Vestibular nystagmus with interstitial keratitis is known as Cogan syndrome. Labyrinthine nystagmus occurs in disease of the internal ear in which the semicircular canals are involved, and can be produced in normal subjects by rotation in a specially designed chair or by syringing the ears. Conjugate movement to the opposite side may be induced by syringing one ear with cold water, mimicking a destructive lesion or to the same side with warm water (remembered by the mnemonic COWS or cold opposite, warm same side). Vertical gaze upwards may be induced by syringing both ears with cold water and vertical conjugate gaze downwards induced by syringing both ears with warm water (mnemonic CUWD or cold up, warm down). The nystagmus is rhythmic, with a rapid and a slow component, is bilateral, and horizontal or rotatory, but varies according to the semicircular canal stimulated. Any pair of semicircular canals can also be stimulated by rotation with the head in a suitable position. Destruction of one labyrinth causes rhythmic nystagmus towards the opposite side, which ceases if the other labyrinth is destroyed.

Miners' nystagmus: This occurs chiefly in those who have worked for a long time at the coal face. The patient complains of defective vision, which is worse at night, headache, giddiness, photophobia, the dancing of lights and movement of objects. The nystagmus is essentially rotatory and very rapid; in latent cases it is elicited by fixing the head and making the patient look up. In severe cases, the lids are nearly closed and the head is held backwards; there is tremor of the head and eyebrows. The frequency of the disease varies inversely with the illumination in the mine, suggesting that fixation difficulties in the dim illumination may be an aetiological factor; it will be remembered that vision in a dull light is carried out almost entirely by the rods. In these circumstances visual acuity is greatest 10-15% outside the fovea, and there is a physiological central scotoma making fixation difficult. There is, however, a large psychoneurotic factor in all cases. Improvement in miners' lamps and in the lighting of mines eliminated the disease.

Differential diagnosis

There are a number of ocular motility disorders, which occur in childhood and resemble nystagmus. This group includes ocular bobbing, flutter-like oscillations of the eyes, ocular dysmetria, opsoclonus, ataxic conjugate movements of the eyes and ocular myoclonus.

In *ocular bobbing* the eyes remain motionless in the primary position and then suddenly the eyes deviate downwards or, less commonly, upwards after which they slowly return to the primary position. Children with this affliction characteristically have loss of caloric responses on cold-water irrigation of the ears with total horizontal conjugate gaze palsies. They usually have a massive neoplastic lesion involving the pontine brainstem and the prognosis is extremely poor.

Flutter-like oscillations of the eyes and ocular dysmetria are ocular signs of interruption of cerebellar connections into the brainstem. They represent the dysmetric overshoots of the eyes and inability to fixate a target accurately when gaze is shifted from one point in space to another. The eyes may either overshoot (or undershoot) the target.

Opsoclonus consists of wild, chaotic, apparently conjugate movements of the eyes. There are frequent myoclonic movements of the face, arms and legs. Patients have a clear sensorium; the disorder often follows an episode of benign encephalitis and usually has a good prognosis.

Oculopalatal myoclonus is an unusual disorder in which the patient develops associated movements of the eyes, palate, face, platysma, larynx, eustachian tube orifice, tongue and occasionally the extremities. It follows severe brainstem damage in the myoclonic triangle, which has as its boundaries the red nucleus above, inferior olive below and dentate nucleus of the cerebellum posteriorly. It occurs most commonly in association with vascular disease or as a sequel of brainstem encephalitis.

Evaluation and treatment

A careful history must be taken to ascertain age of onset, presence of oscillopsia, history of strabismus or amblyopia, or previous treatment, drug or alcohol use, associated symptoms such as tinnitus, vertigo, numbness, motor deficit or diminished vision as well as occupational and family history. Complete ocular examination (look for albinism), recording of eye movements, visual fields, drug levels in the urine, serum or both, neurological examination to rule out diseases of the CNS, and neuroimaging with CT or MRI as needed should be carried out. If the nature of nystagmus suggests lesions in the cerebellum or cervicomeduilary junction, an MR scan is preferable to a CT scan.

Therapeutic modalities available to manage nystagmus include optical aids such as spectacles, prisms and contact lenses; medications for specific conditions; biofeedback training mechanisms to reduce nystagmus; and surgery to reduce nystagmus and eliminate abnormal head posture. Whenever possible, the underlying aetiology must be identified and appropriately treated. Periodic alternating nystagmus may respond to baclofen (5 mg orally thrice daily increased gradually by 15 mg/day every 3 days until a maximum of 80mg/day). Baclofen is not recommended for use in children. Acquired pendular nystagmus is known to respond to gabapentin. Refractive errors must be corrected, preferably with contact lenses, and amblyopia treated by either occlusion or penalization. Attempts have been made to convert the movements of a nystagmus into audible stimuli, which can be heard by the subject who uses this feedback signal to control the nystagmus by maintaining a constant tone.

Nystagmus in the primary position of gaze remains a particularly troublesome disorder, which is relatively refractory to medical intervention. A typical example is downbeat nystagmus seen in lesions of the posterior fossa. T his type of nystagmus sometimes responds to treatment with clonazepam, a long-acting benzodiazepine. The slow eye movement is responsible for the genesis and continuation of the oscillation, with the fast eye movement playing only a corrective role. Clonazepam markedly alters the slow phase of the nystagmus and this effect may improve visual acuity, unless there is some other cause for the lowered vision.

Indications for surgery are visually disabling nystagmus with excessive excursions or a 'null point' in extreme lateral gaze, in which the patient has to maintain an uncomfortable and abnormal head posture to see clearly The basic aim of surgical treatment is to transfer the 'neutral point' (where the nystagmus is least apparent) from an eccentric position to a straight-ahead position so that

there is an elimination of the compensatory head posture. Prismotherapy may be applied to achieve the same effect. The Faden operation is based on the idea that the necessary muscle force for any given ocular movement steadily increases after leaving the arc of contact of the globe. The operation consists of creating a second insertion of certain extrinsic ocular muscles (usually both medial recti) at least 10 mm behind the physiological insertion. Surgery to shift the null point to the primary position (Kestenbaum or Anderson procedure), or to generally reduce the amplitude (supramaximal recession of all four horizontal recti) is sometimes needed for congenital nystagmus. Severe, disabling nystagmus can be treated with retrobulbar injections of botulinum toxin.

VASCULAR DISORDERS

Intracranial aneurysms

Aneurysms that are of ophthalmological interest affect the circle of Willis, its branches or the major arteries forming the circle (Fig. 31.4). Sites of aneurysms most likely to have ophthalmological manifestations are (i) the junction of the internal carotid-posterior communicating artery causing third nerve palsy; (ii) the carotid-ophthalmic artery junction causing compression of the optic nerve and/or chiasma; (iii) the intracavernous carotid artery causing extraocular muscle paresis, facial sensory loss over the region of the trigeminal nerve and rarely optic nerve compression and (iv) giant aneurysms of the basilar top which can produce ocular nerve palsies. Aneurysms of the internal carotid artery above the anterior clinoid process are termed supraclinoid and those below it, infraclinoid aneurysms.

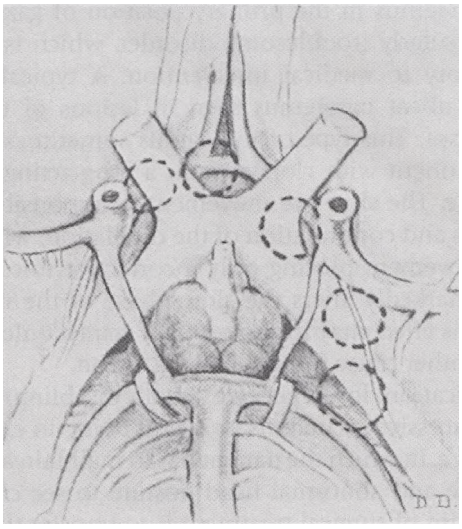


Fig. 31.4 The common sites of aneurysms in the chiasmal region. (By courtesy of Russell Brain)

In general, intracranial aneurysms are usually congenital or developmental in origin, though they frequently manifest later in life. They usually arise at the bifurcation of the vessels, for example, internal carotid artery into the middle and anterior cerebral arteries, internal carotid-posterior communicating artery, basilar artery bifurcation, etc. and give rise to ophthalmic symptoms in three ways as described below.

Mechanical pressure

Aneurysms may exert mechanical pressure on neighbouring structures by their slow growth, causing symptoms characteristic of a tumour in the chiasmal region, or oculomotor nerve palsy with pupillary involvement due to a posterior communicating artery aneurysm pressing on the oculomotor nerve. An intracranial aneurysm is the commonest cause of painful ophthalmoplegia.

Infraclinoid aneurysms produce symptoms by dilatation of the internal carotid artery within the cavernous sinus which affects the motor nerves to the eye and the ophthalmic and maxillary divisions of the trigeminal nerve. Expansion of the aneurysm gives rise to a slowly progressive ophthalmoplegia, severe pain and paraesthesia in the face associated with corneal anaesthesia. These aneurysms often grow to a large size and do not usually rupture but they may thrombose completely and thus cure spontaneously. Alternatively, the artery may dilate or expand and produce erosion of the optic canal with compression of the optic nerve.

Production of an arteriovenous fistula

Sometimes aneurysms of the internal carotid artery in its intracavernous part may rupture within the cavernous sinus and produce a carotid-cavernous fistula.

Production of subarachnoid haemorrhage

Aneurysms of the circle of Willis tend to rupture suddenly, resulting in subarachnoid haemorrhage. The majority of patients presenting with rupture of such an aneurysm are middle-aged women. There is a severe headache of sudden onset on one side of the head due to meningeal irritation followed later by a third nerve palsy with pupillary dilatation. Subarachnoid haemorrhage is in fact characterized by sudden violent pain in the head followed by photophobia and unconsciousness. Sudden loss ofvision is extremely rare. Abrupt loss of vision, swollen discs and exophthalmos are uncommon. A subhyaloid and vitreous haemorrhage *(Terson syndrome*) may present at the posterior pole. Death may occur from a subarachnoid haemorrhage or from bleeding into the brain tissue.

The first diagnostic procedure in a patient in whom subarachnoid haemorrhage is suspected should be a CT scan. Lumbar puncture shows fresh blood which on standing becomes xanthochromic, as opposed to a

traumatic tap. The current recommendation is that, as far as possible, lumbar puncture should be avoided so that a rebleed is not precipitated.

Vascular malformations of the nervous system

These are divided into four groups and include some varieties of a group of disorders called the phacomatoses (such as the Sturge-Weber syndrome, von-Hippel Lindau disease, etc.):

1. Capillary telangiectases
2. Cavernous angiomas
3. Venous malformations
4. Arteriovenous malformations

Capillary telangiectases are relatively common lesions generally found at necropsy. They are small and cause no symptoms. The commonest location is the pons.

Cavernous angiomas are an important potential source of bleeding. If they rupture there is severe intracranial haemorrhage. They can also manifest as space-occupying lesions and MR scan is the best diagnostic procedure. The lesions are usually solitary and well defined, often located on the surface of the cerebrum or within the brainstem and can be removed surgically.

Venous malformations are commonly found in the spinal cord and meninges but often occur in the scalp and the orbit. In the latter situation they cause intermittent exophthalmos, made worse on stooping. Histologically they are similar to arteriovenous malformations, except that arterial structures are absent. They consist of multiple veins of varying calibre. They can be seen on a venous angiogram and, if present in the orbit, are associated with a raised intraocular pressure and, eventually, a secondary form of glaucoma.

Arteriovenous malformations are the commonest of the four groups. Grossly they appear as a tortuous mass or a 'bag of worms'. They are composed of arteries and veins of abnormal calibre and length. They are classified according to their arterial supply, from the pial vessels, or the dural vessels derived from the internal or external carotid or vertebral artery; or from both the pial and dural vessels. They mostly manifest with acute haemorrhage and epilepsy and sometimes present with features of a space-occupying lesion (Fig. 31.5).

Arteriovenous fistulae

Arteriovenous fistulae are abnormal communications between the arterial and venous channels. Carotid-cavernous fistulae are the most important in relation to ophthalmology. These are abnormal communications between either the carotid arterial system and the cavernous sinus or between the dural veins and the cavernous sinus. They can be classified according to the anatomy *(direct arterial* versus *dural; internal carotid* versus *external carotid),* velocity of blood flow *(high flow* versus *low flow)* and aetiology *(traumatic* versus *spontaneous).*

Carotid-cavernous fistulae involve a direct communication between the wall of the internal carotid artery and the sinus itself. Such a fistula is a high-flow, high-pressure system which causes the arterialized blood to flow from the cavernous sinus forwards into the ophthalmic veins in the orbit. The ocular signs are related to venous congestion and reduced arterial blood flow to the orbit. These produce the classical signs and symptoms of severe ipsilateral headache, a homolateral carotid bruit, progressive exophthalmos, dilated and frequently pulsating episcleral blood vessels (Fig. 31.6), raised episcleral venous pressure and glaucoma, ocular ischaemia and

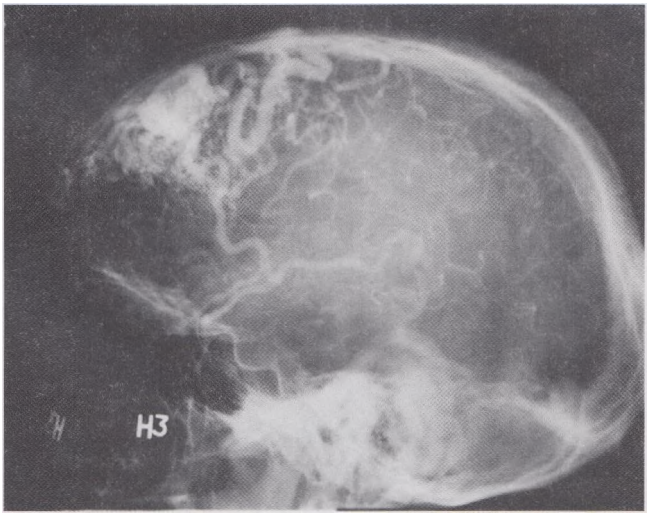


Fig. 31.5 Carotid angiogram showing an arteriovenous malformation with a 'bag of worms' appearance in the frontoparietal area. (By courtesy of PN Tandon)

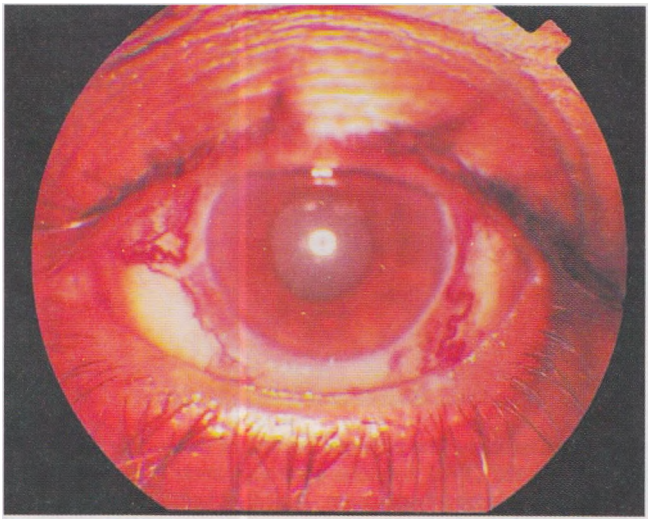


Fig. 31.6 Dilated episcleral vessels in a patient with carotid–cavernous fistula.

varying degrees of ophthalmoplegia. It may lead to progressive blindness due to a carotid-ophthalmic artery steal syndrome. There is a loud bruit audible over the carotid artery and the eye, which diminishes on manual compression of the carotid artery in the neck. Of carotid-cavernous fistulae, most (75%) are traumatic and are more common in young men; a few (25%) are spontaneous. Symptoms and signs usually respond to occlusion of the internal fistula by balloon catheterization or surgical ligation.

A slow-flow *cavernous sinus dural fistula* or malformation is derived from the dural blood vessels in the cavernous sinus. The signs and symptoms associated with these dural shunts are essentially the same as those seen with classical carotid-cavernous fistulae except that they are more subtle. The dural arteriovenous shunts may be within the cavernous sinus or directly adjacent to it, or they may involve a more distant sinus and subsequently drain into the cavernous sinus. They are more common in the elderly especially women and may develop spontaneously or in the presence of underlying systemic conditions such as atherosclerosis, hypertension, collagen vascular disease, during or after childbirth and, in some cases, are probably due to a local congenital vascular malformation. Associated symptoms are headache which is severe, unilateral, often localized to the orbit, temple or forehead. Proptosis is minimal. Dilated conjunctival vessels are common and produce a red eye without pulsation. Raised intraocular pressure is common but mild. Unilateral sixth nerve palsy is a frequent finding. An objective bruit is heard in half the cases. Dural arteriovenous fistulae may be associated with spontaneous choroidal detachments. Misdiagnosis is more common with dural shunts than with carotid-cavernous fistulae. Dural shunts have been misdiagnosed as chronic conjunctivitis, orbital cellulitis, orbital pseudotumour or thyroid eye disease.

Radiographic diagnosis requires CT scan, MR imaging, computer Doppler imaging and complete selective cerebral angiography using subtraction and magnification techniques (Figs 31.7 and 31.8).

Because these lesions involve the dural vessels they may be amenable to embolization in selected cases. Selective catheterization with embolization of the feeding vessels by a transfemoral artery approach and the use of ground-up pieces of gel-foam may close the shunt.

Vasculopathies and cerebral occlusive disease

Occlusive vasculopathies could be embolic, thrombotic or vasospastic. They could be due to underlying systemic cardiovascular disorders such as cardiac arrhythmias of which atrial fibrillation is a common culprit, atherosclerosis, hypertension, diabetes, migraine, inflammatory arteritis such as that associated with giant cell arteritis, polyarteritis nodosa and systemic lupus erythematosus, further aggravated by additional risk factors such as obesity and smoking. The classic visual symptom is that of amaurosis fugax.

Amaurosis fugax

Aetiopathogenesis: A transient decrease in blood supply to the eye or optic nerve could occur due to (i) an embolus from the carotid artery (which is most common), heart or aorta; (ii) vascular insufficiency due to arteriosclerotic or atherosclerotic occlusive vascular disease of the vessels anywhere along the path of blood flow to the eye from the aorta to the globe. This causes hypoperfusion which may be precipitated by a sudden postural change

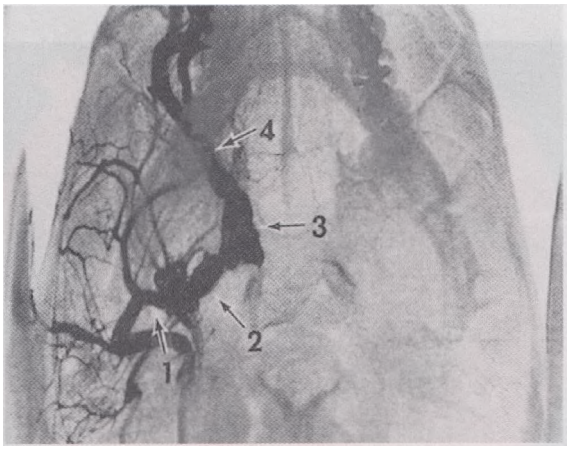
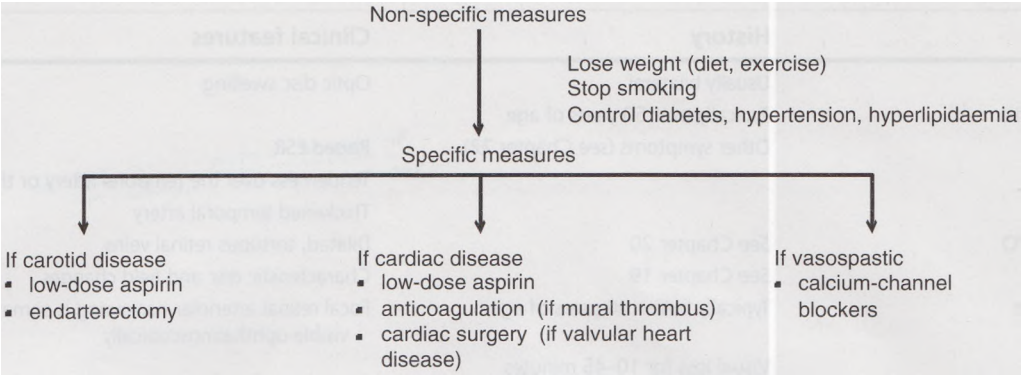


Fig. 31.7 Base view. The proximal portion of the middle meningeal vessel is dilated (1). A fistulous communication is present in the region of the foramen spinosum. A dilated vein (2) extends from the region of the foramen spinosum to the posterior portion of the cavernous sinus (3). The superior ophthalmic vein (4) fills in a retrograde direction. (By courtesy of Costin)



Fig. 31.8 After embolization the middle meningeal and superficial temporal arteries fill normally. The fistulous communication to the cavernous sinus has been occluded. (By courtesy of Costin)



Flowchart 31.1 Treatment of amaurosis fugax.

or cardiac arrhythmia; (iii) hyperviscosity or a hypercoagulable state of the blood such as polycythaemia vera, thrombocytosis and chronic myeloid leukaemia and rarely (iv) an intraorbital tumour compressing the optic nerve or a nourishing vessel in certain gaze positions causing transient visual loss.

Clinical features: Monocular transient, recurrent episodes of visual loss characterize this syndrome. Visual loss lasts for seconds to minutes, but may last up to 1-2 hours and then return to normal. Ophthalmoscopy may reveal an embolus visible within a retinal arteriole or ocular examination may even be completely normal. Sometimes other signs of ocular ischaemia (*see* Fig. 9.3), old branch retinal artery occlusion (BRAO), or other neurological signs caused by cerebral ischaemia such as a history of transient ischaemic attacks (TIA) and contralateral arm or leg weakness may give supportive evidence of an underlying vasculopathic disease.

Differential diagnosis: Other causes of transient visual loss must be excluded (Table 31.2). Relevant investigations include

- recording of the blood pressure;
- urgent erythrocyte sedimentation rate (ESR) to rule out giant cell arteritis;
- complete blood count with differential leucocyte and platelet counts to rule out polycythaemia, thrombocytosis and leukaemia;
- medical examination including cardiac and carotid auscultation;
- fluorescein angiography;
- ophthalmic colour Doppler ultrasound to look for retrolaminar central retinal artery stenosis or embolus;
- non-invasive carotid artery evaluation by colour Doppler, ultrasound and MR angiography;
- echocardiogram for cardiac evaluation and
- serum biochemistry including fasting and postprandial blood glucose, glycosylated haemoglobin and serum lipid profile to rule out diabetes mellitus and hyperlipidaemia.

Treatment: This consists of treating the general systemic diseases resulting in transient visual loss, as well as undertaking certain specific measures for cardiac or carotid diseases (Flowchart 31.1).

Carotid occlusive disease or ocular ischaemic syndrome

Aetiopathogenesis: Atherosclerotic occlusive carotid artery disease usually causes more than 90% stenosis before it manifests as ocular ischaemia syndrome. An ulcerative atherosclerotic plaque in the carotid artery may produce ischaemic syndromes even before the narrowing of the artery reaches this level. It can also occur with involvement of the ophthalmic artery but this is less common.

Clinical features: These include decreased vision, ocular or periorbital pain, sometimes a history of amaurosis fugax, and delayed dark adaptation with an after-image or prolonged recovery of vision after exposure to bright light. It is usually unilateral, males being more commonly affected (2:1), and occurs typically in the older population (50-80 years of age). Ocular signs include dilated retinal veins with irregular calibre but no tortuosity. There is narrowing of the retinal arterioles. Mid-peripheral retinal haemorrhages are seen in 80% of patients, rubeosis iridis or neovascularization of the iris in 66% and posterior segment neovascularization in 37%.

Non-ophthalmic manifestations of carotid artery insufficiency *include* TIA, i.e. features of focal motor or sensory deficit which resolve spontaneously within 24 hours.

Differential diagnosis: Carotid occlusive disease has to be differentiated from the following:

- Central retinal vein occlusion (CRVO), but this usually has tortuous veins, disc oedema and sometimes opticociliary shunt vessels can be seen on the disc.

Table 31.2 Conditions which produce transient visual loss

Condition	History	Clinical features
Papilloedema	Usually bilateral	Optic disc swelling
Giant cell arteritis	Typically over 50 years of age	
	Other symptoms (see Chapter 22)	Raised ESR
		Tenderness over the temporal artery or the scalp
		Thickened temporal artery
Impending CRVO	See Chapter 20	Dilated, tortuous retinal veins
Glaucoma	See Chapter 19	Characteristic disc and field changes
Retinal migraine	Typically below 40 years of age	Focal retinal arteriolar narrowing is sometimes visible ophthalmoscopically
Migraine	Visual loss for 10–45 minutes prior to headache	
Vertebral artery dissection (from atherosclerotic disease or trauma)	Headache	Consistent with those of sudden arterial dissection

CRVO, central retinal vein occlusion.

- Diabetes mellitus (may produce similar manifestations), but is usually bilateral, with characteristic hard exudates.
- Aortic arch disease caused by Takayasu arteritis, aortoarteritis, atherosclerosis and syphilis should also be looked for and excluded.
- Hyperlipidaemic ophthalmopathy.

Evaluation includes examination of the peripheral pulses, cardiac and carotid auscultation, echocardiogram, recording of the blood pressure and investigations for diabetes mellitus and hyperlipidaemia. Non-invasive carotid artery evaluation by Doppler ultrasound and magnetic resonance angiography (MRA) should be done. Orbital colour Doppler ultrasound and ophthalmodynamometry can be helpful. The latter is useful if central retinal vein occlusion cannot be excluded, in which case the ophthalmic artery pressure is normal to raised, whereas in carotid artery disease it is low.

Treatment: This consists of controlling chronic systemic diseases such as diabetes mellitus and hypertension. The patient should be advised to stop smoking and lose weight and reduce cholesterol levels if raised. If required, carotid endarterectomy should be carried out and panretinal photocoagulation (PRP) performed if neovascularization is detected.

Glaucoma, if detected, is controlled with either drugs or surgery.

Vertebrobasilar insufficiency

Aetiopathogenesis: This is a vasculopathic disease affecting the vertebrobasilar arterial supply. It manifests with symptoms due to ischaemia of the brainstem and occipital cortex. Risk factors include diabetes mellitus, hypertension, hyperlipidaemia and cervical spondylosis.

Clinical features: These include episodes of transient blurred vision occurring bilaterally, lasting a few seconds to a few minutes which are sometimes accompanied by flashing lights. Other associated symptoms that may be present are transient diplopia, ataxia, vertigo, dysarthria, perioral paraesthesia, dysphasia, hemiparesis or hemisensory loss. The patient may also give a history of drop attacks (sudden episodes of falling to the ground without warning or loss of consciousness). However, the eyes are completely normal on examination.

Differential diagnosis: This includes other causes of transient visual loss (Table 31.2). A complete work-up should be carried out which includes all the tests as for carotid occlusive disease, ECG and 24-hour Holter monitoring to rule out sick sinus syndrome and ventricular ectopics, and MRA or transcranial and vertebral Doppler ultrasound to evaluate the posterior cerebral blood flow. X-rays of the cervical spine to rule out compressive disease of the cervical spine (degenerative changes especially osteophytes encroaching on the arterial foramina) are also required.

Treatment: This consists of non-specific measures as in occlusive carotid artery disease. Rarely, vertebral artery decompression may be required.

Cerebral haemorrhage and thrombosis

In the *occipital cortex,* the posterior cerebral artery is usually involved; it supplies most of the occipital cortex and much of the temporal lobe. A lesion of this vessel thus causes a crossed homonymous hemianopia often with disturbances of the visuopsychic areas *(see* Fig. 31.2A); the fixation area is usually spared owing to an overlapping blood supply from the middle cerebral artery at the

posterior pole. Obstruction of the middle cerebral artery produces visual agnosia with a crossed homonymous field defect affecting, preferentially, the upper quadrants of the field by involvement of the inferior optic radiations looping forward in the temporal lobe.

An acute lesion of the *premotor frontal cortex* affecting the *frontal eye field* causes a conjugate deviation of the eyes away from the side of the lesion as an irritative phenomenon, which is reversed later when paresis sets in so the deviation is to the same side as the lesion. These deviations are generally only observed in unconscious patients.

A haemorrhage in the *internal capsule* produces a conjugate deviation of the head and eyes towards the side of the lesion, with a contralateral hemiplegia. A haemorrhage into the *pons* (below the decussation of the corticofugal fibres) produces conjugate deviation of the head and eyes away from the side of the lesion, that is, towards the hemiplegic side, and a palsy of horizontal conjugate gaze to the side of the lesion. The pupils are extremely small—an important diagnostic sign in a comatose patient. Pin-point pupils are also seen in patients with thalamic haemorrhage.

Obstruction of the branches of the *basilar artery* in the brainstem produces symptoms depending on the implication of the ocular motor nuclei and the pyramidal tracts.

Obstruction of the *posterior inferior cerebellar artery* gives rise to a characteristic clinical picture resulting from infarction of a wedge-shaped area on the lateral aspect of the medulla. In addition to vertigo, dysphagia, signs of cerebellar deficiency and sensory disturbances due to trigeminal involvement, there is nystagmus and Homer syndrome (miosis, enophthalmos and ptosis) on the affected side.

Cortical blindness

Aetiopathogenesis: The most common cause is bilateral occipital lobe infarction. Unilateral infarction leads to contralateral homonymous congruous hemianopia. In both cases, the central macular region is spared with preservation of some central vision due to dual blood supply from the posterior cerebral artery (a branch of the vertebral artery), and the posterior communicating artery (a branch of the internal carotid artery system). Bilateral occipital infarcts result in cortical blindness characterized by its denial (Anton syndrome). Head injury is the second most common cause of Anton syndrome. A less common cause is a neoplasm involving the occipital cortex which could be a falcotentorial meningioma or multiple metastases.

Clinical features: Vision and visual fields are markedly decreased in both eyes when there is bilateral involvement, usually with sparing of the macula, but sometimes there may be complete visual loss with no light perception. Pupillary responses are normal. In unilateral cases there is contralateral congruous homonymous hemianopia.

An investigative work-up should be carried out as in other vasculopathic conditions, including a CT or MRI scan to identify the anatomical extent and nature of the lesion.

Treatment: It is guided by the underlying disease condition. Patients with stroke may recover vision partially or completely.

Giant cell arteritis

See Chapter 22.

Migraine

This is a periodic, typically unilateral, throbbing or boring headache accompanied by nausea, vomiting, mood changes, fatigue and visual disturbances. The term originated from Galen's usage of the word 'hemicrania' to describe a periodic disorder comprising paroxysmal blinding hemicranial pain, vomiting and photophobia, relieved by dark surroundings and sleep, known to recur at regular intervals. The word hemicrania was, with the passage of time, cormpted to hemigranea and then migrania, until the French translation migraine gained acceptance.

Aetiopathogenesis: For many years a purely 'vascular' hypothesis postulated that the headache phase of migrainous attacks was produced by extracranial vasodilatation, which corroborated with the prominent painful temporal artery pulsations described by many patients during headache, and that neurological symptoms were produced by intracranial vasoconstriction. However, over the past 50 years, attention has been focused on the concept that migraine is analogous to epilepsy and that clinically apparent circulating phenomena are actually secondary to neurophysiological changes in the cerebral cortex.

As currently understood, the pathogenesis is divided into three phases. The first is brainstem generation, the second vasomotor activation in which arteries, both within and outside the brain, may constrict or dilate, and the third is activation of cells of the trigeminal nucleus caudalis in the medulla (which is the brain's pain-processing centre of the head and the face), and the subsequent release of vasoactive neuropeptides at the vascular terminations of the trigeminal nerve. Activation of any one of these phases is sufficient for the production of headache and one phase may appear to dominate in a particular migrainous syndrome. Pharmacological data suggest serotonin receptors as being mainly responsible for triggering the neural origin of migraine. Migraine has been postulated to represent a hereditary perturbation of serotonergic neurotransmission.

Clinical features: Migraine affects nearly 10% of the population and is characterized by headache, but has been

Table 31.3 Classification of migraine based on clinical presentation

Clinical subtype	Frequency	Clinical features
Common migraine (headache without aura)	80%	Nausea, vomiting, mood changes and fatigue
Classic migraine (headache with aura)	10%	Headache is preceded (15–45 minutes) by visual disturbance or transient focal neurological symptoms
Acephalic migraine	Rare, debated	Visual aura of classic migraine without headache. May have focal neurological disturbances without headache or vomiting and are referred to as migraine equivalents or accompaniments. These are more common between the ages of 40 and 70 years.
Complicated migraine		Migraine with dramatic focal neurological features, thus overlapping with classic migraine, but in the latter the symptoms precede the headache while in complicated migraine they occur at the peak of the headache and persist longer. The term connotes a persisting neurological deficit that is a residuum of a migraine attack or when the neurological deficit outlasts the headache

classified into various subtypes according to the constellation of symptoms seen (Table 31.3). The usual site of headache is the frontotemporal region. It is usually unilateral but can be bilateral. When unilateral, in the majority of cases the headache changes sides to the other side of the head in different episodes. It affects all ages with the highest incidence in children and young adults. Among adults it is more common in females but among children girls and boys are equally affected. A family history is common. There may be a past history of car sickness or cyclical vomiting as a child. Migraine in children may manifest as recurrent abdominal pain and malaise. The episodes may start after awakening and are generally relieved by sleep.

The symptoms of migraine have been observed to have certain known associations or precipitating factors which include menstrual cycles, puberty, birth-control or hormonal pills, foods containing tyramine or phenylalanine (such as vintage cheeses, wines, chocolates, cashew nuts), nitrates or nitrites, monosodium glutamate, alcohol, fatigue, lack or excess of sleep, emotional stress or bright lights. The duration of each attack varies from 6 hours to 2 days. In migrainous women, the attacks are known to stop during pregnancy after the second trimester. Attacks occur in cycles of several months to a year, and become less frequent and less severe with increasing age.

Characteristic visual disturbances associated with classical migraine include zigzagging flashing lights *(fortification spectra),* blurred vision, or a visual field defect lasting 15-30 minutes, usually preceding the headache. The migraine may often be preceded by an 'aura' or an inexplicable 'sensation' of an impending migrainous attack. Patients may experience photophobia during the headache phase. Other neurological deficits such as hemiparesis may occur.

Neurological deficits that may accompany migraine can be of four types.

1. *Cerebral*—motor, sensory or visual. The onset can be at the height of the headache but, more commonly, it follows the headache. Focal motor deficits, speech disorder, paraesthesiae of the extremities, face, tongue or lips and even hemiplegia with total paralysis or weakness on one side of the body (hemiplegic migraine) are all known to occur.
2. *Ophthalmoplegic*—ipsilateral paralysis of one or more extraocular muscles usually occurs as the migrainous headache is resolving. This is more common in childhood.
3. *Retinal*—sudden monocular visual loss without flashes may occur.
4. *Basilar artery migraine*—mimics vertebrobasilar arterial insufficiency with bilateral blurring of vision or blindness, diplopia, vertigo, gait disturbances, formed visual hallucinations and dysarthria.

Differential diagnosis: This includes all other causes of headache (Table 31.4). It is worth remembering that the majority of unilateral migraine headaches do, at some point, change sides, so patients who always develop a headache on the same side of the head may have a more serious neurological disorder. Secondly, one should pay close attention to the temporal sequence of symptoms. If headache precedes the visual symptoms, even though this can occur in complicated migraine, the possibility of other conditions in which this order of events is more likely, such as arteriovenous malformations, mass lesions with cerebral oedema and an epileptiform seizure focus, must be considered and ruled out.

Work-up of patients includes a detailed history and careful ocular examination including refraction and neurological examination, preferably by a neurophysician. Hypertension and a low blood sugar level should be looked for as hypoglycaemic headaches may be triggered by stress and fatigue.

Neuroimaging with CT or MRI of the head is warranted in patients with (i) atypical migraine, i.e. pain always on the same side of the head or atypical sequence

Table 31.4 Differential diagnosis of headache

Condition	Clinical features
Life-threatening or vision-threatening	
Malignant hypertension	Raised blood pressure, hypertensive retinopathy, headache typically occipital
Raised intracranial pressure	Papilloedema. Headache usually worse in the morning and worsens with Valsalva manoeuvre
Intracranial infection(meningitis, brain abscess)	Fever, neck stiffness, photophobia, neurological signs
Subarachnoid haemorrhage	Extremely severe headache of sudden onset, neck stiffness, sensorial disturbances with or without focal neurological defects
Epidural or subdural haematoma	Following trauma, altered level of consciousness
Structural abnormality in the brain (tumour, aneurysm, arteriovenous malformation)	Signs of raised intracranial pressure, focal neurological deficit
Giant cell arteritis	Age more than 55 years, raised ESR, jaw claudication, scalp tenderness, malaise
Acute angle-closure glaucoma	Decreased vision, painful red eye, dilated vertically oval pupil, shallow anterior chamber, raised intraocular pressure
Ocular ischaemic syndrome	Periorbital pain, mid-peripheral retinal haemorrhages, dilated veins, rubeosis, amaurosis fugax
Others	
Tension headache	Affects females more than males. Generalized nondescript band-like discomfort present continuously
Cluster headache	Unilateral, periorbital, frontal or temporal headache with ipsilateral epiphora, rhinorrhoea, sweating, nasal stuffiness and ptosis. Lasts minutes to hours, recurs once or twice daily for several weeks followed by symptom-free intervals of months to years. Affects men (90%) and may be precipitated by alcohol or nitroglycerin
Herpes zoster ophthalmicus	Dermatome distribution, unilateral, followed by rash
Tolosa-Hunt syndrome	Orbital apex or superior orbital fissure or cavernous sinus syndrome with optic nerve involvement and varying degrees of ophthalmoplegia
Trigeminal neuralgia	Facial pain restricted in area to the distribution of the trigeminal nerve or its branches
Convergence insufficiency	Poor convergence fusion range
Spasm of accommodation	Blurred distance vision, relieved by cycloplegic therapy
Anterior uveitis	Acute red eye, blurred vision, small miosed pupil

with visual symptoms persisting after the onset of the headache or appearing after the headache phase and
(ii) complicated migraine.

Treatment: Patients should be asked to avoid all agents or stressful events known to trigger attacks as far as possible. Appropriate spectacles should be prescribed for any refractive error. Antinausea medication may be needed during the acute episodes. Patients with infrequent headaches should be advised to take analgesics (such as aspirin, paracetamol, ibuprofen, naproxen sodium, nimesulide) as soon as possible after the onset of the headache. If initial therapy fails, more potent therapy with one dose of 2 mg of ergotamine (contraindicated in elderly individuals or those with cardiovascular, cerebrovascular, renal or hepatic disease and pregnant patients) or equivalent drugs should be given. Muscle weakness and pain or even cardiac ischaemic pain are described with this drug. Other medications that can be taken after the onset of headache are ergotamine 1 mg with 100 mg caffeine, dihydroergotamine 4 mg as a single dose, butorphenol nasal spray one puff in each nostril, and sumatriptan 6 mg as a single dose subcutaneously. Sumatriptan should not be used if ergotamine has been given in the past 24 hours as their vasoconstrictive effect is additive; a maximum of two doses should be given in 24 hours, but the second dose should not be given if the first is ineffective. Sumatriptan can be given orally as a single, 25 mg dose and the second dose is repeated if there is no relief after 2 hours. This can be repeated every 2 hours up to a maximum of 300 mg in 24 hours, or sumatriptan 20 mg nasal spray can be given as a single dose.

Patients with severe or frequent attacks of two or more headaches per month or those with neurological changes should be treated with prophylactic medication which includes propranolol (10-80 mg orally daily in divided doses initially and slowly increased by 10-20 mg every 2-3 days until the desired effect is obtained. The dose can be increased up to a maximum of 160-240 mg/day). Propranolol is contraindicated in patients with asthma, bradycardia, hypotension and congestive cardiac failure. Amitriptyline (25-200 mg four times daily, starting at the lower dose and increasing by 25 mg every 1-2 weeks if needed) and calcium channel blockers such as flunarizine 5-10 mg daily have also been found to be effective. It is worth noting, however, that so far no 'cure' has been found and most prophylactic regimes are inconsistent in their effect.

INFECTIONS

The role of the ophthalmologist in infections of the CNS is in assisting the neurophysicians and neurosurgeons in establishing baseline clinical ophthalmic features including the presence or absence of papilloedema and protecting the eye from exposure keratopathy.

Meningitis

Meningitis is an infection involving the pia-arachnoid resulting in the collection of inflammatory exudate in the subarachnoid space and cerebrospinal fluid. If the brain parenchyma is also affected meningoencephalitis is a better term. It is due either to a systemic infection with organisms such as meningococci, pneumococci, viruses, etc. or as a result of spread from a neighbouring infective focus (for example, the paranasal sinuses, middle ear), or from a distant septic focus with haematogenous spread. The clinical presentation can be a fulminant acute infection which progresses in a few hours, a subacute infection that progresses over several days and a chronic meningitis which evolves as a neurological syndrome and persists for more than 4 weeks.

Acute bacterial meningitis, acquired in the community is most commonly due to *Streptococcus pneumoniae* (approximately 50% of cases), *Neisseria meningitides* (approximately 25%), group B streptococci and *Listeria monocytogenes.* The incidence of *Haemophilus influenzae-induced* meningitis has decreased following near universal immunization with the H. *influenzae* type b (Hib) vaccine. Hospital-acquired infection following neurosurgical intervention is more commonly due to *Staphylococcus aureus* and coagulase-negative staphylococci. Viruses causing acute meningitis include enteroviruses (poliovirus), arboviruses, HSV-1, HSV-2, HIV, mumps, cytomegalovirus, measles, influenza A and B, rubella and varicella zoster virus. Chronic meningitis can be due to partially treated suppurative meningitis, *Mycobacterium tuberculosis,* Lyme disease among the bacterial pathogens; secondary or tertiary syphilis among *spirochaetes; Cryptococcus neoformans, Coccidiodes immitis, Candida* spp., *Aspergillus* spp., *Histoplasma capsulatum* and *Sporothrix schenckii* among fungi, *Toxoplasma gondii, Acanthamoeba* spp. and trypanosomiasis among protozoal pathogens; cysticercosis due to cysts of *Taenia solium, Gnathostoma spinigerum* and *Angiostrongylus spinigerum* among helminthic organisms.

The classic clinical features include fever, headache and neck stiffness, which are seen in over 90% of cases. Other features include altered sensorium seen in 75% of cases, nausea, vomiting and photophobia. Seizures and features of raised intracranial pressure may be associated and, in meningococcaemia, a typical skin rash is seen. Neck rigidity, which is pathognomonic of meningeal irritation, is demonstrated or confirmed by examination of the patient in the supine position. Resistance to passive neck flexion, presence of pain on passively extending the flexed knee with the thigh flexed on the abdomen (Kernig sign) and spontaneous flexion of the knees and hips induced by flexion of the neck (Brudzinski sign) are all classic signs to be carefully looked for.

In *acute meningococcal* (*epidemic*) *meningitis* papillitis due to a descending infective perineuritis is frequently present; rarely papilloedema may develop. In the early stages there is often kinetic strabismus or conjugate lateral deviation of the eyes. A characteristic sign is the widely open palpebral aperture, often associated with very infrequent blinking. Paralysis of the sixth nerve, usually unilateral, is more common than that of the third, although divergent strabismus due to the latter cause has been frequently reported. Total third nerve paralysis is rare. The pupils vary in size, usually showing miosis in the early stages and mydriasis when coma sets in; loss of reaction to light is relatively rare. Metastatic endophthalmitis in children is an uncommon complication.

Sporadic *acute basal meningitis* may be associated with complete amaurosis with normal fundi and pupillary reactions, pointing to the action of toxins on the higher visual centres. The blindness may persist for many weeks after the other symptoms subside, but sight may be ultimately restored. *Chronic basal meningitis* sometimes shows the same feature, but in these cases optic neuritis and postneuritic atrophy may occur from secondary hydrocephalus and pressure of the distended third ventricle upon the chiasma and tracts or meningeal adhesions in the chiasmal region.

In meningitis of *middle ear* origin, papillitis or papilloedema is usually due to complications such as sinus thrombosis or cerebral abscess. When ocular paralysis occurs, the sixth nerve is usually affected, rarely the third (compare with intracranial abscess). The facial nerve is most frequently involved, the paralysis often causing lagophthalmos. Conjugate deviation of the eyes is not uncommon.

Chronic chiasmal arachnoiditis is a localized infection in the meninges around the chiasma and optic nerves; the aetiology is obscure although sepsis of the nasal sinuses or sarcoidosis may account for some cases. A primary optic atrophy usually develops bilaterally, with a central scotoma and irregular contraction of the visual fields, either concentrically or with bitemporal loss. The differential diagnosis from a pituitary tumour is based on negative radiological and other evidence, and deformation of the chiasmal cistern on CT cisternography.

In *tuberculous meningitis* a moderate degree of papillitis is common (about 25%) and is generally bilateral. Miliary tubercles in the choroid, though reported in the earlier literature, are only infrequently reported in

several large series of tubercular meningitis from India, except when associated with miliary tuberculosis. There is often partial ocular pareses, usually of the sixth and third nerves. Bilateral third nerve paralysis is almost unknown, a point of distinction from syphilitic basal meningitis. Not infrequently there is a kinetic (not paralytic) conjugate deviation of the eyes and head to one side. *Intracranial tuberculomas* manifest ocular signs like any other brain tumour. Antitubercular treatment must be administered with isonicotinic acid hydrazide (INH), rifampicin, ethambutol and pyrazinamide initially for 2-3 months followed by INH and rifampicin for 18 months in infections of the central nervous system.

Diagnosis: This is established by blood culture and lumbar puncture. The cerebrospinal fluid shows an increase in cells with predominantly polymorphonuclear neutrophils in bacterial and lymphocytic pleocytosis in tubercular, viral and fungal infections. There is a decrease in glucose content in bacterial infections in contrast to normal glucose concentration in viral. Other changes seen in acute bacterial meningitis include an increase in protein content, positive Gram stain in 70%-90% of fresh cases and positive culture in 80%. India ink stain is useful for detecting cryptococcal infection. If neuroimaging is indicated, MRI is preferred to CT in detecting cerebral oedema, associated lesions in the brain parenchyma and areas of ischaemia.

Treatment: The condition constitutes a medical emergency and as soon as samples are sent for culture, empirical therapy with intravenous anti-biotics must be started. Third-generation cephalosporins such as ceftriaxone or cefotaxime and vancomycin provide good coverage for most organisms. Ampicillin should be added to cover for *Listeria monocytogenes* in infants less than 3 months of age, those over 55 years of age or those with depressed cell-mediated immunity. Iatrogenic and nosocomial infections, which could include *Pseudomonas aeruginosa,* should be treated with ceftazidime and vancomycin.

Sequelae and complications can result due to inflammatory damage, vasculitis, ischaemia and raised intracranial pressure, and include a mortality rate varying from 3 to 20%, impairment of intellectual functions, loss of memory, seizures, disturbances of gait and balance, and loss of hearing or loss of vision.

Encephalitis

Inflammation predominantly affecting the brain parenchyma is known as *encephalitis.* Enteroviruses, herpesviruses, arboviruses, influenza virus, rabies virus, amoebiasis and toxoplasmosis can cause encephalitis. Ocular palsies usually usher in an attack of *encephalitis lethargica.* Ptosis is the commonest feature, and other branches of the third nerve are especially involved. The muscles are often only partially paralysed and generally recover. Diplopia is an early symptom and nystagmus may be present. Papilloedema is rare and the pupils are usually normal. The general symptoms are lethargy, great muscular debility and other signs of an acute general infection. The disease is often followed by parkinsonian tremor (paralysis agitans) and, in the later stages, spasmodic conjugate deviation of the eyes occurs, usually upwards (*oculogyric crises),* accompanied by synergic movements of the head and neck. Oculogyric crises may be relieved by Benzedrine (up to 30mg a day). They are sometimes a result of phenothiazine idiosyncrasy.

Acute *polioencephalitis* can lead to paralytic squint following a febrile attack in young children. The sixth nerve is most often involved.

Other infections

A collection of pus in the subdural space (*subdural empyema),* extradural space (*epidural abscess),* or in the brain parenchyma with necrosis (*brain abscess)* can manifest as a space-occupying lesion with focal neurological signs depending on the location. MRI scans are preferred to CT in imaging these lesions because of their greater sensitivity. Stereotactic needle biopsy can be done in certain situations. Treatment by neurosurgical drainage under cover of antibiotics is needed.

Another special form of intracranial infection of ophthalmological relevance is *suppurative thrombophlebitis,* especially *cavernous sinus thrombosis.* The latter can develop as a consequence of suppurative infections in the 'danger area' of the face or the orbit. Septic cavernous sinus thrombosis presents with fever, headache, retro-orbital and frontal pain, restriction of extraocular movements, chemosis, proptosis, ptosis, absent corneal sensations and hypoesthesia of the face along the ophthalmic and maxillary divisions of the trigeminal nerve, tortuous dilated retinal veins, papilloedema and loss of vision due to exposure keratopathy, or optic nerve involvement due to raised intraorbital pressure or secondary to septic vasculitis and ischaemia.

Syphilitic infections

Treponema pallidum was a major cause of CNS infection with considerable morbidity and was commonly prevalent in the pre-penicillin era. It has always been of great interest to ophthalmologists as it affects the eyes in various ways. There has been a resurgence of this infection accompanying the human acquired immune deficiency syndrome (AIDS) and hence it is still of some relevance today. However, the late tertiary manifestations of untreated disease such as the previously common granulomatous lesion—the gumma, and cardiovascular

syphilis due to occlusive endarteritis—are uncommon nowadays in communities with good access to health care. Sporadic cases of neurosyphilis, particularly in those simultaneously infected with the HIV virus, are still seen. Neurosyphilis in the pre-penicillin era manifested as a variety of lesions involving the CNS both in the secondary and tertiary stages. These included cranial nerve palsies, Argyll Robertson pupil, chronic basal meningitis, opticochiasmatic arachnoiditis, meningovascular syndromes, gumma, tabes dorsalis and general paralysis of the insane. Fortunately, these lesions are now rarely seen. Hence these are not detailed here except to mention a few which are of interest to ophthalmologists.

Congenital syphilis: This is acquired from the mother during any stage of pregnancy but the lesions are generally known to develop after the fourth month of gestation when the foetal immunological system begins to develop. This is because the pathogenesis of congenital syphilis is more dependent on the immune response of the host than on the pathogenic effect of the organism.

Acquired syphilis: This sexually transmitted disease can also be acquired by exposure to infected blood. The stages of acquired syphilis in an untreated patient are (i) *primary syphilis* (chancre at the site of inoculation which usually heals within 4-6 weeks), (ii) *secondary' syphilis* (diffuse lymphadenopathy, mucocutaneous lesions, rash and constitutional symptoms), (iii) *latent syphilis* (clinically asymptomatic with positive serological evidence of infection; early latent, i.e. within a year; or late latent, i.e. more than 1 year after infection) and (iv) *late syphilis* (slowly progressive inflammatory damage leading to tertiary manifestations such as gummas, aortitis and neurosyphilis).

Among untreated patients, about 30% of those with latent syphilis go on to develop features of late syphilis but 70% do not ever develop clinically manifest late syphilis. However, remain positive for evidence of infection with more sensitive treponemal antibody tests.

Neurosyphilis may be asymptomatic or symptomatic. CNS invasion by *Treponema pallidum* can occur within the first few weeks of infection but this may or may not lead to clinical neurological disease. *Treponema pallidum* has been isolated from the cerebrospinal fluid in 40% of patients during primary and secondary syphilis and in 25% of untreated late latent syphilis. Asymptomatic neurosyphilis is diagnosed on the basis of abnormalities in the cerebrospinal fluid [mononuclear pleocytosis, increased protein concentration and a reactive Venereal Disease Research Laboratory (VDRL) test]. Those with untreated latent or asymptomatic neurosyphilis have a 20% overall risk of progressing to clinical neurosyphilis in the first 10 years and the risk increases with the degree of abnormality of the cerebrospinal fluid and with time.

Symptomatic neurosyphilis can present as *meningitis* (usually in less than 1 year of acquiring infection), *meningovascular* disease (usually presents 5-10 years after first exposure) or *parenchymatous involvement* (general paresis at 20 years and tabes dorsalis at 25-30 years), or a combination of the three in different degrees. Acute meningitis is seen only in secondary syphilis and that itself is a rare presentation seen in less than 2% of cases.

Cerebral syphilis was the term usually applied to relatively early, direct syphilitic disease of the brain and meninges, which was essentially a gummatous inflammation of the meninges and the walls of the cerebral blood vessels.

Basal gummatous meningitis was a common manifestation arising in the subarachnoid tissue in the region of the chiasma and spreading thereafter over the optic nerves, tracts and the base of the brain. In such infections papillitis, papilloedema, or postneuritic atrophy is frequently found (about 13% each), and is usually bilateral. Visual defects are very common. As with all types of basal meningitis, such as tuberculosis and sarcoidosis, the third, fifth and sixth nerves can be paralysed and, least frequently, the fourth. Pupillary changes occur, depending upon the third nerve lesions. A very characteristic feature of basal gummatous meningitis is the inconstancy and variability of the symptoms, temporary and recurrent visual and ocular motor disturbances being very common.

Tabes dorsalis: This is a syphilitic demyelination of the posterior columns, dorsal roots and the dorsal root ganglia leading to ataxic gait, paraesthesiae, loss of deep pain, temperature and joint position sensation, areflexia, bladder disturbance and impotence. *Syphilitic optic atrophy* is common and occurs in about 10-20% of cases of *tabes dorsalis.* Involvement of the optic nerve is probably a primary interstitial perineuritis causing a secondary degeneration of the nerve fibres and their parent ganglion cells. Optic nerve involvement may precede the appearance of typical tabetic symptoms by some years.

The *fields* show progressive contraction, *pari passu* with the failure in central vision. It is rare for the failure of sight to commence with a central scotoma, thus differing from the onset in MS. Two types of field are met with: (i) general concentric shrinkage, the colour fields for red and green being lost early, and central vision being greatly impaired and (ii) irregular sectorial defects, which are sharply defined but gradually spread, although central vision may be good.

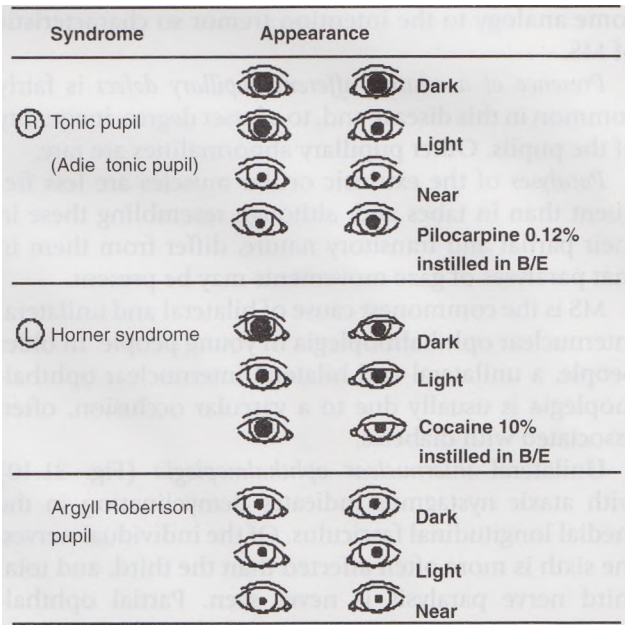
The characteristic *pupillary signs* include the so-called spinal miosis, the Argyll Robertson pupil reaction, inequality of the pupils and distortion of the pupillary aperture. These signs are found in other diseases and are to be regarded as signs of syphilis of the CNS rather than as pathognomonic of tabes; their combination is of great diagnostic significance.

Argyll Robertson pupils are found in 70% of tabetics and are almost invariably bilateral. Unequal pupils are found in 30% of tabetics, but are met with still more frequently in general paralysis. Ophthalmoplegia interna, i.e. paralysis of the sphincter pupillae and the ciliary muscle, occurs in about 5% of tabetics and is generally unilateral. It is due to a lesion in the nucleus of the third nerve.

Paralyses of the extrinsic ocular muscles: This is common in tabes, occurring in about 20% of cases. It is characteristic of tabetic paralyses that they are partial pareses rather than paralyses, variable and transitory. The pareses of the ocular muscles nearly always occur in the pre-ataxic stage; when they occur at a later stage they are more likely to be permanent. They generally clear up rapidly, but show a marked tendency to recur.

General paralysis of the insane (progressive paralysis, paralytic dementia): This form of syphilitic disease reflects parenchymatous damage which is widespread and is often accompanied by signs and symptoms which are due to lesions of the posterior tracts of the cord, identical with those in tabes. The mnemonic 'paresis' is useful in remembering the varied manifestations: personality change, affect, reflexes, eye, sensorium, intellect and speech. The ocular symptoms are most common and unequivocal and have been attributed the same pathogenic mechanism as in tabes.

The pupillary changes are characteristic. In the early stages inequality is often accompanied by slight deformation in the shape of the pupil and irregularity of the pupillary margin is common. An Argyll Robertson pupil (Fig. 31.9) occurs in nearly half the cases. In about 5% of cases the reactions both to light and convergence are lost, a condition which is rare in tabes and especially frequent in the juvenile form of general paralysis. The sensory reaction is very often lost with the light reaction. Bilateral Argyll Robertson pupils (spinal miosis) is commoner in tabes, unequal pupils in general paralysis. Ophthalmoplegia interna is rarer in general paralysis.



Fig, 31.9 Diagnostic features of important pupillary abnormalities.

Primary optic atrophy: This occurs in about 8% of cases showing the same type and course as in tabes. Like pupillary signs, it may precede the onset of the typical cerebral symptoms by a considerable period, especially in those cases which commence with tabetic symptoms.

Paralyses of the extrinsic ocular muscles: This occurs about half as frequently as in tabes, with exactly the same characteristics, the third nerve being most frequently involved.

DEMYELINATING DISEASES

Multiple sclerosis

MS is currently considered to be an autoimmune disease with a relapsing-remitting or progressive course, pathologically characterized by focal inflammation, demyelination and gliosis or scarring. The lesions are disseminated throughout the brain and occur at varying intervals, hence the disease was also called 'disseminated sclerosis'. Selective demyelination with relative sparing of the axons is the hallmark of this disease but partial or total destruction of axons correlating with irreversible neurological damage may also occur. Multiple greyish, sclerotic lesions scattered in the white matter, varying from 1 mm to several centimetres in size, are visible on macroscopic examination of the brain and these are termed *plaques.* Epidemiological evidence suggests that it is a disease occurring in genetically predisposed individuals combined with appropriate environmental influences and possibly triggered by unrelated events such as non-specific upper respiratory infections. This may be due to some molecular similarities between myelin antigens and certain viruses.

MS occurs between adolescence and middle age, is known to occur all over the world, in all regions and communities, but is twice as common in females than males and shows an increasing prevalence with increasing distance from the equator. It is less commonly seen in India and other tropical countries, at least in its classical form. However, with the availability of MR scan it is being diagnosed more frequently than previously. Its more frequent occurrence in high socioeconomic groups has been attributed to better sanitation and delayed initial exposure to infectious agents.

The clinical manifestations are varied, with involvement of white matter tracts of the CNS. The initial onset can be insidious (15%) or abrupt (85%). A remitting

and relapsing course is the most common, with either complete recovery or progressive residual damage with each attack. Primarily and secondarily progressive varieties are also seen. Limb weakness (35%), sensory loss (37%), paraesthesiae (24%) and optic neuritis (37%) are the commonest symptoms. Diplopia, vertigo and ataxia are relatively less common and Lhermitte sign (a transient electric shock-like sensation shooting down the spine into the legs induced by neck flexion), gradual visual loss, facial palsy, seizures and impotence are rarer manifestations.

Clinical work-up includes detailed neurological examination and further investigations as indicated. Analysis of the cerebrospinal fluid, MRI of the head and spine, serum vitamin B_{12} levels, serum VDRL test, ESR, autoimmune serological screening for rheumatoid factor, antinuclear antibody, anti-DNA antibodies and angiotensin-converting enzyme estimation are the investigations usually advised. Owing to the frequent involvement of the optic pathways and spinal cord—latent or overt—visual evoked potentials (VEP) and somatosensory studies provide valuable information. Similarly, visual field charting by threshold automated perimetry may reveal visual field defects earlier than their clinical manifestation. There is no specific diagnostic test but diagnostic criteria for clinically definite MS are (i) documentation of two or more episodes of symptoms (which must last more than 24 hours and should be at least 1 month apart), and (ii) two or more signs (at least one must be demonstrated by neurological examination and the second sign could be an abnormal paraclinical test such as an MRI or an abnormal visual, auditory, or somatosensory evoked electrical response) that reflect involvement of anatomically non-contiguous white matter tracts.

As regards the prognosis, eventually most patients experience progressive disability to a greater or lesser extent with only 20% having no functional limitation. Initial presentation as isolated optic neuritis, or purely sensory symptoms, complete recovery from the first episode, a relapsing-remitting course with less than two episodes in the first year, age of onset less than 40 years and female sex are all associated with a better prognosis. In cases presenting with a single episode of optic neuritis, if MRI of the brain is normal there is a less than 10% chance of developing a second episode of symptoms within 10 years. If, however, the MRI reveals multiple T_2-weighted lesions there is a 70-80% risk of developing definite MS within 10 years.

Ophthalmic manifestations

Lesions in the visual pathways often occur in MS (50% of cases). Unlike the lesions of tabes, the medullary sheaths of the nerve fibres are especially attacked, the axons remaining relatively little affected. Hence, during the acute stage, defects in conductivity are especially prominent, but high degrees of functional restoration are possible. The optic nerves are most frequently attacked with all the clinical signs of typical retrobulbar neuritis, but patches of degeneration in the chiasma, optic tracts or optic radiation may cause characteristic hemianopic or quadrantic changes in the fields.

The frequency of attacks of unilateral *retrobulbar neuritis,* which clear up and recur, often many years before the disease becomes generalized, has already been noted. The visual defect may clear up entirely but may be followed by irregular field defects—central scotomata, concentric contraction of the field and irregular peripheral defects, sometimes only for colours, showing variations from time to time. Some degree of optic atrophy usually develops eventually, the appearance of which bears no relation to the functional defect, but permanent blindness almost never occurs. Often eyes with apparently normal vision demonstrate a prolonged latent period on testing the pattern VEP.

Retinal venous 'sheathing' is sometimes found in MS and is either active periphlebitis or resultant venous sclerosis, associated with foci of inflammation throughout the eye and CNS. It is a concurrent part of a multifocal process in the neural tissue and is probably a component of an immune response in the nervous system, either to exogenous or endogenous antigen.

Nystagmus occurs in 12% of cases, but nystagmoid jerks are much more common (50% of cases). True nystagmus is a very important diagnostic sign since it is rare in other acquired diseases of the CNS. Both are probably due to central changes, and the latter show some analogy to the intention tremor so characteristic of MS.

Presence of a relative afferent pupillary defect is fairly common in this disease and, to a lesser degree, inequality of the pupils. Other pupillary abnormalities are rare.

Paralyses of the extrinsic ocular muscles are less frequent than in tabes and, although resembling these in their partial and transitory nature, differ from them in that paralyses of gaze movements may be present.

MS is the commonest cause of bilateral and unilateral internuclear ophthalmoplegia in young people. In older people, a unilateral and bilateral internuclear ophthalmoplegia is usually due to a vascular occlusion, often associated with diabetes.

Unilateral *internuclear ophthalmoplegia* (Fig. 31.10) with ataxic nystagmus indicates demyelination in the medial longitudinal fasciculus. Of the individual nerves, the sixth is more often affected than the third, and total third nerve paralysis is never seen. Partial ophthalmoplegia externa also occurs; ophthalmoplegia interna is unknown.

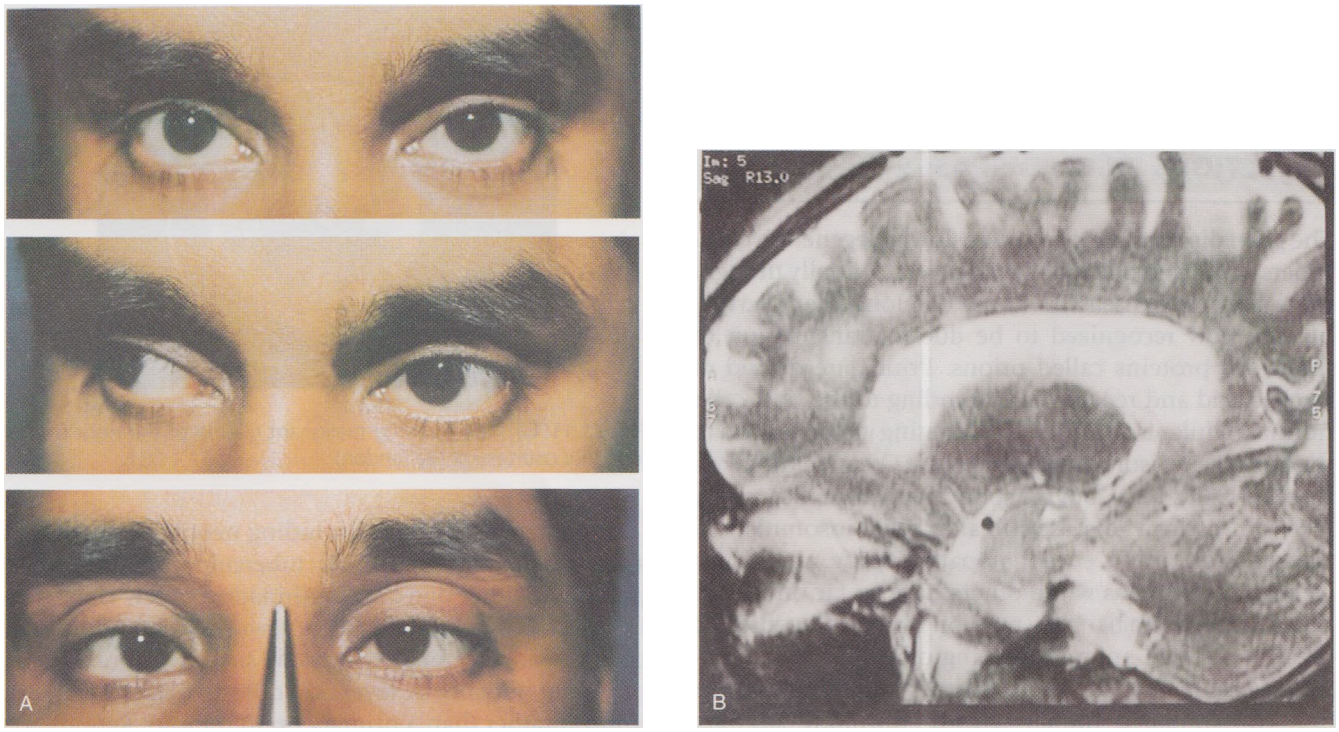


Fig. 31.10 Internuclear ophthalmoplegia. (A) Demonstrating poor adduction left eye on dextroversion but normal adduction on convergence; (B) plaques of demyelination seen on MRI.

Treatment

This is guided by the extent and nature of involvement. In those with relapsing-remitting disease, acute neurological exacerbations without significant functional impairment are treated symptomatically with supportive therapy. Those with functional impairment are treated with intravenous methylprednisolone as pulse therapy. In those with progressive disease, supportive therapy is the mainstay but other disease-modifying modalities such as interferon IFN-^la or IFN-(31b, intravenous immunoglobulin, and high-dose methylprednisolone in bimonthly cycles are being used in some countries. Supportive physiotherapy and psychotherapy are helpful in such an incapacitating prolonged illness.

Neuromyelitis optica (Devic disease)

Devic disease is considered to be a variant of MS. There is an association of bilateral optic neuritis with myelitis; the visual defect usually precedes the signs of myelitis. Its onset is sudden, but one eye may be affected a day or so before the other. Complete amaurosis generally supervenes rapidly. There may be an initial central scotoma and pain on moving the eyes, pointing to a retrobulbar neuritis. There is usually only slight neuritis, but considerable swelling of the disc has been seen. The site of the myelitis may be lumbar or dorsal. There are no signs of general meningitis and the other cranial nerves are not involved. In patients who recover, the blindness passes off and vision is restored.

Acute multiple sclerosis (Marburg variant)

This occurs in young people and is characterized by an extensive fulminant demyelination of the entire white matter of the cerebral hemispheres and brainstem with no remissions; death usually occurs within 1 year of onset. Ocular symptoms appear early. Blindness is common, due to destruction of the optic radiations; optic neuritis or retrobulbar neuritis follows demyelination of the optic nerve. Ocular motor palsies and nystagmus are common. Diagnosis is usually established only on post-mortem examination.

Acute disseminated encephalomyelitis

In contrast to MS this has a monophasic course and has frequently a direct temporal association with infection (*postinfectious* encephalomyelitis) or vaccination (*postvaccinial* encephalomyelitis). Widely scattered foci of perivenular inflammation and demyelination is the pathological hallmark. Smallpox, certain rabies and rarely live measles vaccine have been implicated. Viral infections, such as measles, mumps, influenza, parainfluenza, chickenpox and infectious mononucleosis, can all predispose to this disease. Optic neuritis tends to be more commonly bilateral at presentation as opposed to

MS. In the absence of a specific prodromal viral infection or history of immunization the condition can be indistinguishable from MS. Treatment is similar to MS.

INFECTIOUS PRION DISEASES

The *prion* diseases are a group of slowly degenerative disorders of the nervous system which were initially thought to be slow virus diseases because of a long latent period, but are now recognized to be due to transmission of infectious proteins called prions. Prions are devoid of nucleic acid and reproduce by binding to the host cell's normal cellular isoform and stimulating its conversion to the pathogenic isoform. Examples are Creutzfeldt-Jakob disease (CJD), Kuru, bovine spongiform encephalopathy (BSE or 'madcow' disease), fatal familial insomnia and transmissible mink encephalopathy. Some are known to occur in humans while others have so far only been described in animals. Transmission by ingesting infected meat of affected animals, feeding offal of infected animals to cattle and iatrogenic spread by dura mater grafts and contaminated human growth hormone supplies prepared from human pituitary glands have been implicated. Clinical features include non-specific symptoms of fatigue, malaise, loss of weight, headache and disturbed sleep. Visual impairment due to optic atrophy, supranuclear gaze palsy, seizures, cerebellar ataxia and extra-pyramidal dysfunction resembling parkinsonism and progressive dementia can result. No specific treatment is available. Prevention of further transmission of prions by their complete inactivation by sterilization can only be achieved by autoclaving at 132 °C for 5hours. Thus, in the absence of any definite diagnostic test, any patient dying of an undiagnosed neurological disorder is suspected to have prion disease and the organs of the deceased, such as the eyes, kidney, liver, etc., cannot be used for transplantation.

INTRACRANIAL TUMOURS

Primary malignant tumours of the CNS are less common than secondary metastases from malignancies elsewhere. However, because of the confined closed cranial cavity, any space-occupying lesion—whether benign or malignant, neoplastic or otherwise—can produce certain common clinical features. Glial tumours (Fig. 31.11) such as astrocytomas, glioblastomas, oligodendrogliomas and ependymomas are the commonest primary brain tumours (50-60%), meningiomas are next (25%), followed by schwannomas (10%). Sellar and parasellar tumours, pituitary adenomas, craniopharyngiomas or tumours of the Rathke pouch constitute an important group of special interest to ophthalmologists.

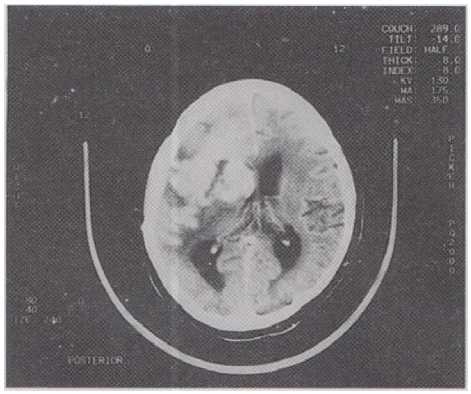


Fig. 31.11 CT scan showing malignant glioma of the right frontal lobe. (By courtesy of PN Tandon)

Intracranial tumours (including neoplasms and such space-occupying lesions as tuberculomata) generally present as either one or a combination of few characteristic sets of symptoms. It is noteworthy that additional general constitutional symptoms such as anorexia, loss of weight, malaise or fever are indicative of a metastatic tumour rather than a primary brain tumour. Retinoblastoma, lung, breast, thyroid, gastrointestinal and germ cell malignancies have a propensity to metastasize to the brain. Symptoms produced by intracranial tumours may be as follows.

1. General 'non-focal' symptoms of *increased intracranial pressure*—headache, vomiting, dizziness, convulsions, somnolence, papilloedema and, occasionally, ocular palsies, particularly of the sixth nerve alterations in the pulse, blood pressure and respiratory rhythm.
2. *Focal neurological deficits* usually progressive, owing to compression or destruction of neighbouring structures, the ophthalmologically important of which are field defects and ocular pareses. Sometimes an acute stroke-like event occurs, possibly because of haemorrhage into the tumour or sudden cystic changes and oedema.
3. *Convulsions* or seizures.
4. *Headache* can arise due to focal irritation, pressure, displacementordistortionofpain-sensitivestructures or due to raised intracranial pressure. Headache associated with the latter may characteristically be precipitated by straining, sneezing or coughing, worsens when recumbent and may even disturb a sound sleep. The headache is initially episodic and may be associated and partly relieved by projectile vomiting, but as the raised intracranial pressure becomes sustained, it becomes continuous.

Papilloedema: This has already been discussed in relation to intracranial tumours (*see* Chapter 23). Precentral and temporosphenoidal tumours are nearly always associated with severe papilloedema, postcentral tumours with moderate papilloedema, often of

short duration. Of the subcortical tumours about one-half cause papilloedema which is, as a rule, moderate and of short duration. Tumours of the optic thalamus and mid-brain are almost invariably associated with papilloedema of great severity. Cerebellar tumours are always and extracerebellar tumours usually accompanied by papilloedema of a grave character. Of the pontine tumours, only about one-half give rise to papilloedema, and only when neighbouring parts of the brain, especially the cerebellum, have become involved. The papilloedema, when it does develop, is usually marked. Ventricular tumours cause a moderate papilloedema. There are three regions of the brain, the pons, central white matter of the cerebral hemispheres and the pituitary gland, in which tumours usually develop without causing papilloedema.

Paralyses of the ocular muscles: Except for the lateral rectus, paralyses of the other ocular muscles as a non-specific sign of raised intracranial pressure are rare.

Focal signs: Apart from the general symptoms of headache and signs of raised intracranial pressure, intracranial tumours produce focal defects which are of localizing value to clinically determine the anatomical site of involvement.

Tumours of the frontal lobe, particularly meningiomata of the olfactory groove, are sometimes associated with a pressure atrophy of the optic nerve on the side of the lesion due to direct pressure, and a papilloedema on the other side due to raised intracranial pressure *(Foster-Kennedy syndrome).* Gliomas may manifest with features of raised intracranial pressure and changes in behaviour (Fig. 31.5).

Chiasmal and pituitary tumours (see Fig. 31.12).

Tumours of the temporal lobe: In 50% of cases these produce a characteristic crossed upper quadrantanopia, usually incongruous, being more accentuated in the ipsilateral field. This sign is due to pressure on the optic radiations as they loop through the temporal lobe. Visual hallucinations may occur owing to irritation of the visuopsychic area. Downward pressure at the tentorial edge may involve the third nerve. Rarely, the fifth nerve may be compressed in the middle cranial fossa causing diminution of corneal sensitivity.

Tumours of the parietal lobe: These produce a crossed lower homonymous quadrantanopia (from involvement of the upper fibres of the radiations), visual and auditory hallucinations, and an abnormal optokinetic response to the revolving drum.

Tumours of the occipital lobe: These produce essentially visual symptoms. Typically, there are crossed homonymous quadrantic or hemianopic defects extending up to the fixation point. Anteriorly situated tumours may cause a crescentic loss in the periphery of the opposite uniocular temporal hemifield. Visual agnosia may also occur.

Tumours of the mid-brain: The localizing signs of tumours in this region depend on involvement of the pyramidal tracts and the ocular motor nerves. All of them may be associated with homonymous hemianopia owing to pressure on the optic tracts.

In the upper part of the mid-brain (the colliculi and pineal gland) the most characteristic sign is initial spasmodic contraction or retraction of the upper lid followed by ptosis, together with loss of conjugate movements upwards, sometimes followed by a similar failure of downward movement. There is light-near dissociation in that the pupillary response to light is impaired as contrasted with the better constriction obtained on testing the near reflex. There may be vertical nystagmus and adduction movements on attempted vertical gaze.

At an intermediate level in the region of the *cerebral peduncles* the third nerve nucleus becomes progressively involved. Ipsilateral ptosis and ultimately a complete third nerve paralysis is associated with a contralateral hemiplegia involving a facial palsy of the upper motor neurone type *(Weber syndrome,* Fig. 31.13). If the red nucleus is involved, tremors and jerky movements occur in the contralateral side of the body. This condition, combined with ipsilateral third nerve paralysis, forms *Benedikt syndrome.* If the lemniscus is involved there may be contralateral hemianaesthesia.

At a still lower level in the *pons,* similar localizing symptoms are found. In the upper part of the pons before the fibres to the facial nucleus have crossed, there is again a third nerve paralysis with contralateral hemiplegia and upper motor neurone type facial palsy. In the lower part of the pons the lateral rectus may be paralysed with a contralateral hemiplegia and an ipsilateral facial palsy *(Millard-Gubler syndrome,* Fig. 31.13); more commonly the sixth nerve palsy is replaced by a loss of conjugate movement to the same side *(Foville syndrome,* Fig. 31.13). The fifth nerve may be paralysed causing loss of corneal sensation which is liable to cause neurotrophic and neuroparalytic keratitis owing to the accompanying facial palsy, and implication of the eighth nerve may cause deafness. Gaze palsy, horizontal or internuclear, is diagnostic of a lesion at this level.

Tumours of the auditory nerve, growing in the cerebellopontine angle, give rise to a fairly characteristic syndrome with ocular signs. Corneal anaesthesia due to involvement of the fifth nerve may be an early occurrence. Early tinnitus and deafness on one side is associated with cerebellar symptoms, among which nystagmus is common. The sixth nerve is usually involved, generally with paralysis of the lateral rectus only, rarely with paralysis of conjugate deviation. As might be expected, there is very often facial paralysis of the peripheral type, including the orbicularis palpebrarum.

Tumours of the cerebellum: Usually these cause nystagmus as well as marked papilloedema.

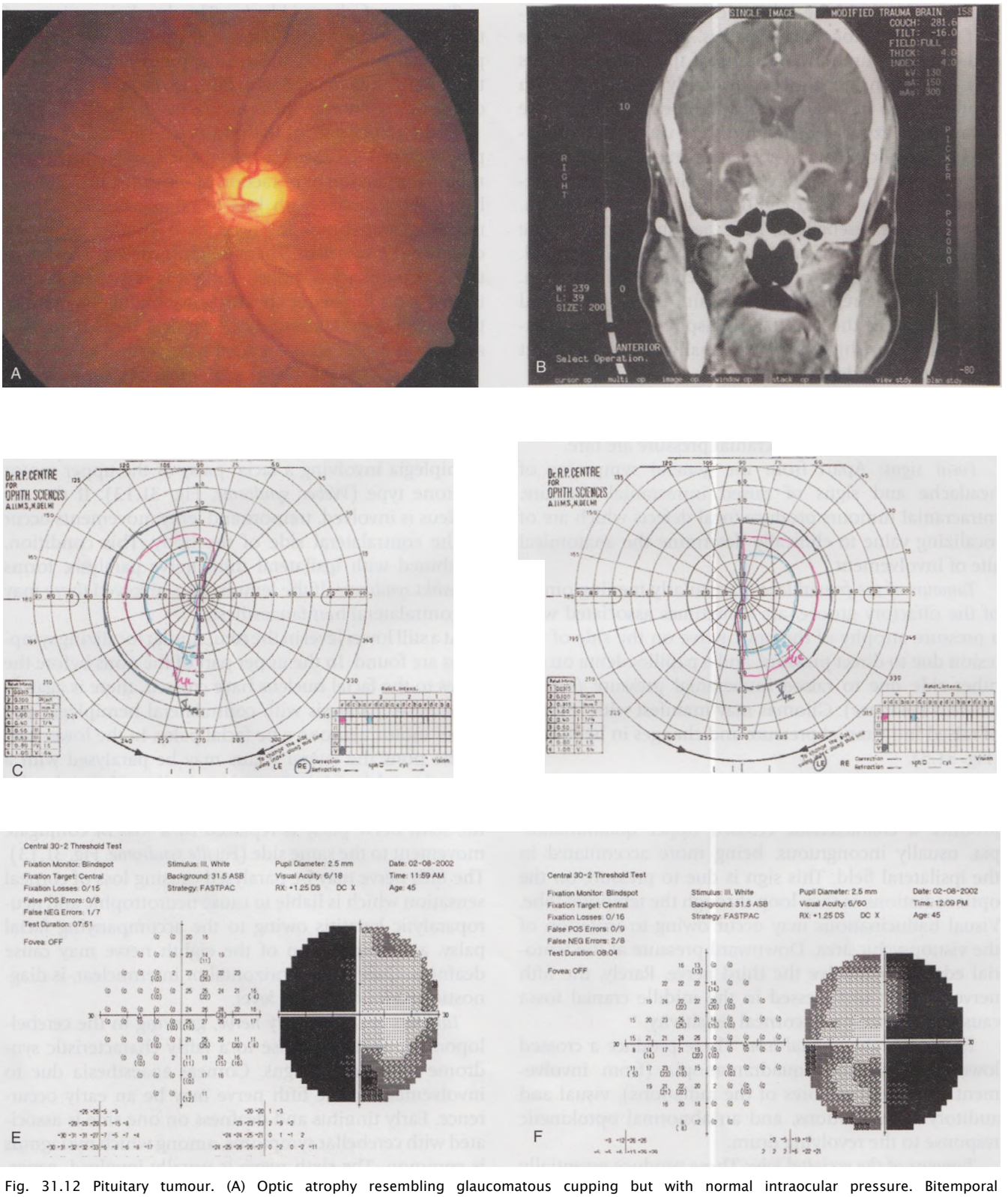


Fig. 31.12 Pituitary tumour. (A) Optic atrophy resembling glaucomatous cupping but with normal intraocular pressure. Bitemporal hemianopia led to the correct diagnosis on Goldman field charting (C and D), which was confirmed by CT scan. (B) Automated static perimetry (E and F).

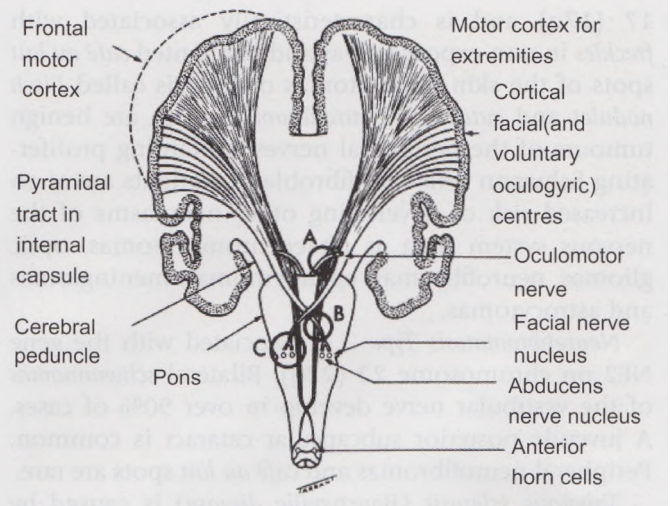


Fig. 31.13 The relation between the pyramidal tracts and the ocular motor nuclei. (A) The site of a lesion causing Weber syndrome (ipsilateral third nerve paralysis and crossed hemiplegia of the face and body). (B) The site of a lesion in the pons causing ipsilateral upper motor neurone palsy, i.e. without muscular atrophy, facial paralysis and contralateral hemiplegia which, on extension downwards, may involve abducens paralysis (Millard–Gubler syndrome). (C) The site of a lesion in the pons causing Foville syndrome, i.e. ipsilateral abducens paralysis with loss of conjugate deviation to the same side, Ipsilateral lower motor neurone facial palsy and contralateral upper motor neurone hemiplegia.

Certain hereditary conditions predispose to brain tumours (*see* below: *phakomatoses,* p. 500) and these include hereditary retinoblastoma, associated with RBI gene on chromosome 13 (13q), which increases the likelihood of associated retinoblastoma, pinealoblastoma and malignant glioma. Werner syndrome or multiple endocrine neoplasia (MEN-1) linked to the MEN-1 gene (llql3) causes pituitary adenoma and malignant schwannoma besides medullary carcinoma of the thyroid and phaeochromocytoma.

Hydrocephalus

In congenital and early acquired hydrocephalus of infancy, optic atrophy is not infrequently found. Papilloedema occurs only rarely, in spite of the increased intracranial pressure, due to the relief of pressure by the enlargement of the skull and the resiliency of the fontanelles and gaping sutures, as well as to the very gradual development. The eyeballs usually deviate downwards, and upward movements are restricted (the 'setting-sun' sign). This is because a dilated ventricular system compresses the vertical upgaze centre in the dorsal mid-brain. It is more often due to a dilated posterior third ventricle, since it is also seen in cases of hydrocephalus due to aqueductal stenosis. In advanced cases there is considerable proptosis. Such children are lethargic, subject to fits and often blind with sluggish pupils and spastic diplegia.

The *acquired hydrocephalus* of later life, after the fontanelles and sutures have closed, can often only be diagnosed with certainty after neuroimaging. The cardinal signs of increased intracranial pressure—headache, vomiting and papilloedema—are present, often associated with ataxia of the cerebellar type. These are often diagnosed as intracranial tumours in which localizing signs are usually absent or masked. Bitemporal hemianopia, due to pressure on the chiasma and tracts by the bulging floor of the third ventricle, may suggest the true aetiology. Defective vision due to secondary or post-papilloedema optic atrophy may persist.

HEAD INJURY

Closed head injuries

Simple *concussion* injuries associated with blunt head trauma are followed by a temporary loss of consciousness with subsequent full recovery, usually spontaneously. They may be associated with partial or total amnesia but rarely have any ophthalmic signs or symptoms. More severe injuries to the brain are frequently followed by *haemorrhage*—subdural, extradural (Fig. 31.14) or intracerebral—often resulting in progressive impairment of consciousness. The pupillary reactions are important since they may be the main diagnostic indication for operation in a comatose patient. At first the ipsilateral pupil is contracted; later, as intracranial pressure increases, this pupil dilates and does not react to light *(Hutchinson pupil);* if pressure increases further, a similar phenomenon occurs in the other pupil. In actual clinical practice the stage of contraction may seldom be observed. The presence of dilated, fixed pupils is a strong indication of life-threatening tentorial herniation and brainstem compression. *Pin-point pupils,* often attributed to brainstem (pontine) injury, though seen uncommonly, have an even worse prognosis than bilateral dilated fixed pupils. The fourth nerve is the most

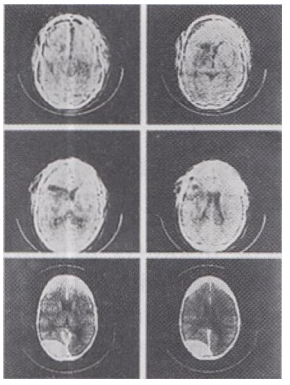


Fig. 31.14 CT scan showing extradural haematoma in the parieto-occipital region. (By courtesy of PN Tandon)

commonly affected among the ocular motor nerves in closed head injuries because it is the thinnest and has the longest intracranial course.

Fractures of the base of the skull

A subconjunctival haemorrhage arising from the fornix whose posterior extent is not visible is a reliable clinical sign of a fracture of the base of the anterior cranial fossa. The latter may also cause blood to track forwards and produce subconjunctival haemorrhage or a 'black eye' without a history of a direct blow to the orbit.

Fractures of the base of the skull commonly involve the cranial nerves. The most common complication is ipsilateral facial paralysis of the lower motor neurone type (22% of cases); the sixth (4%), third (2%), fifth (1.6%) and fourth (1%) follow in order of frequency. Fractures of the base sometimes involve the roof of the orbit but rarely traverse the optic foramen; occasionally both optic foramina are implicated, ft may happen that the nerve is directly injured or compressed by haemorrhage; more frequently, however, owing to the fact that the dura mater becomes the periosteum, the optic nerve is injured indirectly, probably by shearing involving laceration of the small meningeal vessels feeding it. If the injury is severe, in 2-4 weeks signs of primary optic atrophy appear and progress to total atrophy; in this event blindness is absolute and permanent. Disc oedema indicates haemorrhage into the nerve sheath and may occur from basal haemorrhage without fracture of the optic foramen. Such cases have a serious prognosis. These injuries may cause concentric contraction of the field of vision, or quadrantic and other sectorial defects. A central scotoma is rare. Pigmentation in and around the disc may follow haemorrhage into the sheath. The pupillary reactions vary, a relative afferent pupillary defect on the side of the lesion is the most common.

Injuries to the optic nerve and optic chiasma

See Chapter 22.

HEREDITARY AND DEGENERATIVE DISEASES

Neurocutaneous syndromes (phakomatoses)

A group of genetic disorders inherited as autosomal dominant are associated with skin manifestations and a variety of tumours affecting the nervous system. The important ones with relevance to ophthalmology are briefly mentioned.

Neurofibromatosis Type 1 (von Recklinghausen disease) is associated with a gene (NF1) mutation on chromosome 17 (17q) and is characteristically associated with *freckles* in non-exposed areas and pigmented *cafe au lait* spots of the skin, hamartomas of the iris called *Lisch nodules* and *cutaneous neurofibromas* which are benign tumours of the peripheral nerves containing proliferating Schwann cells and fibroblasts. Patients are at an increased risk of developing other neoplasms of the nervous system such as phaeochromocytomas, optic gliomas, neurofibromas, ependymomas, meningiomas and astrocytomas.

Neurofibromatosis Type 2 is associated with the gene NF2 on chromosome 22 (22q). Bilateral *schwannomas* of the vestibular nerve develop in over 90% of cases. A juvenile posterior subcapsular cataract is common. Peripheral neurofibromas and *cafe au lait* spots are rare.

Tuberous sclerosis (Bourneville disease) is caused by two possible gene mutations TSC1 (9q) and TSC2 (16p) and is characterized by the triad of *seizures, mental retardation* and *skin lesions.* The skin lesions are adenoma sebaceum, ash-leaf shaped hypopigmented macules, depigmented naevi and shagreen patches. Calcified subependymomal nodules demonstrated by CT or MRI are characteristic. Patients are predisposed to developing ependymomas and astrocytomas. Potato tumours of the retina, rhabdomyomas of the myocardium, angiomas of the pancreas, kidney, liver and adrenals can occur.

Von Hippel-Lindau syndrome is associated with mutation of the VHL gene located on chromosome 3 (3p). It is characterized by *haemangioblastomas,* which are slowly growing cystic tumours, in the retina, cerebellum and spine. Other tumours which can occur include phaeochromocytoma, renal cell carcinoma or hypernephroma, and cysts or haemangiomas of the parenchymal organs such as the liver, kidneys and pancreas.

Sturge-Weber syndrome, associated with facial angioma, choroidal angioma, glaucoma and cerebral angioma, and *naevus of Ota* are other phakomatoses of ophthalmic interest which are described in Chapter 20.

Chronic progressive external ophthalmoplegia

Chronic ophthalmoplegia of a progressive type, due to a *myopathy* of the extraocular muscles, commences with ptosis or diplopia. In the course of months or years the degeneration spreads to all the ocular muscles of both sides. The intraocular muscles of the iris and ciliary body are not affected. Cases of isolated ophthalmoplegia of *neurogenic* origin are rare, but the condition is occasionally a precursor or symptom of tabes or general paralysis of the insane, rarely of MS. It may become associated later with bulbar symptoms; in these cases the internal musculature may be involved.

Hereditary ataxia (Friedreich disease)

In this condition, optic atrophy and paralyses of the ocular muscles are very rare. Nystagmoid jerks of the eyes, very similar to those occurring in MS, are common, but visual symptoms are absent. The movements are probably due to the same lack of coordination which causes the other ataxic signs of the disease; they occur on voluntary movement and are not usually present in passive fixation.

Status dysraphicus

This results from a defective or anomalous closure of the neural tube and may have various ocular implications. In *syringomyelia* cavities form around which secondary gliosis develops in the cervical and upper dorsal cord; in *syringobulbia* the process extends up to the medulla. The neural symptoms, which develop between the ages of 20 and 40 years, include paralysis of the cervical sympathetic chain (Horner syndrome), the trigeminal nerve and various extraocular muscles.

Lysosomal storage disorders

These disorders and their associated retinal lesions have been described in Chapter 20 (*see* p. 331).

Wilson disease

This is also known as *hepatolenticular degeneration* and is an inherited disorder of copper metabolism due to mutation of the AT P7B gene. There is a defect in maintaining the copper balance with a deficiency of caeruloplasmin and excessive deposition of copper in the brain, liver and various other organs. The disease usually manifests clinically after the age of 6 years with hepatitis, cirrhosis, tremors, disturbances of gait, dysarthria and/or psychiatric disturbances. Criteria for confirming the diagnosis include either demonstration of *Kayser-Fleischer rings* or low serum caeruloplasmin levels of less than 20mg/dl, as well as an increased concentration of copper in a liver biopsy specimen. Successful treatment with agents to remove and detoxify the copper deposits is possible. Penicillamine or trientine is usually the first line of therapy and are replaced with zinc preparations later as maintenance therapy.

Alzheimer disease

First described by Professor Alois Alzheimer in Germany in 1907, it is a common cause of dementia in western countries. It is now known to have a genetic predisposition and risk factors identified include old age, female gender and a positive family history. The pathogenesis is linked to an exaggeration of some physiological changes of ageing. The most important microscopic changes identified are the excess accumulation of cytoplasmic neurofibrillary tangles (NFTs) and neuritic 'senile' plaques. Four different susceptibility genes have been identified: the APP gene on chromosome 21, PS-1 (presenilin-1) on chromosome 14, PS-2 (presenilin-2) on chromosome 2 and Apo E gene on chromosome 19.

A disease of the elderly, it shows an increase in frequency with each decade of adulthood to reach a reported frequency of approximately 20% of the population older than 85 years. Clinical features begin gradually in the early stages with mild memory loss, bewilderment in unfamiliar surroundings, forgetfulness and consequent increase in cognitive problems. As the disease progresses patients are easily lost, confused, display difficulties in language and comprehension, develop various apraxias with difficulties in performing simple routine sequential tasks and begin to require daily supervision.

Some patients develop a cortical blindness with a characteristic denial of the inability to see which has been correlated by autopsy studies with advanced neuropathological degeneration in the visual cortex. In the late stage there is a complete loss of reason, judgement and cognition. Some remain ambulatory but are prone to wander aimlessly. Sleep disturbance, delusions and hallucinations, loss of inhibitions and belligerent behaviour can occur. The clinical course could be steady downhill progression or reach a plateau in some. No definite treatment has shown any convincing benefit and supportive therapy is the mainstay.

Parkinson disease

Parkinson disease is a degenerative disease causing loss of nerve cells in the pigmented substantia nigra pars compacta and locus coeruleus in the mid-brain, which results in a depletion of dopamine and other neurotransmitters such as norepinephrine. The disorder begins in middle age, around 45 years or later, with equal frequency in males and females. Its prevalence in the general population is about 2% in those over 65 years. The constellation of typical symptoms includes *tremors, rigidity* and *akinesia.* This combination of clinical features comprises the syndrome termed as 'parkinsonism' and could be due to other conditions besides Parkinson disease, such as drugs.

Important clinical features are a typical *tremor* which is most prominent at rest and conspicuously increases with emotional stress with typical flexion-extension movements of the fingers, hand (characteristic 'pill-rolling' movement) or foot, rhythmic pronation-supination of the forearm, *rigidity,* slowing of voluntary movements *(akinesia),* loss of facial expression, deterioration in handwriting and disturbance of gait with short shuffling steps, absent arm swing, unsteadiness while turning and sometimes a *festinating gait* at an increasing speed with difficulty in stopping. Ocular manifestations include

blepharoclonus which is a fluttering of the eyelids when closed, *blepharospasm* or involuntary eye closure, widened palpebral aperture and *infrequent blinking.*

Therapy is symptomatic and supportive. Non-specific anticholinergic drugs are used to relieve tremors by their muscarinic antagonist action. Constipation, urinary retention, blurred vision, dryness of the mouth and eyes and the risk of precipitating acute angle-closure glaucoma are important side effects. Amantadine potentiates the release of endogenous dopamine and can benefit all major symptoms in mild disease. Restlessness, confusion, cardiac arrhythmias and skin rashes are possible side effects. Levodopa (which is a metabolic precursor of dopamine) administered with carbidopa relieves most symptoms and is particularly helpful against bradykinesia. Postural hypotension, cardiac arrhythmias, nausea, vomiting, dyskinesias and confusion are troublesome side effects. Stereotactic pallidotomy or thalamotomy is useful in selected cases. It can now be performed using a highly focused proton beam by external radiation (the 'gamma knife').

Progressive supranuclear palsy

Also known as the *Steele-Richardson-Olszewski* syndrome, this neurodegenerative condition is associated with neuronal loss, NFTs (different from the type seen in Alzheimer disease) and gliosis in the mid-brain, pons, basal ganglia and cerebellar dentate nuclei. Seen twice as often in males than females, it begins in those who are 45-75 years old and is characteristically associated with *supranuclear ophthalmoplegia.* Voluntary saccadic gaze and the fast phase of optokinetic nystagmus are absent first in the vertical plane (downgaze is more severely affected) and then in the horizontal plane as well. Reflex conjugate eye movements such as the oculocephalic (doll's head) and oculovestibular (caloric) reflexes are preserved. Additional features include rigidity and bradykinesia which may resemble Parkinson disease, but in progressive supranuclear palsy tremor is uncommon and the dystonic axial posture is in extension rather than flexion. Axial rigidity combined with a disturbance of downgaze is often present with a history of frequent falls. Dysarthria, dysphagia and exaggerated jaw jerks complete the clinical picture of pseudobulbar palsy. Dopaminergic and anticholinergic preparations are partly effective.

OPHTHALMOPLEGIA CAUSED BY DEFICIENCIES AND TOXINS

The chief exogenous poisons causing ophthalmoplegia are lead and ptomaines; the chief toxins, diphtheria and influenza. In *lead poisoning* the onset is slow and the intrinsic muscles of the eye are often involved. In *botulism,* due to food contaminated with *Cl. botulinum,* bilateral ophthalmoplegia interna, with or without ptosis, is typical but total ophthalmoplegia also occurs. In *diphtheria,* isolated ocular palsies are common, but ophthalmoplegia externa is rare; the pupil often escapes, the ciliary muscle never. In *influenza* the palsies are similar, affecting the extrinsic and ciliary muscles, but usually not the pupil; the pupil, however, has been known to be affected without the ciliary muscle. In all cases recovery is common.

In *thiamine deficiency,* frequently associated with alcoholism, the onset is sudden and accompanied by cerebral symptoms—such as headache, delirium and coma. Bilateral ophthalmoplegia externa occurs with or without ptosis, often followed by facial and bulbar paralyses with difficulty in speech and swallowing; the intrinsic muscles usually escape. Pathologically the condition is an *acute haemorrhagic anterior encephalopathy* (Wernicke). It is also characterized by impairment of memory resulting in amnestic-confabulatory behaviour. The prognosis is poor.

CONGENITAL AND DEVELOPMENTAL CONDITIONS

Encephalocele

These are developmental defects resulting in herniation of the brain outside the cranial cavity. The commonest site is the occipital region with involvement of the occipital lobe producing ophthalmic manifestations. Another common site, especially in Asians, is the nasal region. These are associated with hypertelorism and occasionally with other craniofacial deformities such as midline facial clefts. Uncommonly they may protrude into the orbit resulting in proptosis.

Craniosynostoses

This group of disorders is due to premature union of certain cranial sutures which result in characteristic deformities of the skull: frontal metopic suture—*trigonocephaly,* occipitoparietal and frontoparietal—*turricephaly, tower skull,* coronal—*brachycephaly* or sagittal—*scaphocephaly.* Asynchronous fusion of the bones leads to a lop-sided skull—*plagiocephaly.* The greater wing of the sphenoid is displaced so that the orbit becomes shallow, causing some degree of proptosis. In the early stages there is papilloedema, but more commonly, only in the later stages, optic atrophy is seen. The amount of atrophy varies in degree. The papilloedema is probably due to increased intracranial pressure, owing to continued growth of the brain in a restricted space. Most of the patients are males. Craniosynostoses may be associated with other systemic abnormalities such as syndactylism

(Apert disease) or patent ductus arteriosus or coarctation of the aorta with maxillary hypoplasia, shallow orbits and apparent proptosis (Crouzon disease).

Congenital oculomotor apraxia

This is a clinical disorder with a good prognosis. Patients make characteristic thrusting movements of the head opposite to the direction in which they wish their eyes to move. The beginning of the head movement is initiated by a blink, the head is turned considerably past the target, such that the patient overshoots the target and, following fixation on the target, the head is then brought into line with regard to the target. The rapid head movements are thought to be related to the use of vestibular reflexes in changing the position of the gaze. Random eye movements are intact. The condition resolves spontaneously as the child grows older.

Congenital spastic diplegia (little disease)

This is a bilateral spastic paralysis present from birth. Considered previously to be due to meningeal haemorrhage as a result of birth injury, it is probably a degenerative cerebral process of obscure aetiology. Ocular anomalies such as optic atrophy, retinal degeneration, cataract, squint and internuclear palsies may occur concurrently.

SUMMARY

The eye can be affected by diseases of the nervous system in various ways. Direct involvement of the second, third, fourth, fifth, sixth and seventh cranial nerves can occur with intracranial and extracranial lesions. Indirect involvement by raised intracranial pressure and effects on the vascular supply can also occur.

A thorough knowledge of the visual pathway and the oculomotor system is useful in identifying and interpreting clinical symptoms and signs and localizing lesions. Modern techniques of neuroimaging are undoubtedly a great help in assisting the clinician. However, careful documentation and review of clinical findings particularly visual fields, disc appearance by ophthalmoscopy and range of extraocular movements remain important for management and follow-up.

32

Ocular Manifestations of Systemic Disorders

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THE EYE IN SYSTEMIC DISEASE

The eye is intimately linked with the rest of the body in many ways, such as by development, its blood supply and the continuity of the nerve fibres and meninges with the brain. It is therefore to be expected that the eye would reflect changes within the body, especially vascular changes in the smaller vessels. Widespread and major disorders such as diabetes and hypertension have already been covered extensively. However, there are many other systemic disorders with noteworthy ocular components that have received mention in a number of chapters, as the same disease afflicts different tissues of the eye. This chapter seeks to highlight important aspects of ocular involvement in commonly encountered disease processes, particularly if the ocular manifestations contribute to the diagnosis or are a major clinical problem.

IMMUNOPATHOLOGICAL PROCESSES AND THE EYE

Owing to the avascularity of the cornea and lens and the physiological selectivity of the blood—aqueous barrier as well as the absence of lymphatic channels within the globe itself, the eye is in a privileged situation with regard to immunology. However, immunopathological disorders do affect the eye. Hypersensitivity reactions often have an ocular component. Some examples of ocular hypersensitivity are listed below.

Type I hypersensitivity (acute anaphylactic type)

Acute anaphylaxis is mediated chiefly by IgE. Systemic anaphylaxis such as follows the administration of penicillin or the ingestion of certain foods in sensitized individuals may result in severe chemosis of the lids with generalized urticaria. Vernal conjunctivitis is believed to be a localized form of anaphylaxis since IgE has been demonstrated in tear fluid.

Type II hypersensitivity (complement-dependent type)

Antibodies which bind to antigens on the cell surfaces may result in death of those cells due to activation of the lytic complement system or because of C3-mediated macrophage activity. In the eye an example of this type of reaction is the destruction of a malignant melanoma of the choroid following exposure to autologous serum containing tumour-specific antibody.

Type III hypersensitivity (immune-complex type)

When the antibody and antigen present in tissue fluid or the circulating plasma combine, the resulting complex activates components of the complement system with the development of inflammation and polymorphonuclear lymphocyte accumulation, tissue necrosis and vascular thrombosis. This mechanism may be responsible for some cases of recurrent uveitis in man.

Type IV hypersensitivity (cell-mediated)

This delayed type of hypersensitivity is mediated by thymus-dependent lymphocytes. Manifestations of this type of hypersensitivity are seen in corneal graft

rejection, helminthic infestations of the retina, fungal infections of the choroid and conjunctivitis provoked by sensitization to cosmetic eye preparations. It may play a part in sympathetic ophthalmitis, optic neuritis and possibly viral keratitis.

Type V hypersensitivity (stimulating)

An example of a stimulating hypersensitivity is long-acting thyroid stimulation (LATS), which is a non-complement fixing immunoglobulin antithyroid antibody. On contact with a specific site on the thyroid cells and orbital tissue, their activity is stimulated.

As an example, over 90% of patients with ankylosing spondylitis show the presence of HLA-B27 and a normal person who is positive for this antigen is a hundred times more at risk of developing this disease than an HLA-B27 negative person. The precise mechanism of HLA and disease susceptibility is still hypothetical.

Apart from acute anterior uveitis (HLA-B27), optic neuritis (HLA-DRW2 and HLA-DW2) and certain autoimmune diseases such as myasthenia gravis (HLA-B8 and HLA-DRW3) and thyrotoxicosis (HLA-DW3 and HLA-B8), there is little evidence of HLA association with eye disease but further evidence on this aetiological aspect is accumulating day by day. The finding of such an association can help in defining subgroups of clinical disease, occasionally in clinical diagnosis, in defining individuals at risk from a disease (particularly in families) and in providing valuable information as a basis for further research on pathogenesis.

Autoimmune disorders

Ocular involvement occurs as a component of various autoimmune disorders, but the eye can also be involved secondarily, due to post-inflammatory effects of the disease or side-effects of medications. A prominent example is the hypertensive retinopathy seen in systemic lupus erythematosus (Fig. 32.1), polyarteritis nodosa andTakayasu arteritis (Fig. 32.2).

Cataracts and glaucoma can ensue following the prolonged use of corticosteroids and a maculopathy may be seen after chloroquine therapy. Table 32.1 summarizes the important clinical features of common immunological disorders.

Haematological diseases

Blood dyscrasias and haematological malignancies often have ophthalmic features (Table 32.2) and, more importantly, the ocular manifestation may be the initial reason for presentation to an ophthalmologist or physician in some of these disorders. A high index of suspicion is necessary to identify the changes, and order appropriate investigations to arrive at the correct diagnosis.

Infectious diseases

Systemic infections can involve the eye through metastatic foci, directly by local spread or indirectly by immune-mediated inflammation affecting the eye. Examples of direct infection are dendritic keratitis due



Fig. 32.1 Retinal changes in systemic lupus erythematosus.

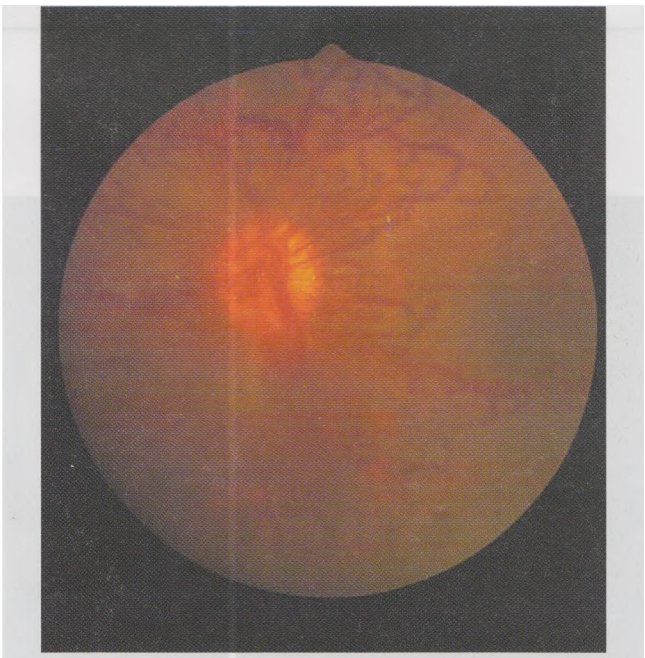


Fig. 32.2 Extensive neovascularization in Takayasu disease. (By courtesy of AH Paul)

Table 32.1 Ocular and systemic features of immunological disorders

Systemic diagnosis	Systemic features	Extraocular features	Intraocular features
Rheumatoid arthritis	Arthritis—hand, wrist and foot, skin nodules, Felty syndrome	'Dry eye', episcleritis, scleritis	Iridocyclitis, corneal melting, cataract
Systemic lupus erythematosus	Butterfly rash, pleuritis, pericarditis, Raynaud phenomenon	Episcleritis	Iritis, retinopathy
Giant cell arteritis	Temporal arteritis, cephalgia, jaw claudication	Extraocular muscle palsies	Anterior ischaemic optic neuropathy
Sarcoidosis	Granuloma of the lymph nodes, lungs, CNS, erythema nodosum	Enlargement of the lacrimal glands	Iridocyclitis, retinal periphlebitis or sarcoid nodule (Fig. 32.3)
Reiter syndrome	Arthritis, urethritis, plantar rash	Conjunctivitis	Uveitis, retinal vasculitis
Periarteritis nodosa	Pyrexia of unknown origin, myalgia, arthralgia, skin nodules, renal and cardiac failure	Episcleritis, extraocular muscle palsy	Uveitis, retinal haemorrhage, papilloedema
Vogt–Koyanagi–Harada syndrome	Meningitis, encephalopathy, dysacusis, vitiligo, alopecia	Poliosis	Uveitis, choroiditis, exudative retinal detachment
Multiple endocrine neoplasia (MEN lib)	Medullary carcinoma of thyroid, phaeochromocytoma	Mucosal neuromas of the lid and conjunctiva	Medullated nerve fibres in the cornea

Table 32.2 Ocular and systemic features of haematological diseases

Systemic diagnosis	Systemic features	Extraocular features	Intraocular features
Lymphocytic leukaemia	Lymphadenopathy, hepatosplenomegaly, anaemia, leucopenia	Proptosis	Iris nodules, retinal oedema, haemorrhages, leukaemic infiltrates, Roth spots
Myeloid leukaemia	Hepatosplenomegaly, bleeding, thrombosis	Orbital chloroma	Retinal oedema, haemorrhages, peripheral retinal neovascularization (Fig. 32.4)
Lymphomas	Fever, lymphadenopathy	Lid/orbital deposits	Uveitis
Sickle cell anaemia	Transient aplastic crisis, stroke, leg ulcers, jaundice, anaemia	Dilated conjunctival vessels	Retinal capillary occlusion, neovascularization, chorioretinal scars

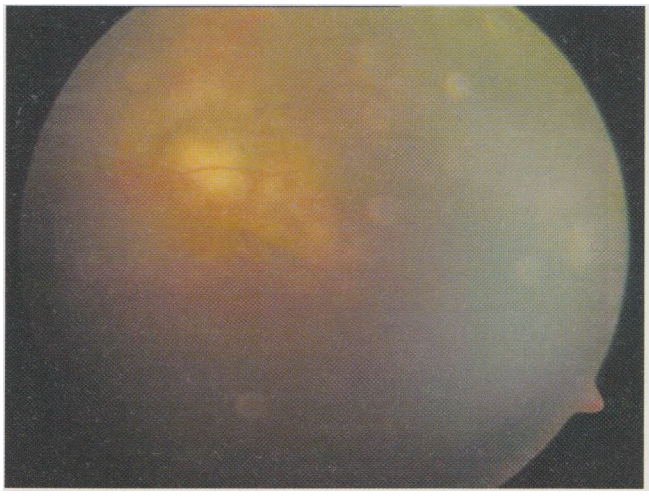


Fig. 32.3 Sarcoid nodule.



Fig. 32.4 Fundus of a patient with chronic myeloidleukaemia.

Table 32.3A Ocular and systemic features of infectious diseases

Systemic diagnosis	Systemic features	Extraocular features	Intraocular features
Viral			
Herpes simplex	Blisters and sores around the mouth and genital area	Vesicles on the lids	Dendritic keratitis, uveitis, acute retinal necrosis
Congenital rubella	Congenital heart disease, sensorineural deafness, mental retardation		Microphthalmos, cataract, glaucoma, chorioretinitis
Measles	Rash, diarrhoea, middle ear infection, encephalitis, precipitates malnutrition	Keratoconjunctivitis, precipitates xerophthalmia	Optic neuritis
Infectious mononucleosis	Fever, malaise, rash, lymphadenopathy, splenomegaly	Conjunctivitis	Uveitis, retinal phlebitis, papillitis
Cytomegalovirus	Immunocompromised adults and newborns—fever, hepatitis, pneumonitis, encephalitis	Microphthalmos	Necrotizing chorioretinitis, optic atrophy
Acquired immune deficiency syndrome	Immunocompromised individuals, Kaposi sarcoma	Kaposi sarcoma (Fig. 32.5)	Cotton-wool spots on retina, cytomegalovirus retinitis
Fungal			
Candida	Oral and genital 'thrush'	Conjunctivitis	Keratitis, retinitis, endophthalmitis
Cryptococcus	Immunocompromised adults, pneumonia, meningitis		Papilloedema, optic atrophy
Bacterial			
Tuberculosis	Fever, malaise, granulomas (lung, lymph node)	Phlyctenular conjunctivitis	Granulomatous uveitis, juxtapapillary choroiditis
Leprosy	Thickened peripheral nerves, hypaesthetic skin lesions, weakness of peripheral muscles	Facial palsy, madarosis	Iritis, secondary glaucoma, cataract

Table 32.3B Ocular and systemic features of parasitic diseases

Systemic diagnosis	Systemic features	Extraocular features	Intraocular features
Toxoplasmosis	Congenital—mental retardation, deafness Immune deficient patient—encephalitis		Macular scarring, retinochoroiditis, vitritis
Toxocariasis	Visceral larva migrans—liver, lungs, heart, brain		Vitritis, choroiditis, vitreoretinal granuloma
Cysticercosis	Cysticerci—subcutaneous, brain, spine, heart	Subconjunctival cysticerci	Subretinal or vitreous cysticerci
Onchocerciasis	Subcutaneous onchocercomas		Sclerosing keratitis, uveitis, cataract

to herpes simplex virus infection and necrotizing chorioretinitis in cytomegalovirus infection. Indirect involvement is illustrated by phlyctenular conjunctivitis in patients with tuberculosis, subacute sclerosing panencephalitis manifesting with chorioretinitis years after an attack of measles and papilloedema due to cryptococcal meningitis.

Acquired immune deficiency syndrome

Acquired immune deficiency syndrome (AIDS) is caused by infection with the human immunodeficiency virus (HIV), an RNA virus of the human retrovirus family. The virus has two subtypes; HIV-1 is responsible for most human infections. Confirmed routes of transmission include sexual intercourse, through infected blood and

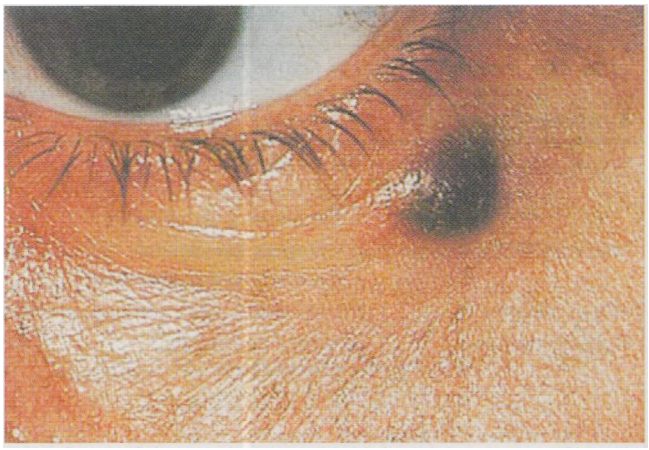


Fig. 32.5 Kaposi sarcoma in a patient with acquired immune deficiency syndrome.

spread from mother to child, which may be either haematogenous or through breast milk.

The disease is characterized by a deficiency of T helper lymphocytes, leading to an inability to combat opportunistic infections. The clinical spectrum of manifestations ranges from an acute infection with an asymptomatic 'window period' before seroconversion, persistent generalized lymphadenopathy and 'full-blown' AIDS. Diagnosis is based on enzyme immunoassay detection of HIV antibodies. The World Health Organization has laid down criteria for making a provisional diagnosis when blood tests may not be available. The presence of any two major signs associated with at least one minor sign is considered to be an indication of AIDS. Major signs include (i) loss of more than 10% of body weight, (ii) chronic fever and (iii) chronic diarrhoea of over 1 month's duration. Minor signs include (i) chronic cough, (ii) itchy dermatitis, (iii) recurrent herpes zoster, (iv) oropharyngeal candidiasis, (v) chronic progressive herpes simplex infection and (vi) generalized lymphadenopathy.

Ocular lesions are a common feature of AIDS. The ophthalmic manifestations of HIV infection itself are a microangiopathy affecting mainly the conjunctiva and retina and Kaposi sarcoma of the lids and conjunctiva. Conjunctival microvasculopathy, seen in about 75% of patients, is characterized by telangiectasia, segmental dilatation, comma-shaped fragments and sludging in the smaller blood vessels. HIV retinopathy is a non-infectious microvascular affection seen in 50-70% of AIDS patients. Superficial and deep retinal haemorrhages, microaneurysms and cotton-wool spots are characteristic features. The cotton-wool spots regress over 6-8 weeks. Other opportunistic infections include (i) adnexal lesions such as herpes zoster ophthalmicus, molluscum contagiosum and pyogenic infections, (ii) anterior segment changes such as infective keratitis and uveitis, (iii) posterior segment diseases such as cytomegalovirus retinitis, progressive outer retinal necrosis, herpes zoster retinopathy, *Pneumocystis carinii* choroidopathy, syphilis, toxoplasmic retinochoroiditis, mycobacterial infections and fungal endophthalmitis, and (iv) neuro-ophthalmic manifestations such as papilloedema, optic atrophy, headaches and nerve palsies.

The CD4 T lymphocyte count correlates to some extent with the clinical manifestations. A count below 500 cells/mm^3 is seen with Kaposi sarcoma, lymphoma and tuberculosis. Counts below 250 cells/mm^3 are associated with *Pneumocystis* and *Toxoplasma* infections, and counts of less than 100cells/mm^{3}with microvasculopathy, CMV retinitis, varicella zoster retinitis, cryptococcus and HIV encephalopathy.

A summary of the clinical features of systemic infections and infestations likely to affect the eye are outlined in Table 32.3A and B.

Endocrine disorders

Apart from diabetes mellitus, other metabolic and endocrine disorders also have important ophthalmic manifestations. In certain disorders the presence of specific ophthalmic features (Table 32.4) can help in reaching a final diagnosis. For example, a Kayser-Fleischer ring (Fig. 32.6) seen in a patient with liver cirrhosis or ataxia can confirm the presence of Wilson disease. Similarly, prominent corneal nerves seen in a patient with medullary carcinoma of the thyroid prompt a careful search for other endocrine neoplasms such as phaeochromocytoma.

Muscular disorders

The extraocular muscles differ from skeletal muscles elsewhere in the body in the nerve to motor end-plate ratio and tonicity of the muscles. This affects the clinical

Table 32.4 Ocular and systemic features of endocrine disorders and disorders of metabolism

Systemic diagnosis	Systemic features	Extraocular features	Intraocular features
Homocystinuria	Mental retardation, tall, arachnodactyly, thromboembolic episodes		Subluxation of the lens
Mucopoly accharidoses	Dysmorphia, behavioural disorders, cardiac anomalies	Corneal opacification	Pigmentary retinopathy, glaucoma, optic atrophy
Wilson disease	Extrapyramidal signs, cirrhosis	Kayser–Fleischer ring (Fig. 32.6)	Sunflower cataract
Diabetes mellitus	Peripheral neuropathy, glomerulosclerosis	Xanthelasma, extraocular muscle palsies, infections	Cataract, iris neovascularization, retinopathy, vitreous haemorrhage, tractional retinal detachment, optic neuropathy (Fig. 32.7)
Hyperthyroidism	Tachycardia, tremors of the hand	Exophthalmos, lid retraction, lid lag	Superior limbic keratitis, disc oedema
Hypoparathyroidism	Tetany, seizures	Fasciculation	Cataract, disc oedema

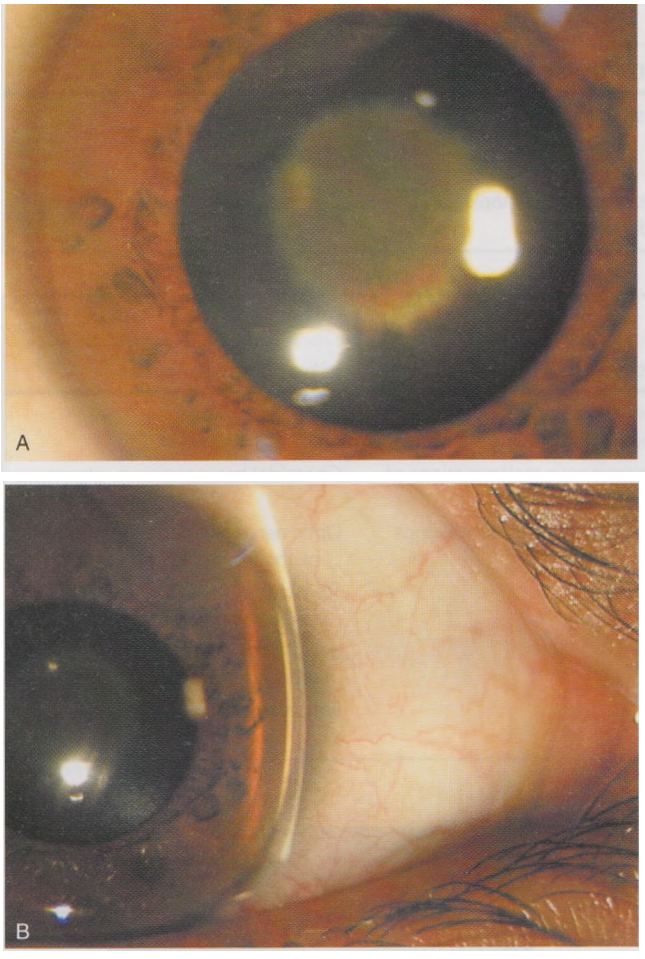


Fig. 32.6 Wilson disease. (A) Sunflower cataract; (B) Kayser-Fleischer ring at Descemet's membrane.

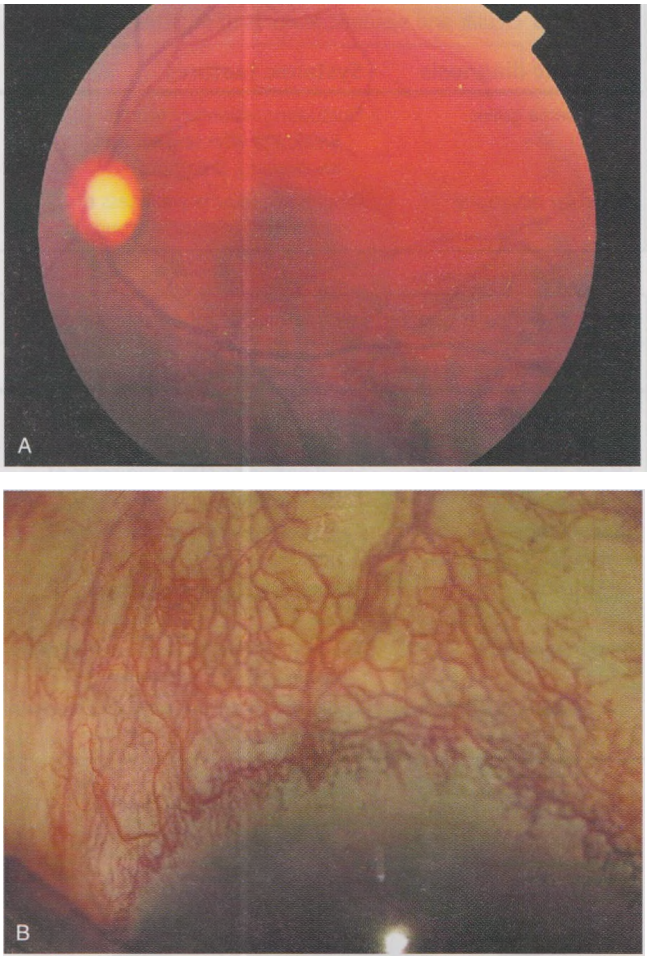


Fig. 32.8 Sturge-Weber syndrome. (A) Choroidal haemangioma; (B) episcleral angioma at the limbus.

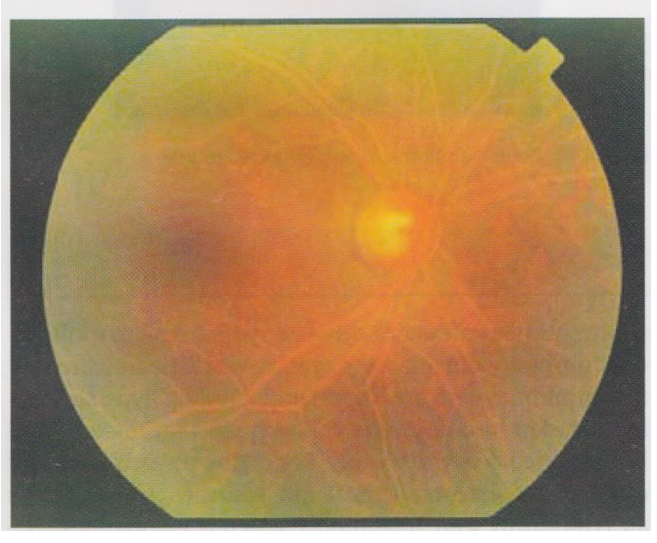


Fig. 32.7 Lipaemia retinalis in a juvenile diabetic. (By Courtesy of PN Tandon)



Fig. 32.9 Plexiform neurofibromatosis of the right side of theface.

Table 32.5 Ocular and systemic features of muscular disorders

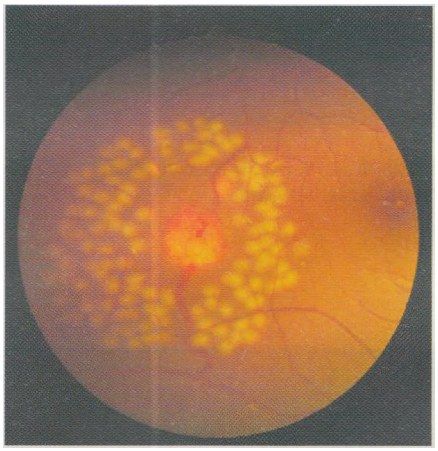
Systemic diagnosis	Systemic features	Extraocular features	Intraocular features
Myasthenia gravis	Fluctuating voluntary muscle weakness affecting speech, swallowing, breathing	Ptosis, diplopia	
Muscular dystrophy	Progressive muscle weakness of characteristic muscle groups	Ptosis, exophthalmoplegia, dry eye	Cataract, pigmentary retinopathy

Table 32.6 Ocular and systemic features of inherited disorders

Systemic diagnosis	Systemic features	Extraocular features	Intraocular features
Down syndrome	Mental retardation, muscle hypotonia, congenital heart disease	Mongoloid slant of eyes, epicanthic folds, keratoconus	Cataract, iris spots
Sturge–Weber syndrome (Fig. 32.8)	Facial port-wine stain, angiomas of the occipital meninges	Arteriovenous malformations of episclera	Choroidal haemangioma, glaucoma
Neurofibromatosis (Figs 32.9 and 32.10)	*Cafe au lait* spots, subcutaneous neurofibromas	Ptosis, pulsating exophthalmos	Optic nerve glioma, neurofibromas of the iris, retina and choroid
Albinism	Hypopigmented skin and hair	Nystagmus	Translucent iris, albinotic fundus, foveal hypoplasia
Marfan syndrome	Tall, arachnodactyly, aortic aneurysm, cardiac valvular anomalies		Subluxation of the lens, myopia, retinal detachment
von Hippel—Lindau disease	Angiomatosis of the central nervous system and kidneys		Retinal angiomas (Fig. 32.11)



Fig. 32.10 Lisch nodules on the iris in a patient with neurofibromatosis type 1. (By courtesy of E Ravindra Mohan)



Fig, 32.11 Retinal angioma in angiomatosis retinae.

presentation of diseases that involve both the skeletal and ocular muscles (Table 32.5).

Inherited disorders

The list of inherited disorders which can affect the eye is too long to be discussed in detail. A few relatively prevalent disorders with prominent ocular features are detailed in Table 32.6. Most diseases would present initially to a paediatrician, but the frequent association of ophthalmic features demands an ophthalmic work-up to prevent needless ocular morbidity.

SUMMARY

A large number of systemic diseases which lead to multisystem morbidity can affect the eyes as well. Diseases affecting the immune system are important including hypersensitivity disorders, autoimmune collagen vascular diseases and immunodeficiency disorders. Endocrine diseases, vascular diseases and haematological malignancies and diatheses are commonly seen. In addition, systemic myopathies, dystrophies and various inherited disorders can have prominent and pathognomonic ocular manifestations.

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Chapter 33

Genetics in Ophthalmology

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FUNDAMENTALS OF HUMAN MOLECULAR GENETICS

DNA, RNA and the basic building blocks

Genes are made of DNA (deoxyribonucleic acid), which acts as a carrier molecule and contains all the information required for protein synthesis and creation of a composite living being. The DNA molecule has a double helical structure. Each strand is composed of a sequence of four different nitrogenous bases joined to a sugar (deoxyribose) and a phosphate, each structural unit constituting a nucleotide. The actual sequence varies from individual to individual in some regions while it is identical in others, and it is this which maintains the uniformity of the species but, at the same time, gives rise to characteristics which are unique for an individual. The four nitrogenous bases are *adenine* (A) *and guanine* (G) which are purines, and *thymine* (T) and *cytosine* (C) which are pyrimidines. The double strand of the DNA is held together by hydrogen bonding between the nucleotides of opposite strands. The pairing is specific: adenosine always pairs with thymine (A-T) and guanine with cytosine (G-C). RNA (ribonucleic acid) is a single-stranded nucleic acid chain composed of the same nucleotides as DNA except that it has the sugar ribose instead of deoxyribose and a uracil base instead of thymine. Accurate copying of the DNA sequence is essential during DNA replication, which is required for cell division. Accurate transcription of DNA into RNA is a prerequisite for gene expression and protein synthesis. The pattern of hydrogen bonding between specific base pairs is the molecular basis for these processes.

DNA, chromosomes and genes

Chromosomes are simply described as packages of human DNA located in the nucleus of the cell. Chromosomes are composed of individual strands of DNA. Each double-stranded DNA is wound around histone proteins. The combined DNA-histone complex then further coils to form a nucleosome. Nucleosomes coil further, and are complexed with additional proteins to form chromatin, which then form the chromosomes. The composite group of human chromosomes is called the *human genome* and includes two sex chromosomes (X, Y) and 22 paired chromosomes (autosomes). Women have two X chromosomes and men have one X and one Y chromosome. *Genes* are specific DNA sequences that contain the code for specific proteins that lead to individual characteristics or functions. Genes are located on the chromosomes and the position is defined as a locus. At a particular locus there is one pair of genes or alleles on the pair of chromosomes, i.e. one on each chromosome.

Gene expression and protein synthesis

The genetic information in the DNA is transferred to RNA by a process called *transcription* and converted into protein synthesis by a process termed as *translation.* The 'expression' of a gene (*see* Fig. 33.3) basically involves the recognition by the enzyme RNA polymerase of a particular DNA sequence known as the *promoter sequence,* as a site for starting RNA synthesis. Once initiated to start 'reading' the DNA sequence in a particular order by the recognition of the promoter sequence, the RNA polymerase assembles a complementary strand of RNA to that specific portion of DNA.

The process by which an RNA strand is synthesized from a DNA template is called *transcription* and the RNA strand produced is called a *transcript.* There are three different types of RNA which are transcripted and participate in protein synthesis: (i) *messenger* RNA (mRNA); (ii) transfer RNA (tRNA) and (iii) ribosomal RNA (rRNA).

In addition to genetic material for selecting the correct amino acids for protein synthesis, human genes contain intervening DNA sequences that are not translated into polypeptides and proteins. These intervening sequences are called introns. They do not have any specific function, and constitute the portion which is transcribed by RNA polymerase but is spliced out of the initial RNA strand (termed heteronuclear RNA or hnRNA) to leave the residual mRNA. The mRNA is the template for protein synthesis and passes from the nucleus into the cytoplasm where it is decoded or 'translated' by tRNA. Each tRNA molecule carries a specific amino acid and has a 'recognition' region consisting of three base units which pair with a corresponding complementary unit of three bases on the mRNA. The amino acids are then joined together to form a polypeptide chain or protein on the rRNA in cytoplasmic organelles called ribosomes. The amino acids are thus attached sequentially to the polypeptide chain in the correct order as determined by the mRNA template. This process of polypeptide and protein synthesis from the RNA is called *translation.* The actual process of polypeptide synthesis takes place on cytoplasmic organelles called ribosomes. The major portion of ribosomes is constituted by rRNA.

In other words, the sequence of bases in the mRNA determines the sequence or order of specific amino acids that make up the polypeptide chain(s) that constitute various proteins. Each individual amino acid is encoded by a unit of three nitrogenous bases in mRNA known as *codons.*

Transfer RNA molecules bind specific amino acids and 'recognize' the corresponding three-base codon in the tRNA. Ribosomes bind to the mRNA and, with the help of the tRNA and rRNA, the amino acids carried by the tRNA are aligned to form the polypeptide. The polypeptide chain undergoes post-translation modification to form the mature protein.

Cell division, replication and the cell cycle

Replication of a cell occurs by the process of cell division. Before cell division, DNA replication takes place. This is a process by which the entire DNA sequence, which comprises the complete human genome, is duplicated or copied by the enzyme DNA polymerase. Once the DNA is replicated, the cell either divides by mitosis or meiosis. In *mitosis,* one copy of each chromosome pair passes to each new daughter cell so that cell division produces two identical daughter cells, each of which is an exact copy of the dividing mother cell.

The other type of cell division is by *meiosis* which is the special process by which the genetic material of a cell is divided to produce the reproductive cells, i.e. sperms (males) and eggs (females). Meiosis, too, begins with DNA replication following which there is a pairing of homologous chromosomes and an exchange of genetic material between the chromosome pairs by crossing over, resulting in recombination. Following this, the doubled chromosomes are distributed to separate daughter cells which are genetically identical at this stage. A second cell division then occurs, this time without further DNA duplication or replication. The doubled chromosomes separate at this stage and each of the two resultant daughter cells have half of the genetic material of the somatic tissue cells.

Genetic disorders, mutations and DNA-based diagnosis

Mutations are changes in the so-called 'blueprint' of human characteristics, i.e. changes in the DNA sequence of a gene that result in a change which is biologically significant. The resultant defect may either be that the protein product is not synthesized at all or might be formed but not function properly. Sometimes mutations create proteins that have a new function which may have an adverse effect on the cell. If the normal protein product of a particular gene is necessary for a crucial biological function, an alteration as a result of a mutation in that gene would lead to an alteration of the normal phenotype.

The most common mutations encountered in humans are *point mutations* which arise due to a single base change in the amino acid sequence. Point mutations that result in a change in the amino acid sequence of the polypeptide chain of a protein arising from replacement of nucleotides are called *missense mutations.* Sometimes point mutations alter the polypeptide production by interrupting the promoter sequence or creating a premature stop codon earlier on in the sequence which is known as nonsense mutation.

Another less common type of mutation is the insertion or deletion of large segments or blocks of DNA

Table 33.1 Detection of gene mutations

Method	Approach	Basis	Example
Genetic linkage analysis	Indirect	Whether or not an individual has inherited a chromosome carrying the abnormal gene responsible for the disease is determined by segregation of genetic markers linked to that specific gene	Any genetically mapped disorder
Direct mutation analysis	Direct	The specific base-pair change in the DNA sequence of the gene which is responsible for the disease is identified. Specific DNA probes which are allele-specific oligonucleotides and only hybridize to the abnormal mutated gene are used	When the DNA sequence of the gene is known and is not very long such as the cystic fibrosis gene

which may also severely affect gene expression. Such mutations may result in a more severe change in the functioning of the protein produced.

Another mechanism of genetically inherited disorders is breaks in specific genes caused by an interruption in their DNA sequence, which occur during chromosomal rearrangement. Usually such a break in the DNA sequence leads to an unstable, incomplete and dysfunctional protein. Sometimes a 'fusion polypeptide product' which may have a completely different new activity in the cell is produced if a broken gene fuses with another gene.

The identification of individuals likely to be affected by an inherited disorder, using the modern technology of molecular genetics to demonstrate DNA mutations known to lead to the disease, is called DNA-based diagnosis (Table 33.1). The aim is essentially to easily recognize a condition so that early intervention can be tried to prevent or reverse the underlying pathological process.

TRANSMISSION OF GENETIC DISORDERS

Genetic disorders are transmitted within a family for generations. The origin would be by a mutation and subsequent propagation is by hereditary transmission. Depending on the type of genetic defect the pattern of transmission can be predicted and *vice versa.* Four basic types of genetic defects are known in humans: (i) monogenic or single-gene defects transmitted by Mendelian inheritance, which can be dominant or recessive and autosomal or X-linked; (ii) polygenic or multifactorial; (iii) chromosomal and (iv) cytoplasmic or mitochondrial.

A detailed family history must be obtained and involvement of family members documented on a pedigree chart or family tree. The abnormal phenotype is coloured solid and may be determined by history alone or based on clinical examination by a qualified expert. Sometimes from history it is not clear whether a particular family member is affected or not. If that individual is not available for clinical examination, then it should be indicated by a query on the pedigree chart *(see* Figs 33.1-33.5).

The pattern of inheritance of some relevant ophthalmic conditions is summarized in Table 33.2.

Monogenic or Mendelian inheritance

Gregor Mendel, an Austrian monk in the nineteenth century, did a series of experiments involving the reproduction of plants and, based on his experiments, laid down two important rules which are applicable to humans as well for diseases which are transmitted by a single gene.

1. The first rule is the *principle of segregation.* This simply states that genes exist in pairs called alleles and that from each biological parent only one member of each pair is transmitted to the off-spring. The law of segregation refers to the behaviour of the chromosomes in meiosis.
2. The second rule is the *law of independent assortment.* This rule essentially states that genes at different loci segregate and are transmitted independently from there.

Mendel's work also demonstrated the concept of dominant and recessive traits. A *dominant* trait is one which manifests itself even if it is represented by a single gene. A *recessive* trait is one which must be present on

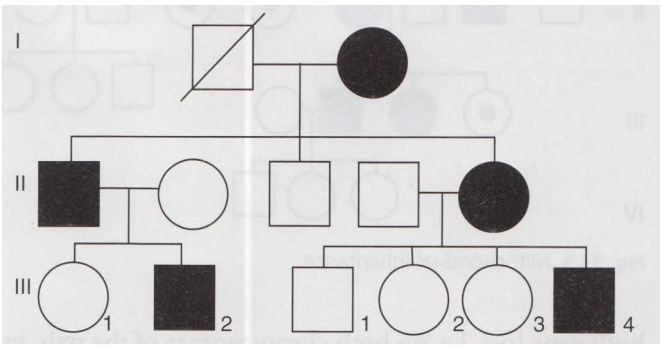


Fig. 33.1 Autosomal dominant inheritance. Pedigree of a family with Marfan syndrome. Affected members who could not be examined were known to be excessively tall and some were known to have dislocated lenses and retinal detachment.

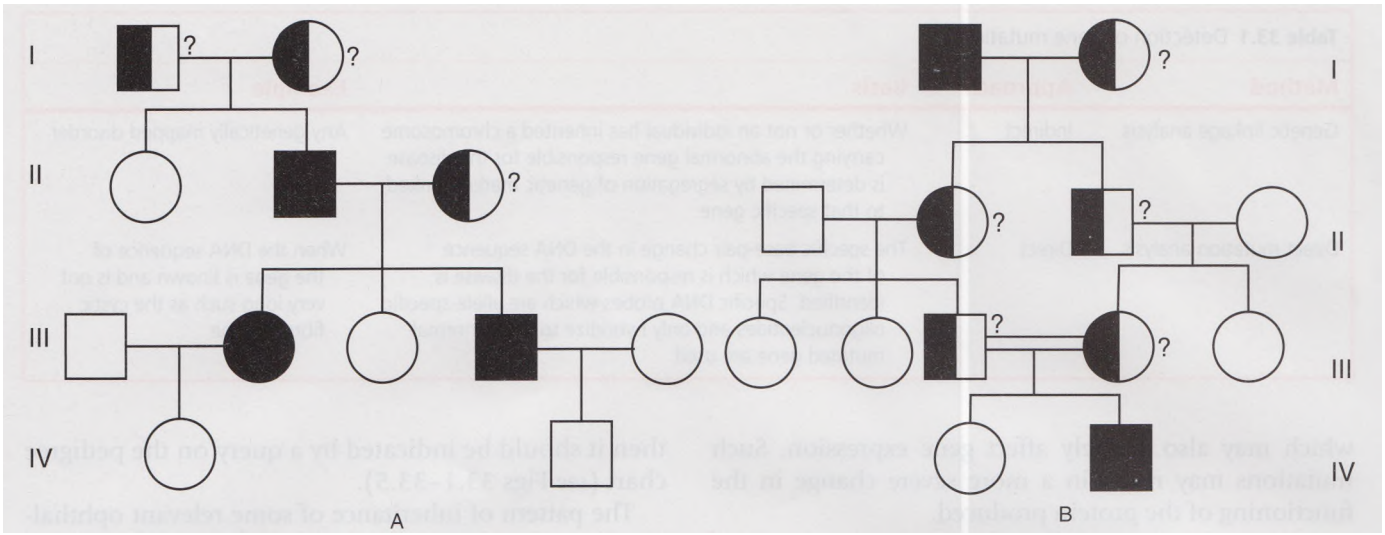


Fig. 33.2 Autosomal recessive inheritance. Pedigree charts of two families with bilateral simple ectopia lentis. Question marks indicate that the carrier state has been assumed according to the history.

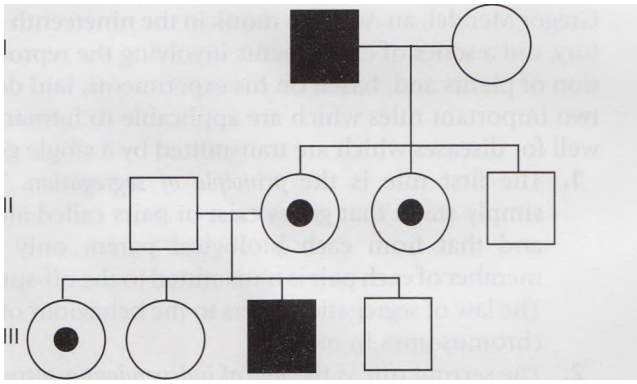


Fig. 33.3 X-linked recessive inheritance. Pedigree chart of a family with severe retinitis pigmentosa.

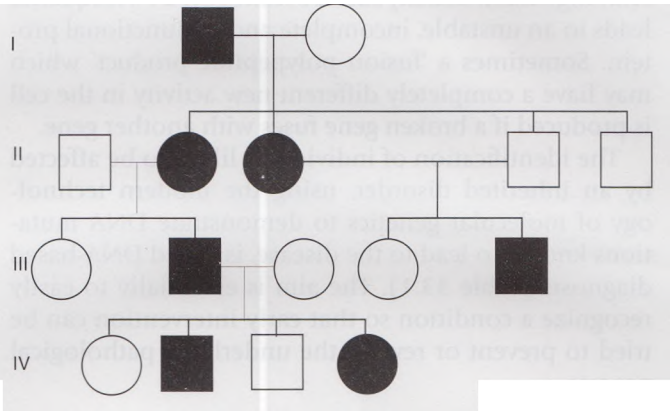


Fig. 33.4 X-linked dominant inheritance.

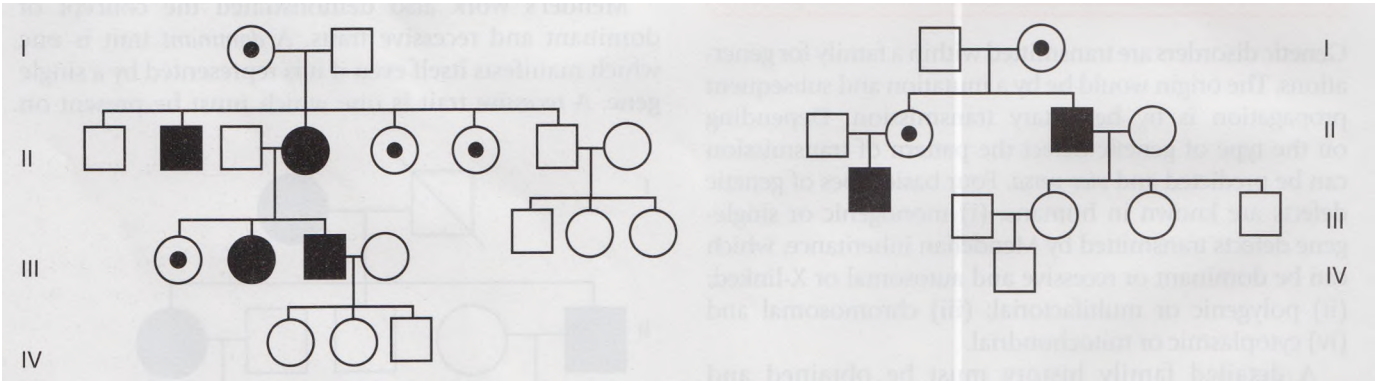


Fig. 33.5 Mitochondrial inheritance.

both gene loci, i.e. on both chromosomes of the pair, in order to manifest the clinical characteristics. Individuals who have two alleles of the same kind are called *homozygous* and those with only one, *heterozygous* for that particular trait.

An example to illustrate this is the inheritance pattern of the colour of the eyes and hair. The principle of independent assortment means that inheritance of eye colour is independent of hair colour. A brown-haired person (brown hair colour is a dominant and blonde

Table 33.2 Hereditary ophthalmic diseases

Disease	Inheritance pattern
General	
Refractive error*	Component ametropia, AR
	Overall ametropia, multifactorial
Dyslexia*	Multifactorial, AD
Nystagmus*	AD/XD/XR
Anterior segment	
Lattice corneal dystrophy	AD
Macular corneal dystrophy	AR
Avellino corneal dystrophy	AD
Reis-Buckler corneal dystrophy	AD
Meesman corneal dystrophy	AR
Juvenile glaucoma*	AD/AR
Primary open-angle glaucoma	Multifactorial
Primary congenital glaucoma*	Sporadic/mutation/AR/AD/AR
Rieger syndrome	
Aniridia*	AD, AR
Non-syndromic congenital cataract*	AD, AR, XR
Ectopia lentis*	Sporadic/AD or rarely AR
Retina	
Retinoblastoma	AD
Kearns-Sayre syndrome	Mitochondrial
Tritanopia	AD
X-linked colour blindness	XR
Blue cone monochromacy*	XR/AR
Total rod monochromacy	AR
Wagner syndrome	AD
Goldmann-Favre syndrome	AD
Angioid streaks	AR
Disciform macular degeneration (Kuhnt-Junius syndrome)	AD
Retinitis pigmentosa*	AR/AD/XR
Congenital stationary night blindness	AR/AD/XR
Norrie disease	XR
Leber congenital amaurosis	AR
Gyrate atrophy	AR
von Hippel-Lindau disease	AD
Ocular albinism	XR
Oculocutaneous albinism*	AR, AD
Neuro-ophthalmic	
Leber optic atrophy	Mitochondrial
Systemic malformations	
Neurofibromatosis	AD
Waardenburg syndrome	AD
Stickler syndrome	AD
Marfan syndrome	AD
Down syndrome	Chromosomal trisomy 21

*Heterogeneic disorders with more than one pattern of inheritance: AD, autosomal dominant: AR, autosomal recessive: XR, X-linked recessive: XD, X-linked dominant.

hair is a recessive trait), therefore, could have either blue eyes or brown eyes (blue eyes is a recessive trait and brown pigmented irises a dominant trait). By the law of segregation, if a parent is heterozygous for brown hair, i.e. one gene is for brown hair and the other gene on the paired chromosome is for blonde hair, but the parent's hair is brown because the latter is the dominant trait, then the individual offspring of that person will only get one gene for hair colour from that particular parent, i.e. either for blonde hair or brown hair. The offspring's own hair colour will depend on what combination of genes he or she receives from both parents.

In his study on inheritance of different traits in pea plants, Mendel observed that most traits segregated independently of each other but some traits segregate and get inherited together. This observation is explained by the fact that genes which are located close together on, a chromosome are usually inherited together, as recombination is unlikely to occur between them. On the other hand, genes located on distant loci are likely to be passed on separately to the offspring as recombination is more likely to occur.

Monogenic disorders have a relatively high risk of transmission with fixed predictable risk ratios and the risk can be theoretically predicted. The severity of the defect in affected individuals does not affect the risk of transmission to their offspring; there is a variation in phenotypes which, however, is discontinuous and the severity of the defect is not generally influenced by environmental factors.

Autosomal dominant traits

Autosomal dominant disorders are more commonly related to genes coding for non-enzymatic structural proteins, collagen or cell membrane components and manifest or express the abnormal phenotype when only one abnormal gene is present, i.e. heterozygotes manifest the disease. Homozygous states with two defective genes are generally lethal. The majority of phenotypes are relatively mild compared to recessive traits. Genotypes are usually manifested as phenotypes, except in cases with reduced penetrance, and the carrier state does not occur. However, for diseases known to manifest late in life such as Huntington chorea, certain types of macular degeneration and autosomal dominant retinitis pigmentosa, younger heterozygotes who carry the trait but have not yet expressed the disease could theoretically be considered as 'carriers'. This has to be accounted for when plotting the family tree for members who are younger than the age of manifestation of the disease.

If one parent is affected the risk for the offspring being affected is 50%, and is 75% if both parents are affected. Both males and females are equally at risk but sex influence is sometimes seen such as in Fuchs endothelial dystrophy which is seen more in females and hereditary

baldness is more frequent in males. Variable expressivity is a well-known feature, incomplete penetrance may lead to 'skipping' of a generation in a family. Compared to recessive traits, mental retardation is rare.

Certain forms of autosomal dominant mutations, such as those causing Marfan syndrome and achondroplasia, have a higher risk of the mutation occurring with advanced paternal age. Fig. 33.1 is an example of a family tree for an autosomal dominant disorder.

Autosomal recessive traits

Homozygous individuals manifest the phenotype, heterozygous persons are 'carriers' and generally clinically normal, though some subtle defects may be detectable such as a mildly depigmented retina in 'carriers' of albinism and Stargardt disease. Parents of affected persons could either both be carriers or one could be affected and the other a carrier. Risk to the off-spring is 25% if both parents are carriers, 50% if one is affected and the other a carrier and 100% if both are affected. Fig. 33.2 is an example of a family tree for an autosomal recessive disorder.

X-linked recessive trait

Many ocular diseases are inherited as X-linked recessive traits. The affected gene is present on the X chromosome. The genotype manifests as the phenotype in males but females are 'carriers' if heterozygous, and clinically affected if homozygous. Carrier females will rarely manifest the disease if by 'lyonization' an exceptional number of normal X chromosomes become inactivated. There is a 50% risk for the daughters of a female carrier to become carriers and a 50% risk for her sons to be affected. An affected male does not transmit the trait to his sons but transmits the gene to 100% of his daughters. Fig. 33.3 is an example of a family tree for an X-linked recessive disorder.

X-linked dominant trait

There are few ocular anomalies that are inherited this way. Myoclonic nystagmus has been suggested to be possibly transmitted as a X-linked dominant trait. The phenotype reflects the genotype, all daughters and no sons of an affected male are affected. Female-to-female transmission of disease is seen, unlike in X-linked recessive and there is a theoretical risk for female members in the family to be affected at a rate twice as high as males. Fig. 33.4 is an example of a family tree for an X-linked dominant disorder.

Multifactorial or polygenic inheritance

There are several phenotypic traits that are dependant on multiple genes for expression. This is termed as polygenic or multifactorial inheritance. It differs from monogenic inheritance in several ways: (i) it has a relatively low risk for transmission; (ii) the risk increases with each affected sibling; (iii) variable phenotypes have a continuous distribution such as height, intelligence or refractive error, the severity being significantly influenced by environmental factors; (iv) there is increasing risk to the offspring with severity of the defect in the parent and (v) it has, at best, only an empirical risk prediction. Refractive errors, strabismus, primary open-angle glaucoma, hypertensive retinopathy and diabetic retinopathy are some examples.

Chromosomal inheritance

Change in the structure of the chromosomes can occur by changes in number or aneuploidy (deletions, duplications, translocations or the attachment of a deleted segment to another non-homologous chromosome), and inversions, where a portion breaks in two places and rejoins the same chromosome after rotation. Structural defects in chromosomes are detected by karyotype analysis and band-staining techniques using peripheral lymphocytes obtained by venepuncture. Earlier, bone marrow cells and fibroblasts obtained from skin biopsies were used for cytogenetic studies but lymphocytes are the most commonly used today.

Most chromosomal errors involving the autosomes are either lethal or cause severe morbidity and are in fact responsible for 50% of spontaneous abortions and stillbirths. Severe mental retardation is very common. Chromosomal abnormalities of the sex chromosomes are less severe. Important disorders of relevance to ophthalmology are trisomy 21 (Down syndrome), deletion of part of the long arm of chromosome 13 (13q associated with retinoblastoma), deletion of a part or the entire short arm of chromosome 5 (5p or *cri du chat* syndrome) and fragile X syndrome.

There is usually no previous family history in these disorders and pedigree analysis is usually difficult. Advanced maternal age is correlated with an increased frequency of Down syndrome. Biochemical assays are not feasible and karyotype analysis by amniocentesis between the sixteenth and twentieth week of pregnancy or chorionic villus sampling by the tenth week after conception are methods used for prenatal diagnosis when indicated.

Cytoplasmic or mitochondrial inheritance

Also known as maternal inheritance, cytoplasmic or mitochondrial inheritance is applicable to the chromosomes contained within the mitochondria as their own circular double-stranded DNA which replicates autonomously and codes for enzymes or subunits of enzymes. Their primary function is to participate in the energy reactions of the cell. Mitochondria are present in the cytoplasm of the ova but are

lost by spermatozoa, and the few remaining to supply the sperm with energy to 'seek' the ova do not enter the ovum at fertilization. Hence all our mitochondria and the mitochondrial DNA are inherited exclusively from our mother. The inheritance is differentiated from the X-linked recessive pattern by the observation that none of the offspring of an affected male will have the trait but all children of an affected mother have the trait (Fig. 33.5). Neuromuscular defects and neuro-degenerative disorders such as myotonic dystrophy and Leber hereditary optic atrophy are of ophthalmic interest which are inherited in this manner.

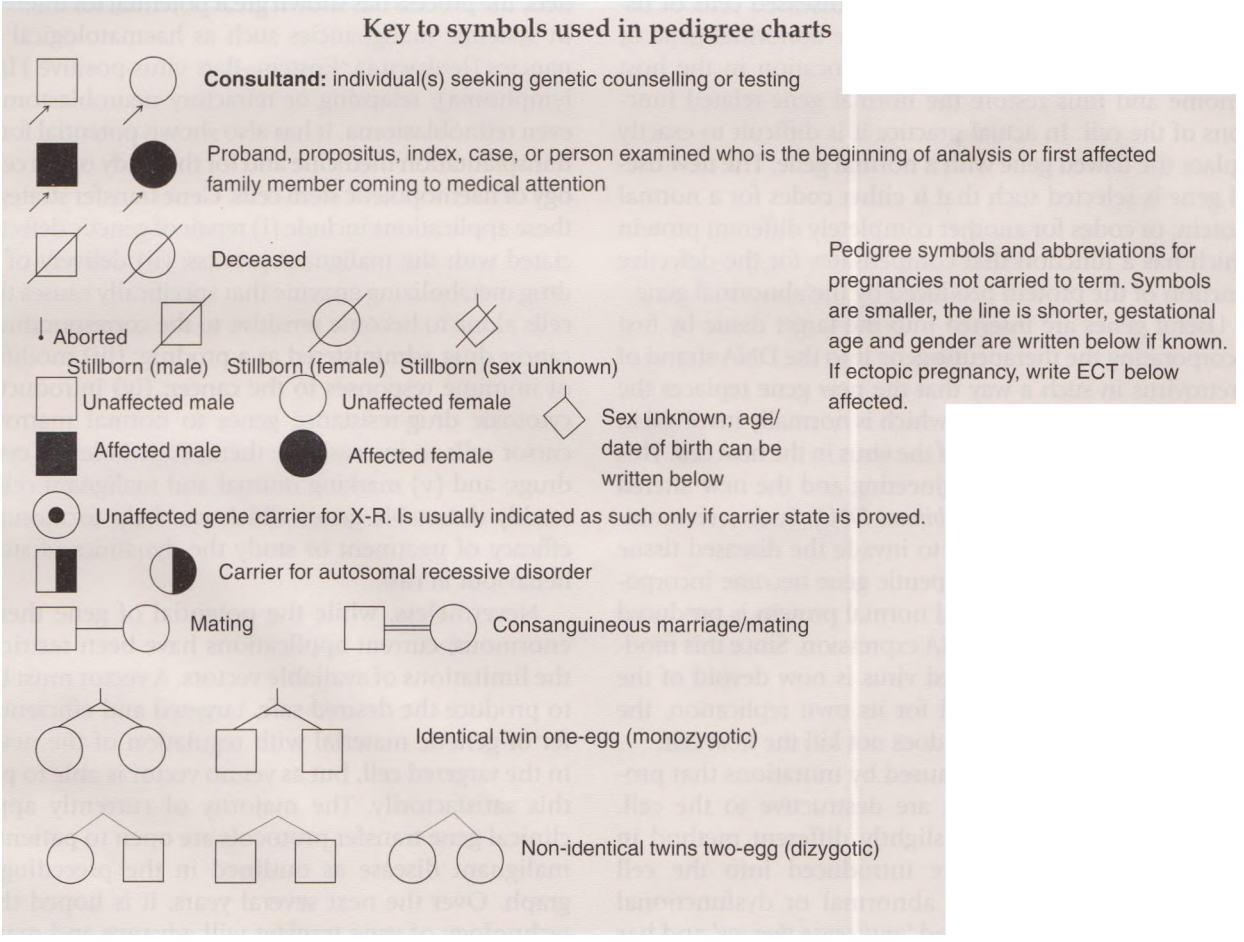
TREATMENT AND PREVENTION OF GENETIC DISEASES

Advances in human ocular molecular genetics have identified the genes responsible for several ocular diseases.

Knowledge of molecular genetics and the precise identification of the location and characteristics of a defective gene gives us a better understanding of human genetics in general. This enables us to protect future generations, to some extent, by genetic counselling, and opens the door to the possibility of cure by gene therapy. This therapy for ocular disorders has promise as there are advantages due to the relatively easy accessibility of the eye, the ability to directly visualize the diseased tissue and the large number of gene-specific defects known to cause many inherited eye diseases.

Several inherited eye diseases are due to defective genes which have been isolated and characterized or the chromosomal location determined. Better knowledge and understanding of how mutated genes cause human ocular disease will lead to improved methods of diagnosis and treatment and eventually will improve the prognosis for vision.

There is no true cure for most genetic diseases. The symptoms can be treated by medication, replacement therapy with the missing enzyme or hormone (such as insulin in juvenile diabetes), controlling the diet or other environmental factors, or surgical procedures such as organ transplantation (as in corneal dystrophies) or excision (as in retinoblastoma). In some diseases a true



Symbols in pedigree charts vary slightly among different genetic counselling services. Each generation is denoted by Roman numerals. The female is shown on the right of the male in mating pairs. Offspring are depicted from left to right in descending order of age and denoted by Arabic numerals. For example, in Fig. 33.5 1112 is the index case.

cure at the molecular level can be attempted. The field of gene therapy is still in its infancy, but will undoubtedly become more advanced and applicable in the future.

At present, recognition of the limitation of therapy in genetic disorders and the reliable predictability of the pattern of transmission of genes from one generation to the next has led to the realization that prevention is the most reliable and effective means of dealing with hereditary disorders. This approach includes genetic screening, genetic counselling and prenatal diagnosis.

Concept of gene therapy

Any mutation in a particular gene due to an alteration in its DNA composition results in a defect in protein production either in the form of (i) complete absence of the protein or (ii) formation of a defective protein, which may not function normally or attain a new function that may be harmful or destructive to the cell.

The basic principle of gene therapy is to treat genetic mutations by introducing normal genes into the cells that are affected by the defective gene. The idea is that the copy of the normal gene delivered to the diseased cells or tissues will either physically replace the abnormal gene or function independently at another location in the host genome and thus restore the normal gene-related functions of the cell. In actual practice it is difficult to exactly replace the flawed gene with a normal gene. The new useful gene is selected such that it either codes for a normal protein, or codes for another completely different protein which has a function that compensates for the defective function of the protein produced by the abnormal gene.

Useful genes are inserted into the target tissue by first incorporating the therapeutic gene into the DNA strand of a retrovirus in such a way that the new gene replaces the portion of DNA of the virus which is normally involved in replication or proliferation of the virus in the host cell. This process involves genetic engineering and the new altered viral DNA is termed a *recombinant DNA.* Such a recombinant virus is then delivered to invade the diseased tissue whereby copies of the therapeutic gene become incorporated into the host DNA and normal protein is produced by the normal process of DNA expression. Since this modified recombinant engineered virus is now devoid of the normal viral genes required for its own replication, the virus cannot proliferate and does not kill the host cell.

There are also diseases caused by mutations that produce gene products which are destructive to the cell. These can be treated by a slightly different method in which oligonucleotides are introduced into the cell to inactivate the mutated, abnormal or dysfunctional gene. This is essentially called *'anti-sense therapy'* and has proved to be a useful approach for those diseases that are caused by mutations which lead to some new function *('gain of function mutations'*) such as cancers.

In summary, most approaches to gene therapy are presently targeted to the restoration of function in the somatic cells of the particular tissue affected (*somatic cell therapy).* Evaluation of alternative (non-viral) means of introducing therapeutic genes is under way. Delivery of these 'good genes' is tailored to target the specific somatic cells affected by the disorder. This target-specific modality of treatment, where the target is the diseased cells, does not affect the rest of the body so that the non-targeted cells and tissues and even the germ-line cells are not affected. Hence, as the germ cells continue to carry the mutated genome, the disease may still be transmitted to the offspring of the affected patient. In order to prevent transfer of the disease to the progeny or offspring of the affected individual, the gene therapy must be targeted at the germ-line cells. *Germ cell therapy* has raised ethical and moral concerns and some scientists feel that it should not be developed further.

The current position of gene therapy is still not well established. Although this modality of treatment was originally conceived as a means to replace or correct defective genes in patients with inherited or heritable genetic disorders, the process has shown great potential for intervention in systemic malignancies such as haematological malignancies (leukaemia, Epstein-Barr virus-positive Hodgkin lymphoma), relapsing or refractory neuroblastoma, and even retinoblastoma. It has also shown potential for use in transplantation medicine and for the study of the cell biology of haemopoietic stem cells. Gene transfer strategies for these applications include (i) repair of genetic defects associated with the malignant process; (ii) delivery of a prodrug metabolizing enzyme that specifically causes tumour cells alone to become sensitive to the corresponding anticancer drug administered as a prodrug; (iii) modification of immune responses to the cancer; (iv) introduction of cytotoxic drug-resistance genes to normal marrow precursor cells to increase the therapeutic index of cytotoxic drugs; and (v) marking normal and malignant cells with readily detectable genes which can help to monitor the efficacy of treatment or study the dynamics of stem cell behaviour *in vivo.*

Nevertheless, while the potential of gene therapy is enormous, current applications have been restricted by the limitations of available vectors. A vector must be able to produce the desired safe, targeted and efficient transfer of genetic material with regulation of the new gene in the targeted cell, but as yet no vector is able to provide this satisfactorily. The majority of currently approved clinical gene transfer protocols are open to patients with malignant disease as outlined in the preceding paragraph. Over the next several years, it is hoped that the technology of gene transfer will advance and many further clinical applications will be developed.

In summary, gene therapy has the potential to revolutionize the way in which diseases are treated but the field

needs time to mature scientifically with due attention to the future medical, economic and ethical ramifications of this form of treatment.

Genetic screening

Genetic screening programmes are for autosomal recessive disorders and are of two types: (i) homozygote screening or the search for individuals who have the disorder and (ii) heterozygote screening or the search for individuals who are carriers of a mutant gene and are thus at risk of having offspring with a particular disorder if the partner is also a carrier. Successful homozygote screening programmes have been put into practice in screening newborns for diseases such as phenylketonuria, homocystinuria, maple syrup urine disease, galactosaemia, cystic fibrosis, hypothyroidism and sickle cell disease. For a screening programme to be effective there should be an inexpensive and reliable test, some tangible benefit in the form of treatment and/or counselling, early diagnosis and education of the individuals and/or screening of families so that they understand the significance or implications of the results. In successful neonatal screening programmes early detection provides the opportunity to initiate appropriate therapy prior to the onset of irreversible damage. Also, the parents can be made aware of the risk to future offspring and can be offered the option of prenatal diagnosis in case of subsequent pregnancy.

Heterozygote screening has been effectively used in the detection of carriers of Tay-Sachs disease, which is a fatal lysosomal storage disease with no effective treatment. Screening of defined populations at risk (e.g. Ashkenazi Jews, in whom carrier frequency is as high as 1 in 25 as compared to approximately 1 in 300 in Anglo-Saxons) is undertaken to identify couples at risk. In case both potential parents are carriers they have a 25% chance of having an affected child. Prenatal diagnosis is available for this disease and provides an option for the couple to have unaffected children.

Genetic counselling

Prospective parents who have a known genetic disease or hail from a family with a known inherited disorder must be offered genetic counselling by the treating physician. Familiarity with the principles of medical genetics is therefore a must for every physician who should use this knowledge to understand and counsel patients. One aspect of genetic counselling involves determination of the risk for having an affected child. In addition, the reliability of the diagnosis must be determined. A family pedigree up to a minimum of three generations must be charted (Figs 33.1-33.5). The information must then be assembled to determine the pattern of transmission within the family and compare it with the pattern expected for that particular disease condition. Depending on the type of inheritance of disease (monogenic, multifactorial or chromosomal) and the reliability of the diagnosis, the risk to subsequent offspring may be predicted with a fair degree of accuracy. In addition to determining the risk, other information to be obtained prior to counselling includes the prognosis and treatment of the disorder and the availability of prenatal diagnosis and testing for the carrier state.

Counselling for many common multifactorial disorders such as diabetes mellitus, hypertension, atherosclerosis, certain congenital malformations and psychiatric disorders is presently imperfect and will remain so until we have a better insight into the complex interaction of the various genes and environmental factors which lead to the manifestation of the disease.

In single-gene disorders, once the diagnosis and family history are established, the risk prediction for the remaining family members, both existing and yet to be born, can be calculated. Autosomal dominant disorders have a 50% chance of being transmitted to the offspring. The risk will be somewhat less if the disease gene exhibits incomplete penetrance. For example, hereditary retinoblastoma, inherited as autosomal dominant trait with 80-90% penetrance will mean that only 40-45% of the children at risk will be affected because 5-10% of children who have inherited the abnormal gene still do not manifest the disease.

Individuals suffering from an autosomal recessive disorder will not have affected children unless they produce offspring by mating with a person who is either a carrier or is affected by the same disease. In the latter case they will produce only affected progeny, though there are rare exceptions to this rule such as if there are different mutations in the same gene which compensate for each other. If an affected person partners a heterozygous carrier, there is a 50% chance that their child will be affected. If a carrier mates with another carrier, the chance that they will have an affected child is 25%. In the case of a person who is affected by an autosomal recessive disease (homozygous for the defective gene), 50% of the offspring will be carriers. If the person is heterozygous for an autosomal recessive trait and partners a normal person, then 50% of their offspring will be carriers.

X-linked recessive disorders are passed from an unaffected female carrier to her daughters who will also be carriers with a risk of 50% for transmitting the disease. Fifty per cent of sons born to female carriers are affected by the disease. These disorders can also be passed from an affected father to all his daughters, who will be carriers and at risk to a tune of 100% of becoming carriers, but are never passed from an affected father to his son. All the sons of an affected male will be normal.

Table 33.3 Indications and methods of prenatal diagnosis

Indication	Method
Chromosomal disorders	Chromosome analysis of cells
Maternal age >35 years	Chorionic villus biopsy (9–12 weeks' gestation)
Parent with a known translocation	Sampling or amniocentesis (15–18 weeks' gestation)
Previous child with chromosomal abnormality	Maternal serum screening using biochemical markers
	Ultrasonography for stigmata of chromosomal disorder
Monogenic disorders	
Autosomal recessive inborn error of metabolism by family history	Biochemical and/or molecular analysis of cells, obtained by chorionic villus sampling or amniocentesis
Couple at risk for a disorder which does not have any molecular or biochemical markers	Fetal imaging by ultrasound (6–40 weeks' gestation)
Couple at risk for a disorder with available molecular markers	Molecular analysis of cellular DNA obtained by chorionic villus sampling or amniocentesis
Malformation disorders	
Couple at risk for having a child with a neural tube defect such as anencephaly, meningomyelocele or other multifactorial malformation syndrome	Fetal imaging by ultrasound, and measurement of alpha fetoprotein in serum and amniotic fluid (15–18 weeks' gestation) for neural tube defects

X-linked dominant disorders will pass from an affected male to 100% of his daughters and none of his sons. If a female is affected then 50% of her sons and 50% of her daughters have a chance of being affected.

Mitochondrial disorders are inherited from the mother by both sons and daughters. The frequency and severity of the disease in the offspring depend on the number of abnormal mitochondria that are present in the mother's egg that produced the affected child. Very few mitochondria in the developing embryo are derived from the sperm; so males affected by mitochondrial disease rarely have affected children.

Prenatal diagnosis

Following genetic counselling, the couple at risk for having a child with a genetic disorder has certain options, depending on the type of disorder (Table 33.3). With low risk or mild disease they may be reassured and may proceed to have a child despite the risks, without any subsequent monitoring. On the other hand, in the case of high-risk diseases with high morbidity they may perceive the risk as unacceptably high and decide to have no additional biological children or may consider adoption. In case both parents are heterozygous for an autosomal recessive disease, they may choose to utilize artificial insemination by an unaffected donor to reduce the risk. The magnitude of the decrease in risk will depend on the carrier frequency for that abnormal gene in the general population. Finally, if the disease can be detected antenatally, the couple may plan for another child and exercise the option of prenatal diagnosis with elective termination of pregnancy if the fetus is affected. The risk of having an affected fetus ranges from less than 10% for nearly all chromosomal and multifactorial disorders and up to 50% for autosomal dominant disease.

The indications for prenatal diagnosis are based on a comparison of the risk of the diagnostic procedure with the risk of having an affected child. The choice of a particular method of diagnosis is determined by the disease and family preference (Table 33.3). The options include estimation of maternal serum alpha-fetoprotein and other fetal proteins, which are non-invasive tests. In addition, ultrasonography is useful in detecting many fetal malformations. Obtaining samples of fetal cells and testing for enzymes, DNA and chromosomal defects is the third method. Fetal cells are obtained by second-trimester (15-16 weeks of gestation) amniocentesis or by transcervical and transabdominal chorionic villus samples. The latter can be performed at 9-12 months' gestation, and thus has the advantage of earlier diagnosis. The tissue obtained is fetal trophoblastic tissue which is an excellent source of fetal DNA and expresses nearly all the enzymes found in amniotic fluid. The risk of chorionic villus sampling in experienced hands is comparable with those of amniocentesis.

SUMMARY

Genetics has always been a very important branch of medicine and recent advances have made a major contribution in understanding and treating many ocular diseases. More and more genes are being identified with a direct relationship with ocular pathology. Examples include retinoblastoma, retinitis pigmentosa, congenital glaucoma and various corneal dystrophies. Myopia, age related macular degeneration and diabetic retinopathy are some examples of multifactorial disorders where both genetics and environmental influences play a role in clinical presentation and course.

34

The Causes and Prevention of Blindness

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Blindness is a devastating physical condition with deep emotional and economic implications. The consequences affect not only the individual but also the family and the community. A blind person loses his or her independence and is prone to experience a sense of profound loss and depression arising from being plunged in darkness. The family directly shares the economic and emotional burden and indirectly so does the community. Blindness from birth or early childhood has unique problems. Thus, much time and resources are spent to reduce this burden of blindness with an aim to prevent it as far as possible.

Prevention of blindness needs to be considered in view of the following four questions:

- How do we *define* blindness?
- How many people are blind, or what is the *magnitude* of blindness?
- Why are people blind or what is the *aetiology* of blindness?
- What can we do to *control* blindness?

WHAT IS BLINDNESS?

The World Health Organization (WHO) has classified defective vision into various grades. Categories of visual impairment 1 and 2 are referred to as 'low vision', 3, 4 and 5 as 'blindness' and category 9 as 'unqualified visual loss'.

If the extent of the visual field is also accounted for, patients with a field less than 10° but greater than 5° around central fixation should be placed in category 3 and patients with a field less than 5 ° around central fixation should be placed in category 4, even if visual acuity is not impaired (Table 34.1 and Fig. 34.1).

Applying the WHO criteria for definition of blindness, i.e. a visual acuity of less than 3/60 in the better eye with best possible refractive correction, approximately 45 million people in the world are estimated to be blind. Another 135 million people are deemed to be visually disabled, i.e. are either visually impaired or severely visually impaired. All these people require rehabilitative support services to a greater or lesser extent. The extent of disability perceived by an individual is related in some degree to the general level of affluence and health of the individual and the society in which he or she lives. This concept of functional blindness occurring before the vision drops to 3/60 necessitated terms such as 'economic' blindness in the past. This, however, led to confusion in nomenclature because the standard of what was perceived as economic blindness varied from country to country. For example, in a developing country such as India, vision less than 3/60 was classified as 'legal blindness' and vision less than 6/60 was termed 'economic blindness'. On the other hand,

Table 34.1 Classification of visual impairment and blindness

Category of visual impairment*	Best corrected visual acuity (BCVA) in the better eye
0 'Normal'	6/6 to 6/18, i.e. can see 6/18 or better
1 'Visual impairment'	<6/18 to 6/60, i.e. cannot see 6/18, can see 6/60
2 'Severe visual impairment'	<6/60 to 3/60, i.e. cannot see 6/60, can see 3/60
3 'Blind'	<3/60 to 1/60, i.e. cannot see 3/60, can see 1/60
4 'Blind'	<1/60 to only light perception, i.e. cannot see 3/60, can see light
5 'Blind'	No light perception, i.e. cannot see light
9 'Undetermined or unspecified'	

*Adapted from International Statistical Classification of Diseases and Related Health Problems, tenth revision. Geneva, World Health Organization, 1992.

in a developed country such as Australia, it was perceived that 'economic blindness' probably better relates to a vision worse than 6/12, as vision below this level adversely affects the ability of a person to drive or function independently at the place of work. However, by changing the level accepted for functionally significant visual impairment, there will be an automatic alteration in the statistics for global blindness. Hence, it is now generally accepted world wide that the standard nomenclature using standard criteria laid down by the WHO be followed uniformly so that there is no confusion in interpreting data from different countries.

The geographic distribution of'bYmdness shows that the developing countries bear the burden of having more than 90% of all the blind and visually disabled people in the world. This is because in developed countries such as those in Europe and North America, effective measures to prevent blindness have been instituted, which have helped to reduce and almost eliminate 'avoidable' blindness (i.e. 'preventable' and 'treatable or curable' blindness). On the other hand, many people in developing nations are deprived of adequate health care and have no access to well- established measures to prevent blindness. At the same time, one must appreciate that the population all over the world is growing and ageing, so that globally the absolute number of people with impaired or poor vision is increasing, together with the prevalence of profound vision loss.

CAUSES OF BLINDNESS

The major aetiological factors responsible for blindness have changed with time and are different in different parts of the world. For instance, two centuries ago, smallpox was a major cause of blindness but with an extensive campaign for immunization, the disease was finally eradicated in 1980. Similarly, blinding gonorrhoea infections in neonates are no longer common due to improved hygienic conditions, so much so that Crede's prophylaxis of instilling silver nitrate eye drops in newborn babies is no longer practised and is not routinely recommended.

In the early half of the twenty-first century, cataract was another major cause of blindness worldwide. Moreover, visual recovery after cataract extraction was unpredictable and often poor. In addition, since thick,

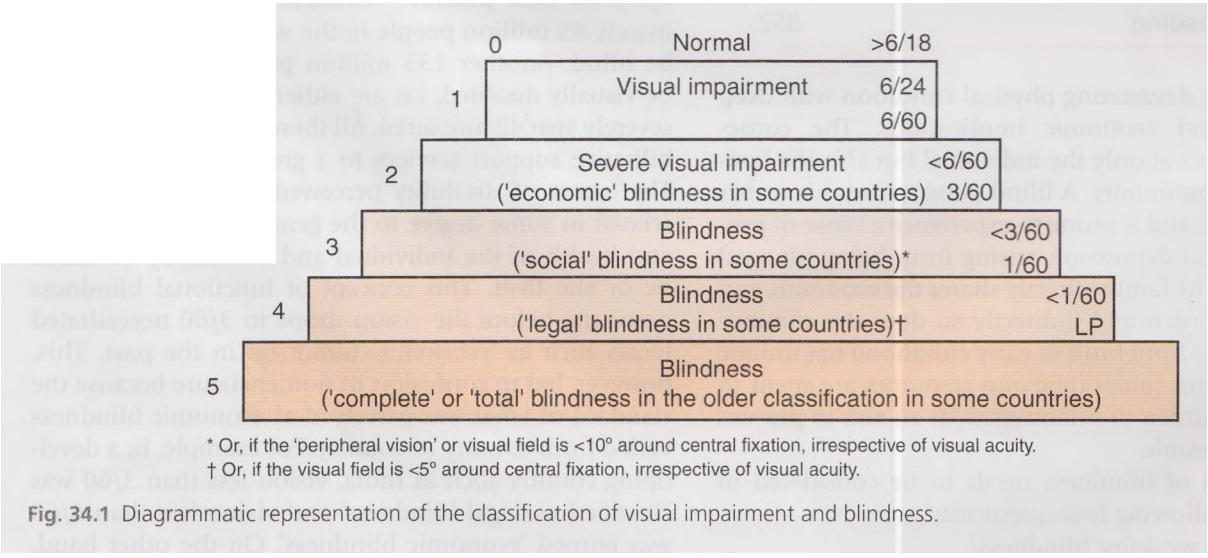


Fig. 34.1 Diagrammatic representation of the classification of visual impairment and blindness.

heavy, aphakic glasses were the only means of optical rehabilitation following cataract surgery, patients were encouraged to wait for their cataract to 'mature' before undergoing surgery to ensure that the benefits of surgery definitely outweighed the possible risks and the relatively poor quality of vision expected with aphakic correction. The advent of microsurgery with operating microscopes, better quality of instruments, change to extracapsular cataract extraction from the intracapsular cataract extraction technique and the invention of the intraocular lens implant has remarkably improved the results of cataract surgery. With the ready availability of quality eye care services to the population at large, cataract blindness has been effectively conquered in the developed world.

Aetiology of blindness: a global perspective

Table 34.2 gives the major causes of blindness, based on WHO reports.

The major proportion of blinding eye diseases are accounted for by the six diseases listed below:

1. Cataract 43%
2. Glaucoma 15%
3. Diabetic retinopathy 8%
4. Trachoma 11%
5. Vitamin A deficiency 6%
6. Onchocerciasis 1%

Diseases 1-3 occur globally, affect individuals (predominantly adults), require surgery or laser therapy and need an eye specialist for treatment or cure.

On the other hand, diseases 4-6 are focal diseases, i.e. occur in specific localized areas of the world, affect communities, start in childhood, can be controlled with medicines and do not necessarily need an eye specialist for treatment or cure.

Table 34.3 Major causes of blindness and their geographic distribution

Developing world (0.5-1 % of the population is blind)	Developed world (0.2% of the population is blind)
Cataract	Refractive errors
Glaucoma	Glaucoma
Trachoma	Cataract
Vitamin A deficiency	Diabetic retinopathy
Onchocerciasis	Age-related macular degeneration
Diabetic retinopathy	
Age-related macular degeneration	

The geographical distribution of the major causes of blindness in the world today is another aspect worth paying attention to. The proportion is not uniform throughout the world (Table 34.3).

What can we do to control blindness?

Blindness control measures are undertaken based on the aetiology and prevalence of blindness. National priorities are set and programmes instituted to combat blindness. General and specific details will be elaborated throughout the chapter.

Blindness control can be planned at various levels. The approach to planning and implementation of blindness control measures should be based on (i) strategy, (ii) disease, (iii) services and (iv) community.

I. Strategies for the control of blindness include
   - *primaiy prevention,* or the prevention of the disease occurring in the first place;

Table 34.2 Global data on aetiology of blindness

Year (Total blind) 1998 (40 million) Aetiology^'"₩^		1995 (38 million)
Cataract	43%	50%
Glaucoma	15%	15%
Trachoma	11%	15% (trachoma/corneal scar)
Vitamin A deficiency	6%	4% (childhood blindness*)
Onchocerciasis	1%	1%
Others (diabetic retinopathy, macular degeneration, optic neuropathy, etc.)	24%	8% (diabetic retinopathy) 1 % (trauma) 6% (other)
	100%	100%

'Childhood blindness. In: *Strategies for the prevention of blindness: national programmes,* 2nd edition. Geneva: WHO, 1997:94-101.

- *secondary prevention,* or the prevention of visual loss from the disease once it has occurred and
- *tertiary prevention,* or restoration of 'sight' to a blind person.

II. A disease-oriented approach to blindness involves
- provision of services for cataract surgery;
- provision of vitamin A supplementation;
- control of trachoma;
- screening of schoolchildren for refractive errors and
- distribution of ivermectin for onchocerciasis.

III. A services-oriented approach is based on the concept of organizing the services in a staggered manner. The various levels include
- *primary care services* at the community level;
- *secondary care services* at the eye clinic level. This includes services provided by general medical doctors and non-ophthalmologists and
- *tertiary care services* at the training or referral centre level and includes all eye specialists.

IV. A *community approach* for specific blindness control measures is directed at the target population at risk.

The strategy used to control any particular disease is tailored according to the nature of the disease, its management, prevalence and health care facilities available. For example, the primary health care services and prevention of blindness strategy is useful for the control of vitamin A deficiency, trachoma and trauma. The community-based rehabilitation approach concentrates on increasing awareness, assessment, assistance and reduction of disability or handicap with a focus on managing the disease in such a way so as to prevent blindness. This strategy is useful for cataract, glaucoma and blinding trachoma with trichiasis.

To restore and maintain good health in the community, primary health care should include the following:
- good quality of food, water and a clean environment;
- control and prevention of epidemics;
- control of endemic diseases;
- education and
- improved level of maternal and child health.

Primary eye care services

This is defined as the provision of promotive, preventive and therapeutic measures for eye health to individuals and the community. To be effective it has to be supported and sustained by an effective and adequate referral system and includes regular refresher training courses for primary care workers.

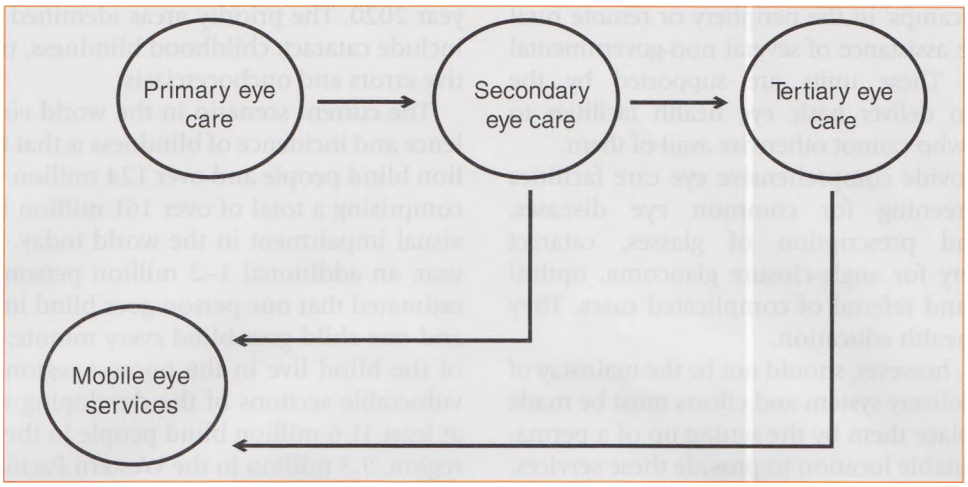
Promotive and preventive activities specifically focus on health education directed at target groups such as village leaders, community councils and local administrative authorities, individual families, patients, school teachers and students. Education is aimed at making the people aware that the majority of blinding diseases are preventable or curable, and the methods for prevention and available avenues for seeking curative measures are clearly indicated. General information regarding the importance of hygiene-both environmental and personal-sanitation, proper nutrition and measures for eye protection at work and play is also made known to the community. In addition, individuals and the community have to be stimulated and encouraged to participate actively in programmes to prevent blindness.

A locally available, willing person is selected and trained as a primary care worker. The clinical activities of the primary care worker are classified as (i) those pertaining to diseases which should be recognized and treated by a trained primary health care worker such as acute conjunctivitis, ophthalmia neonatorum, trachoma, allergic conjunctivitis, styes, chalazia, subconjunctival haemorrhage, conjunctival foreign bodies, corneal abrasions, mild hyphaema and vitamin A deficiency; (ii) conditions that should be recognized and referred to secondary- or tertiary-level centres after treatment has been initiated. These include corneal ulcers, lacerations or penetrating injuries of the eyeball, lid lacerations, entropion and trichiasis, chemical and thermal burns, and any of the conditions in (i) if they do not show signs of resolution in 3-5 days; and (iii) conditions that should be recognized and referred immediately for treatment, such as a painful red eye with visual loss, cataract, pterygium (if the vision is affected), and any patient who has decreased vision which is recorded to be worse than 6/18 in any eye.

Preventive activities include (i) instructing midwives and birth attendants to apply prophylactic treatment to the eyes of newborns for the prevention of ophthalmia neonatorum, i.e. by cleansing of the closed eyelids followed by a single application of tetracycline 1% eye ointment, or with Crede prophylaxis-silver nitrate 1% drops in both eyes (as recommended by the WFIO for deliveries in remote areas in communities with poor hygiene); (ii) administration of vitamin A orally and (iii) application of tetracycline eye ointment in areas endemic for trachoma.

THE DEVELOPMENT OF EYE HEALTH SERVICES, NATIONAL PROGRAMMES FOR THE PREVENTION OF BLINDNESS AND INTERNATIONAL COOPERATION

The establishment of an effective eye care delivery system for the treatment of eye diseases and prevention of blindness is linked to the existing general health services and resources available (Flowchart 34.1). Facilities should be provided using appropriate technology with a flexible approach so that planning and implementation



Flowchart 34.1 Model for an effective eye care delivery system.

are adapted to the existing problems and infrastructure, keeping in mind the priorities for eye health care.

Generally, health services are organized in a standard framework beginning with the basic provision of promotive and preventive requirements at the grassroots level in the community and ending with sophisticated facilities provided by specialized institutions.

Primary eye care

This consists of the following:

- predominantly promotive and preventive measures but includes some curative actions;
- a focus on education and community participation;
- it is community based and the grassroots-level health worker forms the link between the community and the health systems;
- the health worker is trained to recognize common eye conditions and take appropriate action. He or she is taught to identify the three major symptoms of vision loss, pain and red eye. Actions include administration of antibiotics and referral to the next level if needed. The 'kit' includes a hand torch, vision measuring chart, antibiotics (usually tetracycline eye ointment), vitamin A capsules, zinc sulphate eye drops, bandages, sticking plaster, epilation forceps and eye shields.

Secondary eye care

This comprises the following:

- facilities for the management of common blinding conditions;
- a focus on health care delivery but also includes activities related to the training and supervision of health personnel working in the community such as primary health care workers;
- it is hospital based with dispensaries or health centres at the district or provincial level and includes ophthalmic assistants, general practitioners or general medical officers trained in eye care, as well as qualified ophthalmologists;
- an adequate infrastructure (instruments and equipment) to handle common blinding conditions such as correction of refractive errors, cataract, entropion and trichiasis, corneal ulcers, endophthalmitis, ocular trauma and primary angle-closure glaucoma. It could also include screening for open-angle glaucoma and diabetic retinopathy.

Tertiary eye care

Tertiary care units are large institutes in urban centres usually linked to major hospitals and medical colleges, which have all the state-of-the-art diagnostic and therapeutic facilities. These provide the following services:

- management of less common blinding conditions which require highly specialized staff and expensive, sophisticated equipment;
- a focus on the care of diseases that need specialized treatment such as corneal grafting, paediatric cataract surgery, retinal detachment surgery, management of ocular and orbital malignancies and any other disorders that could not be treated or did not respond to treatment at the secondary level;
- provision of expert technical leadership, training of personnel involved at the secondary level, promotion of ophthalmology in relation to public health and conducting research to improve the delivery of eye health services.

Mobile eye services

- In certain countries (Nepal, India, Africa) a team of specialized staff (ophthalmologists, nurses, optometrists and technicians) form a mobile ophthalmic unit which

conducts 'eye camps' in the periphery or remote rural areas, with the assistance of several non-governmental organizations. These units are supported by the government to deliver basic eye health facilities to communities who cannot otherwise avail of them.

- The teams provide comprehensive eye care facilities including screening for common eye diseases, refraction and prescription of glasses, cataract surgery, surgery for angle-closure glaucoma, optical iridectomies and referral of complicated cases. They also provide health education.

These services, however, should not be the mainstay of the health care delivery system and efforts must be made to eventually replace them by the setting up of a permanent base at a suitable location to provide these services.

National programmes for the prevention of blindness are based on comprehensive plans determined by the national policy of an individual country. They are designed to include a range of coordinated activities and implemented by means of the already existing system for provision of health services in the country.

A central organization determines the priorities and then mobilizes and allocates resources accordingly to provide support at all levels of eye health care. The central body organizes health education, training of staff, evaluates and monitors all activities related to the programme. Programmes set the goals according to local problems and priorities and then, based on the financial and human resources available, set targets for achieving the goals. It is recommended that blindness prevention be based on activities related to primary health care (for example, vitamin A deficiency) but also be supplemented by provision of definitive management at the secondary level for the treatment of common blinding conditions such as corneal ulcers, ocular trauma, acute angle-closure glaucoma and cataract surgery.

It is the social responsibility of the government to formulate policies that provide for the training of personnel, implementation and retention of the system, ensure equitable distribution in the country, even in geographically remote areas and under-privileged sections of society who may be physically present in non-remote areas such as urban slums. The best possible utilization of resources allocated for this purpose must be ensured. The monitoring of all activities, maintenance of records and evaluation and analysis of the impact of the programme are also important.

Vision 2020

This is a global initiative launched by the World Health Organisation (WHO) in 1999. It is based on the concept that every living person has a right to sight and aims to eliminate avoidable blindness worldwide by the year 2020. The priority areas identified under this plan include cataract, childhood blindness, trachoma, refractive errors and onchocerciasis.

The current scenario in the world *vis-a-vis* the prevalence and incidence of blindness is that there are 37 million blind people and over 124 million with low vision, comprising a total of over 161 million individuals with visual impairment in the world today. Moreover, every year, an additional 1-2 million persons go blind. It is estimated that one person goes blind in every 5 seconds and one child goes blind every minute. Ninety per cent of the blind live in the poorest regions and affect the vulnerable sections of the developing world. There are at least 11.6 million blind people in the South East Asia region, 9.3 million in the Western Pacific region and 6.8 million in Africa. More than 82% of all blind people are over 50 years old, 1.4 million children under the age of 15 years are blind and females have a significantly higher risk of being visually impaired than males.

Fortunately, 75% of this blindness is in fact treatable and/or preventable. The treatments available for the prevention and cure of blindness are among the most successful and cost effective of all health interventions. It is estimated that unless prompt, effective and preventive health promotional measures are undertaken and implemented the number of blind will increase to 75 million by the year 2020. It is also well recognized that the burden of blindness has an enormous personal, social and economic impact, limiting the educational potential and quality of life of otherwise healthy people, and producing a severe drain on family, community, social and health services. Blindness is also associated with lower life expectancy.

In order to overcome this tremendous shortcoming in the status of health and its delivery systems a global initiative was undertaken to eliminate unnecessary blindness from the world by the year 2020 jointly launched by the WHO and the International Agency for Prevention of Blindness (IAPB) in collaboration with various international non-governmental organizations involved in eye care and prevention and management of blindness.

Vision 2020 focuses on three basic areas, namely, creating adequate eye-care facilities particularly in under privileged areas, creating a foundation of well-trained eye-care workers and implementing specific programmes to control the major causes of blindness. This goal will be attained by a unique multi-pronged approach involving various steps, namely, identification of communities with high levels of blindness, provision of eye-care infrastructure and manpower to these communities and supply of affordable high quality eye care services by virtue of the resources generated. The main responsibilities that the programme has undertaken include increasing awareness of blindness as a major public health issue, control the

major causes of blindness, train ophthalmologists and other eye-care personnel to provide appropriate eye care and create an infrastructure to manage the problem.

Vision 2020's strength lies in partnership between eye-care personnel, ophthalmologists, ophthalmic assistants, nurses and optometrists; International and Organisations (NGDO); National Ministries of Health and Departments of Health Services; and Corporate eye-care service providers. All these individuals and organizations are represented within the IAPB which has an executive task force which collaborates with the WHO in implementing Vision 2020.

Vision 2020 works towards the implementation of National Prevention of Blindness plans in all countries around the world. At the 56th World Health Assembly in May 2003 a Vision 2020 resolution was accepted urging all member states to develop, implement and evaluate national plans and district/region/province plans to enable the Vision 2020 concept to be introduced at the community level, especially in rural areas where the need for blindness prevention is most required and where the greatest progress can be achieved.

The WHO in implementing Vision 2020 or the Right to Sight focuses on five main priorities: cataract, trachoma, onchocerciasis, childhood blindness, refractive errors and low vision. The vision 2020 programme was adopted by the Government of India as a priority area for health development and other diseases of national importance such as diabetic retinopathy, corneal blindness and glaucoma are to be tackled as well.

SPECIFIC BLINDING DISORDERS AND THE APPROACH TO PREVENTION OF BLINDNESS

Cataract

Global view

Cataract is responsible for 50% of blindness in the world; the overall prevalence rate varies from 1 to 4% of the population. Cataract occurs earlier (in the fifth decade of life) in southern Asia and later (in the sixth or seventh decade) in most developed countries in temperate climates. Besides this contributing factor, absence of an effective eye health care delivery system and relatively poor surgical care for cataract leads to a high prevalence of blindness from cataract in the developing countries. Suspected risk factors for development of cataract are mainly exposure to UV-B radiation and sunlight, X-rays, oral and topical corticosteroids, malnutrition and dehydrational states. All these factors contribute to the development of cataract at an earlier age. In addition, cataract progresses faster in diabetics, more so in diabetic women than men. Also, apart from the availability of health care facilities, the visual requirements of the local population and their willingness to undergo surgery also contribute to the final prevalence rate.

Interventions for prevention and treatment

No effective preventive measures in the form of drugs or otherwise have been conclusively established. At the primary level, the health worker screens for cataract and reports those with vision less than a locally determined guideline (usually <3/60 or <6/60) for surgery. He or she plays a role in counselling and motivating those affected to undergo surgery.

At the secondary level, cataract surgery should be performed with equal emphasis on the quality and quantity of surgery. At the tertiary level lies the provision of facilities for surgical treatment of complicated cases such as congenital cataract, subluxated lens, complicated cataracts and cataract associated with systemic diseases such as uncontrolled or inadequately controlled diabetes. In addition, tertiary care centres have the responsibility of training staff at other centres, providing outreach facilities and services, and providing organizational leadership and technical expertise in programmes to eliminate cataract-related blindness.

Glaucoma

Global view

Glaucoma (congenital or infantile, primary open- angle, primary angle-closure and secondary glaucoma) is an important cause of blindness in developing and developed countries. Approximately 15% of all blindness is due to glaucoma and it is estimated that around 600,000 persons per year go blind from glaucoma worldwide. Primary open-angle glaucoma is more common in global distribution. Primary angle-closure glaucoma is comparatively rare in Caucasian populations as it accounts for about 10% of glaucomas in these communities, but it is more common among Asians, accounting for 50% of glaucoma in countries such as India. It is also more common in Eskimos, Japanese, hypermetropes and those with a shallow anterior chamber. Though angle-closure glaucoma usually presents unilaterally, it is primarily a bilateral disease and there is a 40-80% chance that the fellow eye will develop an acute attack in 5-10 years. Considerable progress has been made in studying the epidemiology of and screening in the high-risk Inuit subpopulation but much remains to be achieved in Asia.

Interventions for prevention and treatment

Vision lost due to glaucoma cannot be regained. Early detection and proper treatment is the key to preventing blindness from this disease. Certain risk factors and criteria for identifying people with primary open-angle glaucoma have been determined by epidemiological

studies. These include age above 40 years, raised intraocular pressure, race (Afro-American populations have a 4-8 times higher rate of glaucoma than Caucasians), positive family history, myopia, diabetes, hypertension and possibly alcohol intake and smoking.

Detection and diagnosis have been adequately dealt with in Chapter 18. In a screening programme the intraocular pressure measured by a standard instrument (generally Goldmann applanation tonometer) is useful. A pressure reading of 21 mmHg as the 'cut-off between normal and abnormal is generally accepted and has a sensitivity of 65% and specificity of 91.7%. Programme strategies which include ophthalmoscopy and visual fields would increase the sensitivity. Two-stage screening techniques have often been employed where intraocular pressure readings are taken in large populations, and those with elevated pressures or fundus changes are further subjected to visual field examination. However, only 1 out of 30 people referred with ocular hypertension may actually have a glaucomatous field defect and 30-50% of those with abnormal fields may have a normal intraocular pressure. It is therefore perceived that mass screening for open-angle glaucoma seems inefficient and hence may not be cost-effective. Compared to open-angle glaucoma, acute angle closure glaucoma is easier to diagnose and all primary health care workers must be taught how to recognize that an acute red eye with pain, decreased vision, cloudy cornea, shallow anterior chamber and dilated pupil requires immediate referral to a higher centre. Those at risk for primary open-angle glaucoma should be tested periodically by a qualified eye care practitioner and an iridotomy performed if indicated.

Diabetic retinopathy

Global view

Though originally perceived as being predominantly a disease of developed countries, diabetic retinopathy has shown an increasing incidence in developing countries as well. It is a leading cause of blindness in adults in their productive years and is unique in displaying a generally uniform epidemiological profile worldwide. The incidence of diabetes mellitus increases with the adoption of an urban lifestyle. Risk factors are broadly similar worldwide and the duration of diabetes is the most important predictor for the likelihood of developing diabetic retinopathy. Retinopathy is uncommon with a duration of less than 10 years of the disease, and is virtually present in some degree in 100% of diabetics after 20 years' duration. Sight-threatening retinopathy occurs at the rate of approximately 6% per year; of these, approximately two-thirds will have maculopathy and one-third will have proliferative diabetic retinopathy.

Interventions for prevention and treatment

Like glaucoma, lost vision cannot be recovered. Treatment by laser photocoagulation is at best effective in preventing visual loss and has been shown to reduce the risk of blindness by 60-95%, depending on the type of involvement. Patients must therefore be identified by regular screening and referred judiciously before there is substantial overt visual deterioration.

Screening must be done by a trained medical practitioner or eye care provider. Subjective bias and individual expertise are confounding factors but detection rates with fundus photography are similar if the observer is experienced. Fluorescein angiography to detect or diagnose retinopathy is not recommended as a routine but can be performed when indicated, such as disproportionately severe visual loss indicative of ischaemic maculopathy, in which case macular photocoagulation can be detrimental. Basically the choice of method selected for screening and referral are determined by the availability of personnel and financial resources in the particular community.

Primary prevention by changes in lifestyle of individuals at risk to help prevent or delay the onset of diabetes is ideal. Secondary prevention should be done by early diagnosis of type II diabetes with an initial baseline fundus examination under dilatation at the time of detection of diabetic status for clinically significant macular oedema and proliferative disease. If either is present, referral to a specialist for laser photocoagulation is required. If not, periodic six-monthly or annual review is recommended. Type I insulin-dependent diabetics do not have an asymptomatic latent period before manifesting as diabetics, hence they can be examined for retinopathy 5 years after the onset of diabetes and should be reviewed yearly thereafter. A known diabetic who becomes pregnant is at a high risk for rapid progression of diabetic retinopathy during the pregnancy. A detailed ophthalmic evaluation during early pregnancy and regular review subsequently is recommended. If features indicative of high risk for marked visual loss such as neovascularization of the disc or elsewhere, or clinically significant macular oedema are detected, laser treatment should be performed. Tertiary-level action in restoration of sight-'blind' diabetics is possible in selected patients with vitreous haemorrhage or tractional retinal detachment using sophisticated modern vitreoretinal surgical equipment in an advanced centre.

Childhood blindness

It is estimated that 1.5 million children suffer from severe visual impairment and blindness and, of these, 1 million live in Asia.

The cumulative number of blind-years lived by children is calculated to be 75 million. This is second only to that due to cataract which is 125 million blind-years.

Table 34.4 Regional distribution of blindness in children*

Region	Population in millions (16 years of age)	Prevalence of blindness (per 1000 children)	Estimated number of blind children
Africa	240	1.1	264,000
Asia	1200	0.9	1,080,000
South and Central America	130	0.6	78,000
Europe, Japan, USA	240	0.3	72,000
Total	1810		1,494,000

*Childhood blindness. In: *Strategies for the prevention of blindness in national programmes,* 2nd ed. Geneva: WHO, 1997: 94–101.

Global view

Population-based data are neither extensively available, nor is there any detailed reliable information regarding the incidence of blindness and low vision in childhood. Crude estimates have been made based on blindness registries in industrialized nations and blind school data, with supportive evidence from population-based studies on adult blindness in developing countries. A rough estimate of 1.5 million children are believed to be blind in the world and approximately 3-4 times that number suffer from low vision or, in other words, 5 million children are estimated to be visually handicapped globally. The regional distribution of these figures is outlined in Table 34.4.

It has been calculated that around 500,000 children in the world become blind each year and, of these, almost 50% are believed to probably die in childhood.

Aetiology

Two different classification systems are used to categorize the different causes of impaired vision in children. One is a descriptive anatomical classification and the other is by a prediction of the underlying aetiology based on the stage of development at the time the vision-threatening disease occurred (Table 34.5).

Table 34.5 Causes of impaired vision in childhood*

Anatomical classification

Whole globe: microphthalmos, anophthalmos, phthisis bulbi, atrophic bulbi

Cornea: scar, anterior staphyloma, dystrophy

Lens: cataract, dislocation, aphakia

Uvea: aniridia, coloboma, uveitis

Retina: retinopathy of prematurity, retinal dystrophy, retinal detachment, vasculitis

Glaucoma: buphthalmos

Optic nerve optic atrophy, hypoplasia

Other: cortical blindness, amblyopia

Aetiological classification

Hereditary: chromosomal disorders, single-gene defects

Intrauterine: congenital rubella, foetal alcohol syndrome

Perinatal: ophthalmia neonatorum, retinopathy of prematurity, birth trauma

Childhood: vitamin A deficiency, measles, trauma

Unclassified: impossible to determine the underlying cause

'Childhood blindness. In: *Strategies for the prevention of blindness in national programmes,* 2nd ed. Geneva: WHO, 1997:94–101.

Prevention and treatment

Data from blind school surveys obtained from different regions of the world suggest that approximately 50% of childhood blindness is preventable (Table 34.6).

Action to be taken at the primary care level: The approach to reduction of childhood blindness is tailored according to the predominant locally prevalent disorders; the focus and priorities vary from region to region. Principles include identification of the population at risk and implementing pre-emptive measures.

Vitamin A deficiency is treated according to the schedule (given on p. 204) and prophylactic doses given in areas where the prevalence is high. Prevention of ophthalmia neonatorum includes cleansing the eyes of newborn babies after birth followed by application of 1% tetracycline eye ointment. Immunization against measles and vaccination against rubella in all children at 1 year of age and in pre-pubertal girls 10-12 years of age are other effective measures.

Action to be taken at the secondary level: This includes proper management of eye injuries, corneal ulcers, correction of refractive errors and appropriate referral of cases to a tertiary-level eye facility if required.

Action to be taken at the tertiary level: At this level, screening and treatment of retinopathy of pre-maturity is carried out, as well as management of cataract, corneal scars, glaucoma, strabismus and complicated cases of eye trauma.

Screening for eye diseases in children: There are several disorders that cause substantial impairment of vision but are relatively asymptomatic in very small and even older children and may thus be missed by the parents. Screening for these disorders which are 'silent' in manifestation but for which timely intervention is

Table 34.6 Avoidable causes of childhood blindness based on blind school surveys

Region	Preventable diseases (a)	Treatable diseases (b)	Avoidable (a+b)
West Africa	39% (vitamin A deficiency, measles, harmful traditional eye practices, ophthalmia neonatorum, rubella*)	31% (glaucoma, cataract, others)	70%
South India	37% (vitamin A deficiency, hereditary disease, ophthalmia neonatorum)	10% (cataract, glaucoma, others)	47%
Thailand/The Philippines	33% (vitamin A deficiency, ophthalmia neonatorum, rubella*)	26% (retinopathy of prematurity, cataract, glaucoma)	59%
Chile	18% (hereditary disease, rubella*, ophthalmia neonatorum	36% (retinopathy of prematurity, cataract, glaucoma)	54%

'Rubella causes cataract, glaucoma, microphthalmos.

Table 34.7 Recommendations for screening of children for eye diseases

At birth (examination with a torch)
Buphthalmos
Cataract
Ophthalmia neonatorum
Obvious developmental abnormalities such as microphthalmos and anophthalmos
Nystagmus
Squint
Retinopathy of prematurity (examination with an indirect ophthalmoscope by a trained observer)
Pre-school
Squint and amblyopia
Retinoblastoma
Vitamin A deficiency
School
Refractive error

effective should be specifically identified by screening programmes (Tables 34.6 and 34.7).

Nutritional blindness (vitamin A deficiency)

Global view

Blindness from malnutrition is known to be endemic in South and East Asia, Africa, parts of South and Central America, the Eastern Mediterranean and Western Pacific regions.

Aetiopathogenesis

Nutritional blindness (keratomalacia) results from prolonged and severe lack of vitamin A, usually combined with general malnutrition. Subclinical vitamin A deficiency may manifest as severe clinical deficiency after a precipitating illness, which is most commonly measles, or respiratory tract infections (increased metabolic absorption) or severe diarrhoea (decreased absorption). Vitamin A is required for vision, maintenance of the integrity of epithelial linings, growth and immunity. Deficiency leads to night blindness, dryness of the conjunctiva and cornea and finally liquefactive necrosis (keratomalacia) and ulceration of the cornea.

Corneal damage may be further perpetuated by secondary infections due to poor hygiene. The vitamin A status of an individual depends on the intake of retinal (vitamin A) and carotenoids with vitamin A activity (provitamin A), and the presence of adequate stores in the liver. Neonates get their vitamin A stores from the mother *in utero* and then acquire it from the breast milk after birth. Liver stores, if adequate, can last for up to 6 months.

Epidemiology

Nutritional blindness can occur at any age but is most frequently seen in underprivileged young children in the developing countries because the main contributing factors—measles, frequent diarrhoea, protein—energy malnutrition and other febrile illnesses—are more common in them. Severe keratomalacia is usually seen below 5 years of age and is particularly common in children between 6 months and 3 years of age. Since affected individuals are young, the impact in number of blind person-years is tremendous.

A point worth mentioning here is that severe vitamin A deficiency has also been recognized to occur in affluent communities as well in relation to diseases such as liver cirrhosis or in the elderly population with a poor diet.

Treatment and control

Control is directed at health education, dietary advice, immunization, better hygiene and sanitation. In addition, in disadvantaged communities, vitamin A should be administered prophylactically to the population at risk. The treatment schedule for individuals with keratomalacia is outlined in Chapter 15.

Prophylactic vitamin A administration in areas with endemic vitamin A deficiency is as follows: 200,000 IU vitamin A should be administered orally every 6 months to children 1-6 years of age or weight equal to or more than 8 kg. The first dose can coincide with the administration of the measles or MMR vaccine. Vitamin A can be administered to malnourished mothers in endemic areas at delivery and breastfeeding encouraged. As vitamin A is teratogenic in high doses in early pregnancy, it cannot be given to women with child-bearing potential who may be pregnant again. Thus, the timing of supplementation is critical and should be at birth or within 1 month of giving birth. For infants not on breastfeeding 50,000 IU vitamin A can be administered orally as a single dose.

Any child with measles, severe protein-energy malnutrition, persistent diarrhoea or other prolonged febrile illness should also be given vitamin A according to age, as specified for keratomalacia, but a single dose per episode is recommended as opposed to keratomalacia, in which three doses are administered.

Action at the primary level includes health education, dietary advice and regular administration of prophylactic vitamin A in endemic areas to the population at risk. Provitamin A-rich foods are carrot, mango, papaya, dark green leafy vegetables and are all relatively inexpensive. Foods rich in preformed vitamin A, which is more easily absorbed include egg, fish, milk and whole milk dairy products, but are more expensive and are generally not available to families in high-risk communities. Vitamin A fortification of foods such as cereals, fats and oils has been tried with success.

Trachoma

Global picture

In many rural communities in developing countries, particularly in areas with hot, arid climates, endemic trachoma is still a major cause of blindness. WHO estimates that approximately 150 million people are known to be affected by Uachoma and associated infections, and approximately 6 million people are believed to be blind or severely visually handicapped. Trachoma can be controlled and both visual loss and blindness from the disease can be prevented.

Aetiopathogenesis

Trachoma is a chronic inflammatory disease of the surface of the eye affecting primarily the conjunctiva, but later secondarily affecting the lids and the cornea. The organism responsible is *Chlamydia trachomatis.* There are 11 serotypes identified as A, B, C... to K.

Epidemiology

Trachoma is a potentially blinding disease with a worldwide distribution seen in most developing countries. It is a major public health problem in dry areas of the Indian subcontinent (Bangladesh, India, Pakistan), South-east Asia, Western Pacific region and parts of Oceania, Africa, parts of Central and South America, Australia and the Caribbean. Non-blinding trachoma is also present in other parts of the same areas and other dry subtropical and tropical countries. In regions with better living standards and improved living conditions such as Eastern Asia, Europe, North America, parts of Australia and urban parts of developing countries, trachoma is rarely contracted or transmitted and, if it is, the clinical manifestations are mild and non-blinding.

Trachoma is spread by eye-to-eye transmission through fomites and houseflies. The disease is associated with infections due to other bacteria and viruses which contribute to the disease process. In some communities with blinding trachoma there are regular epidemics of non-chlamydial conjunctivitis once or twice a year, or a continuous prevalence of bacterial and/or viral conjunctivitis all the year round, related to the presence of eye-seeking flies. The combination of active trachoma and recurrent episodes of conjunctivitis from other causes increases the potential severity of the disease resulting in more scarring and consequent blinding complications.

In heavily infected areas almost all the children are infected by the age of 1 or 2 years, with the highest prevalence of active trachoma in children between 2 and 7 years. By adolescence the prevalence of active disease decreases but some individuals continue to have recurring episodes of active disease even in adulthood. Moderate-to-severe inflammatory disease in childhood leads to conjunctival scarring which slowly progresses and leads to entropion and trichiasis, corneal opacities resulting from the constant trauma and repeated secondary infections. The corneal complications usually manifest in adults after the age of 40 years.

It is well known that blinding trachoma is linked with poverty, overcrowding, inadequate face-washing, non-availability of clean water, improper waste disposable leading to breeding of flies and consequent repeated infections of children's eyes with Chlamydia and other micro-organisms causing progressive conjunctival scarring and blinding complications. The active disease either disappears completely or, if present, decreases in severity and prevalence in economically developed communities.

Community diagnosis

Blinding trachoma is recognized to be prevalent in a community if the prevalence of severe visual loss due to corneal opacity is high and if there is a substantial number of people with disabling trachomatous scarring with entropion and trichiasis. Communities with non-blinding trachoma have milder disease, do not have recurring episodes of active disease or secondary infection, have a low prevalence of blinding complications and do not have visual loss from trachoma.

Methods of intervention

The SAFE (Surgery, Antibiotics, Face-washing, Environment) strategy for control of trachoma in communities where it is a major public health problem is directed at eliminating blindness from trachoma by reducing the blinding complications in the short term and taking measures to eradicate or reduce the prevalence and severity of active disease in the long term.

Surgical correction of entropion and trichiasis has an immediate effect in preventing blindness, provided the intervention is made at the appropriate time, i.e. before permanent irreversible corneal scarring.

Antibiotic treatment aims (i) to reduce the severity of inflammation in active trachoma, thereby reducing the potential for scarring and severe blinding complications, and (ii) to decrease disease transmission. Tetracycline (topical and oral), erythromycin (oral), sulphonamides (oral) and rifampicin (oral) are effective drugs.

Tetracycline eye ointment twice daily for 6 weeks is recommended for an individual with active disease but mass therapy of the whole population, particularly children 1-5 years of age, is undertaken in trachoma control programmes in heavily infected areas. Intensive treatment lowers the burden of active infection in the population and the ocular reservoir of *Chlamydia.* This should be followed by intermittent topical treatment to lower eye-to-eye transmission.

Sulphonamides have too many side-effects and rifampicin is better reserved for the treatment of tuberculosis, hence these drugs are not used for the control of trachoma. Though long-acting oral tetracyclines have been effective in mass treatment, they cannot be used in children, which is the group with the highest rate of active infection. Oral azithromycin has a prolonged effect and is now recommended as single-dose therapy. In general, oral antibiotic therapy is currently recommended only for treatment of severe active disease in areas with a high prevalence of trachoma (Table 34.8).

Onchocerciasis

Global picture

Countries lying between 12° north and 15° south of the equator in Africa, some isolated foci in South and Central America and a few pockets in the Republic of Yemen are known to be affected by the disease. Overall, about 100 million people are believed to be at risk, up to 20 million are affected symptomatically, 25,000 are blind and another 50,000 partially sighted due to the disease.

Aetiopathogenesis

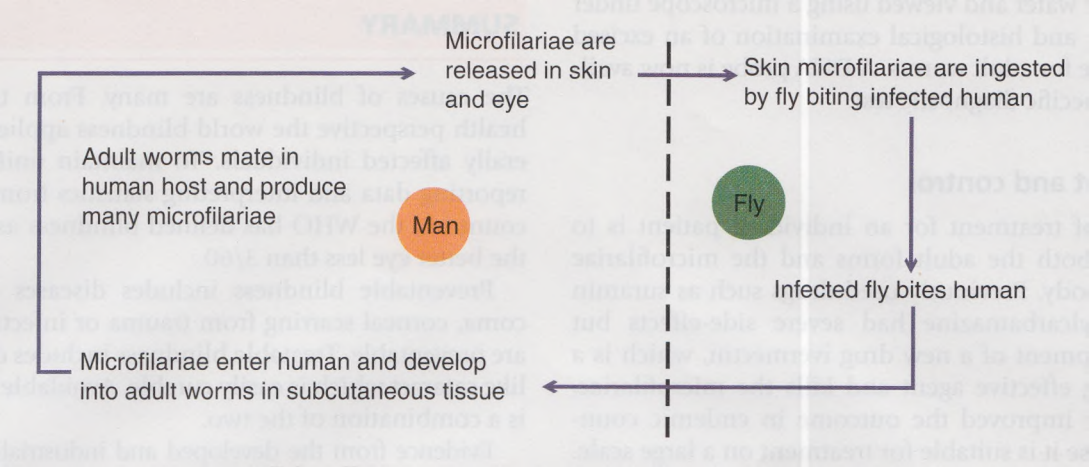
Onchocerciasis is a parasitic infestation by *Onchocerca volvulus,* a filarial worm. The life cycle is completed in humans (definitive host) and a blood-sucking insect vector—the blackfly—known as *Simulium* is the intermediate host. The fly lays its eggs in fast-running water and lives near rivers (Flowchart 34.2).

The adult worms have a life span of up to 14 years and the microfilariae produced can live up to 3 years in

Table 34.8 Treatment and control of trachoma*

Percentage of children 1-10 years of age, with trachoma	Basic treatment	Additional treatment	Eye health promotion
TF+: 20% or more Or TI*: 5% or more	Mass topical antibiotic treatment	Selective systemic antibiotic treatment of severe cases	Improvement in personal hygiene, sanitation, control of flies, improved water supply and waste disposal, distribution of antibiotic ointment during outbreaks of purulent conjunctivitis
TF: 5–20%	Mass or individual/family topical antibiotic treatment	As above	As above
TF: less than 5%	Individual topical antibiotic treatment	Not indicated	Case finding among family members and close contacts

*Childhood blindness. In: *Strategies for the prevention of blindness in national programmes,* 2nd ed. Geneva: WHO, 1997:94–101.
+TF: Trachomatous inflammation, follicular.
*TI: Trachomatous inflammation, intense.



Flowchart 34.2 Life cycle of *Onchocerca volvulus*.

the host. The actively mobile microfilariae spread in the body mainly in the skin but are also present in the urine, sputum, lymphatics, bloodstream and the eye. Eventually these microfilariae will die spontaneously unless they enter the insect vector in which case they develop further and the life cycle is completed.

It is the female fly which feeds on blood, mainly during the day The fly bites the skin and if the victim happens to be infected, microfilariae from his skin enter the fly. These microfilariae migrate to the thoracic muscle of the fly, hence bypassing the digestive system of the intermediate vector host. The microfilariae take about a week to undergo further development and then migrate from their position in the thoracic muscle to the head of the fly where they lodge in a haemocoele in the head. They are infective and can enter a fresh human host when the blackfly bites its next victim. They then develop into adults. The adult worms are coiled in the subcutaneous tissues and form firm subcutaneous nodules about 0.5-10 cm in diameter known as onchocercomas. Adult worms sometimes lodge in other sites such as the brain and can cause epilepsy. In Africans, nodules are more common in the pelvic region while in Central Americans they are more common in the head and neck region. They can also occur on the limbs. The skin manifestations can be asymptomatic or associated with features of dermatitis.

The eyes can be affected by migration of microfilariae into the cornea from the neighbouring skin and conjunctiva, or into the eye along the ciliary nerves and vessels from the periocular tissues, or along the optic nerve sheath from the cerebrospinal fluid, or directly from the bloodstream. The cornea, anterior chamber, iris, ciliary body, choroid, retina and optic nerve can all be affected. Damage occurs by inflammation followed by scarring, cicatrization or atrophy in various degrees. Blindness results from corneal scarring, glaucoma, retinopathy and optic atrophy.

Epidemiology

In hyperendemic areas up to 60% of the local population can be infected and blindness is the most disabling complication, affecting up to 5-10% of the whole population and 30% of males above the age of 40 years. The worst affected area is the West African savannah region. The disease is acquired at an early age but visual loss manifests usually after 15 years of age and the incidence is proportional to increasing age. Visual loss and blindness rates are different from infection rates in various communities and different in individuals, with females being less likely to develop visual loss than males. Though the West African savannah and West African forest regions have a similar prevalence of onchocerciasis, the blindness rate is much lower (1.5%) in the forest area. These differences may be due to variations in distance from the breeding site of the fly, type of clothing worn and differences in the species of the *Simulium* fly. For example in Guatemala, *Simulium ochraceum* is the predominant vector and this species has a preference for biting humans rather than animals, and tends to bite in the upper parts of the body.

In Venezuela the main vector is *Simulium metallicum* which prefers the lower parts of the body and bites both humans and animals. Other factors such as the pathogenicity of *the strain of Onchocerca,* climate differences and exposure to sunlight and dust may also affect the clinical manifestations.

Diagnosis

The skin and eye changes are fairly characteristic and diagnosis is not difficult if the disease is manifest. Screening for the prevalence of the disease should include slit-lamp examination to detect microfilariae in the anterior chamber or cornea, a 'skin snip' examination to look for microfilariae escaping from excised skin placed

in saline or water and viewed using a microscope under low power, and histological examination of an excised skin nodule for adult worms. A DNA probe is now available as a specific diagnostic test.

Treatment and control

The goal of treatment for an individual patient is to eliminate both the adult forms and the microfilariae from the body. Previously used drugs such as suramin and diethylcarbamazine had severe side-effects but the development of a new drug ivermectin, which is a long-acting effective agent and kills the microfilariae, has greatly improved the outcome in endemic countries because it is suitable for treatment on a large scale. The drug is marketed as Mectizan (6 mg per tablet) and is administered as a single dose repeated every 6-12 monthly according to the weight of the patient (150 |jLg/kg). A working dosage chart followed in community control where the drug is administered yearly to all individuals in villages with hyperendemic transmission is given in Table 34.9.

The programme for control of the disease initially focused on control of the vector. It has now shifted focus to concentrating on distribution of ivermectin to affected populations. However, a WHO-sponsored programme to control the fly population in the West African Volta river basin has been successful. The disease can be controlled by actions at the primary level with the village health worker administering the drug according to the weight and maintaining a record. Secondary and tertiary level action include training, supervision and management of complicated cases. Blindness from onchocerciasis is essentially irreversible; thus sight cannot be restored but residual vision can be saved. Death of the microfilariae may worsen glaucoma and optic neuritis, and treatment with topical and systemic steroids may be required in conjunction with microfilarial therapy in individual cases.

Table 34.9 Dosage chart for community control of onchocerciasis*

Weight (kg)	Dose
15–24	3 mg (1/2 tablet)
25–44	6 mg (1 tablet)
45–64	9 mg (1½ tablets)
>65	12 mg (2 tablets)

*The drug is not administered in
- children less than 5 years of age,
- those weighing less than 15 kg,
- pregnant women.
- lactating women with children less than 1 week old and
- severely ill people or those with central nervous system disease.

SUMMARY

The causes of blindness are many. From the public health perspective the world blindness applies to bilaterally affected individuals. To maintain uniformity in reporting data and interpreting statistics from different countries, the WHO has defined blindness as vision in the better eye less than 3/60.

Preventable blindness includes diseases like glaucoma, corneal scarring from trauma or infection which are preventable. Treatable blindness includes conditions like cataract which is easily curable. Avoidable blindness is a combination of the two.

Evidence from the developed and industrialized countries confirms that better standards of living with good nutrition, education, sanitation, hygiene and access to good health care systems reduces the burden of avoidable blindness. The prevalence of blindness in general and the differences in blinding disease distribution and pattern between the developed and developing countries is a reflection of this. The prevalence of childhood blindness, cataract blindness and comeal blindness is higher in developing countries, while proportion of diabetic retinopathy and age related macular degeneration is higher in the developed world. Glaucoma remains an important cause in both regions.

Public health measures to overcome the burden of blindness include upgradation of infrastructure at the primary, secondary and tertiary level along with measures to raise the general standard of living through socioeconomic reforms, education and equitable distribution of wealth and health care facilities.

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Section IX

Surgical Instruments in Ophthalmology

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35

Surgical Instruments in Ophthalmology

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INTRODUCTION

An ophthalmic surgical instrument needs to be precise, efficient and well controlled for a given surgical task. Aspects such as dimensions, weight, centre of gravity, balance and strength need to be thoughtfully incorporated into the design of such instruments. Handling characteristics are controlled by the placement of ridges, grooves or notches to strengthen or weaken a particular instrument consistent with its function. Different tip designs allow for efficient working with a given tissue and minimize trauma.

With the advent of the microscope into the field of ophthalmic surgery, there was a need to change the design and material of ophthalmic instruments which were earlier made chiefly of carbon steel, coated with chrome or nickel. The length of most instruments dropped to about 14 cm in concordance with the working distance of the microscope. A lighter material was required as all manipulations were now being carried out by two or three digits, and the centre of gravity and fulcrum of these smaller instruments ailso moved towards the tip. NorT reflective surfaces are necessary to avoid glare during surgery.

Titanium is lighter than steel, resists corrosion, is non-magnetic and can have a matte finish so that it does not produce glare. Alloys of titanium provide greater hardness and durability and have a low thermal conductivity. However, titaniumlcannot?maintain a^sham edge? Titanium instruments are more expensive than stainless steel, but have a much longer lifespan.

Stainless steel is still used for nltt.ing—instruments, since it'FTolds-a' sharp edge, but it is prone to corrosion especially if not kept clean and dry.

Disposable instruments, equipment and supplies, e.g. blades, sutures with needles, cannulas and drapes are increasingly used today.

There are slightly different designs of some instruments used for specific purposes. The choice of instrument is determined by an individual surgeon's preference and individual needs of the patient.

GENERAL MICROSURGICAL INSTRUMENTS USED FOR OPHTHALMIC SURGERY

Lid speculums (Figs 35.1-35.3)

A lid speculum is essential in ophthalmic surgery for visualization and surgical access in extraocular and intraocular procedures. Their main purpose is to retract the lids and hold the eye open during surgery. They have a self-retaining

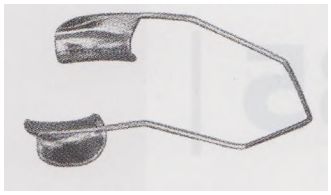


Fig. 35.1 Barraquer wire speculum with solid blades.

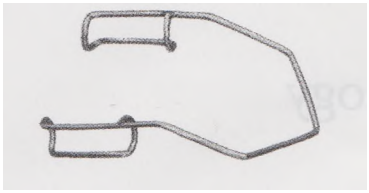
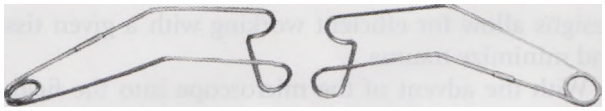


Fig. 35.2 Barraquer wire speculum.



Fig, 35.3 Jaffe wire lid retractors may be clamped to the surgical drape with sutures.

action and are of varied designs that cater to differing needs. Those used during intraocular procedures are light-weight and transmit very little pressure to the eye. Full bladed, larger, rigid speculums are used for strabismus and extraocular surgeries, where a screw allows the palpebral aperture to be maintained as wide as desired.

A smaller pediatric speculum is used for both examination and surgery of children.

Forceps (Figs 35.4-35.13)

Forceps are designed for catching or holding tissues or sutures, and consist of a tip, a shaft and a handle. Toothed forceps are used to hold tissues, e.g. fixation or Pierse-Hoskins forceps. Holding forceps can have three teeth that interdigitate in a one into two pattern. Holding forceps may also have tips that appose, like the cupped ends of the Pierse forceps, for less tissue damage. Smooth tipped forceps are used for holding and tying sutures and manipulating delicate tissues like the lens capsule. Some have both a toothed tip and a flat platform just behind the tip to facilitate both holding of tissues and tying of sutures with the same forceps, e.g. Lim's or Colibri forceps. A forward angulation of the tip permits easier manipulation of ocular tissues.

Needle holders (Figs 35.14-35.16)

Needle holders grasp needles during suturing and therefore vary with both the thickness of the needle used as well as the procedure performed.

Needle holders for extraocular procedures and the application of a superior rectus bridle suture are large and have a locking mechanism to better stabilize the needle, e.g. Arruga needle holder.

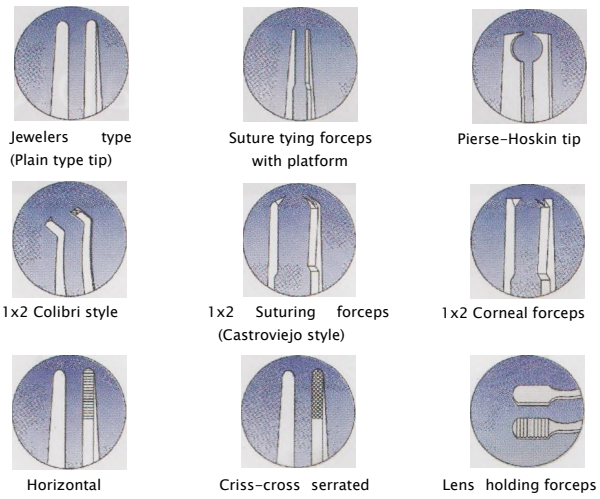
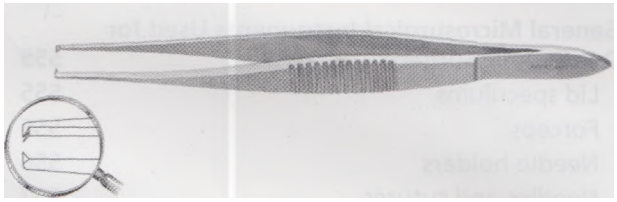


Fig. 35.4 Various types of forceps tips.



Fig, 35.5 Fixation forceps are toothed and are used for grasping the conjunctiva and episcleral tissues, fixing the globe to facilitate surgical manoeuvres.

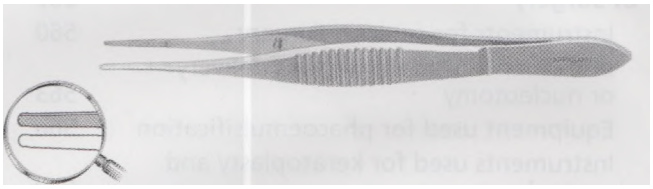


Fig. 35.6 General purpose utility forceps are used for gently holding conjunctiva, muscle, lid tissues, etc.

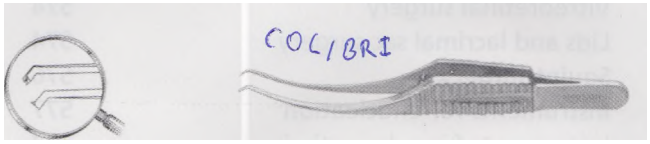


Fig. 35.7 Colibri forceps have fine teeth with a tying platform and are useful for corneoscleral suturing.

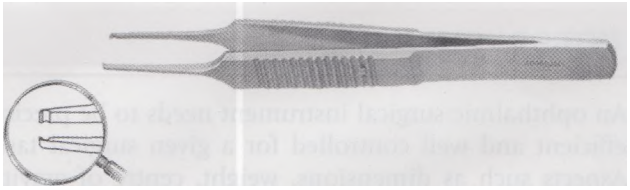
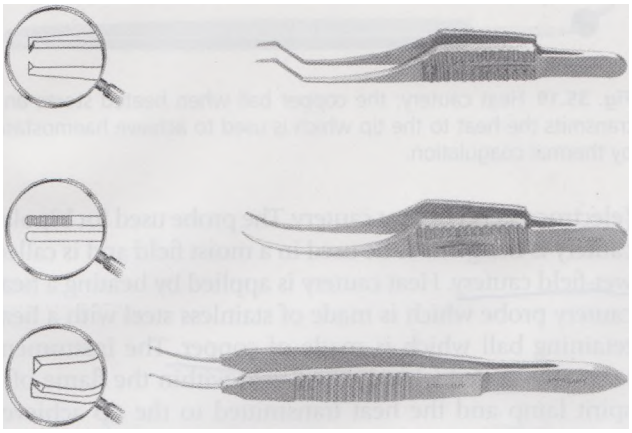


Fig. 35.8 Pierse type microforceps have a straight shaft with fine curved teeth. The curve just proximal to the tip helps in firmly grasping delicate tissues like the cornea without crushing. It is useful fo? corneoscleral suturing.



Fig, 35,9 Iris forceps may be straight or curved.

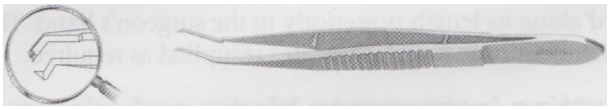


Fig. 35,10 Lim's corneoscleral forceps have a tying platform. They are useful foHiolding the cornea and sclera during dissection and suturing.

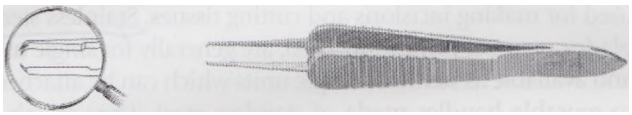


Fig. 35.11 St. Martin forceps are fine, toothed forceps useful for holding delicate tissues like the cornea without crushing.

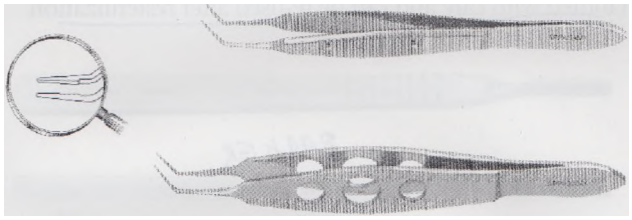


Fig. 35.12 Me Pherson forceps are non-toothed forceps with smooth jaws with an angled 5 mm long platform, ideal for tying 8-0 to 11-0 sutures. They are also useful for holding the lens capsule and handling the intraocular lens during implantation.



Fig. 35 13 ipwplprs fnrrpps are fine, non-toothed forceps with pointed tips that are useful for tying and removing sutures.

Suturing of the skin, conjunctiva and extraocular muscles is done with either the Castroviejo straight tipped or Barraquer curved needle holders.

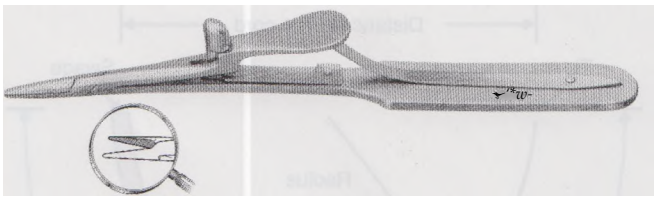


Fig. 35.14 Arruqa needle holder: used for lid surgery, passing bridle sutures under rectus muscles, etc.

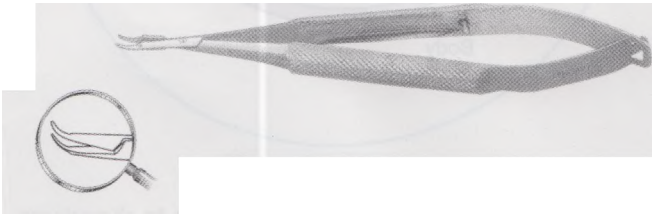


Fig. 35.15 Barraquer needle holder is used when suturing conjunctiva, extraocular muscles, sclera, etc.

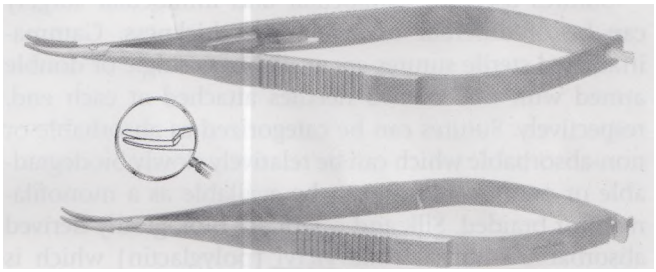


Fig. 35.16 Castrovieio needle holder is used for suturing corneoscleral wounds.

Smaller tipped fine needle holders with a curved tip having a central groove are used to firmly hold curved corneoscleral needles as with 10-0 monofilament sutures and are useful for delicate suturing of the cornea and sclera.

Needles and sutures (Fig. 35.17)

Needles are made of stainless steel and come in many designs, each suited to specific purposes. Spatulated needles cut with both the tips and the sides and stay within a tissue plane. These are the most commonly used needles for corneoscleral, retinal and strabismus surgeries. Round bodied needles have a circular tapering point which is relativelv~atraumatic and are preferred for conjunctival and iris suturing. Reverse cutting needles~have"lTsuperior cutting edge and are used in procedures involving the skin. Needles are commercially available bonded to the sutures as 'atraumatic' needles and are convenient to use. For some procedures such as application of surgical traction, bridle sutures, fornix forming sutures or for performing tarsorrhaphy, larger needles which are reusable after sterilization and require to be threaded with silk or synthetic sutures or sterile cotton thread can be used as an economic alternative.

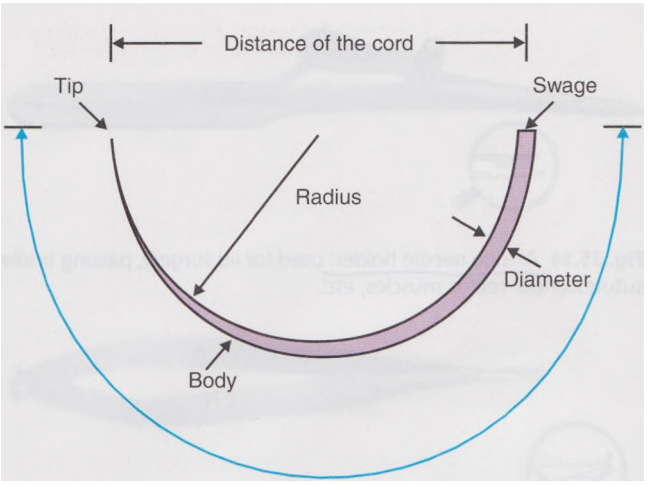


Fig. 35.17 Basic specifications that are important to characterize the different needles used with ophthalmic sutures.

Sutures used for extraocular and intraocular surgery can be of different materials and thickness. Gamma-irradiated sterile sutures are available as single or double armed with one or two needles attached at each end, respectively. Sutures can be categorized as absorbable or non-absorbable which can be relatively slowly biodegradable or permanent and can be available as a monofilament or braided. Silk and catgut are biologically derived absorbable sutures, while vicrvl (polyglactin) which is a co-polymer made from glycolide and L-Iactide is a synthetic absorbable braided suture. Nvlon. Mersilene, polypropylene and surgical stainless steel are synthetic 'non-absorbable suture materials of which nylon slowly degrades with time and steel is truly permanent and non-biodegradable. The thickness of the sutures used varies in a range from 4-0 or SQ-thick sutures for extraocular surgery and fine 10-0 or 11-0 sutures for intraocular surgery.

Cautery (Figs 35.18 and 35.19)

Episcleral and conjunctival blood vessels can be cauterized using electrically operated bipolar diathermy

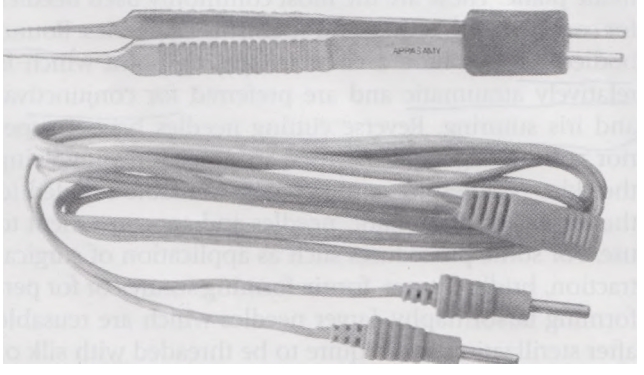


Fig. 35.18 Probe used for electrocautery along with connecting wire.



Fig. 35.19 Heat cautery: the copper ball when heated stores and transmits the heat to the tip which is used to achieve haemostasis by thermal coagulation.

(electrocautery) or heat cautery. The probe used for bipolar cautery is designed to be used in a moist field and is called welrfield cautery. Heat cautery is applied by heating a heat cautery probe which is made of stainless steel with a heat retaining ball which is made of copper. The instrument is simply heated with the ball held within the flame of a spirit lamp and the heat transmitted to the tip achieves haemostasis on direct contact with the bleeding vessels. The copper ball helps to retain the heat for a longer time. The handle is so designed that the heat is not transmitted along its length posteriorly to the surgeon's hand. The instrument can be reheated and reapplied as required.

Cutting instruments: blades and scissors

Blades (Figs 35.20-35.27)

There are a wide variety of disposable and reusable blades made of stainless steel or diamond, respectively, that are used for making incisions and cutting tissues. Stainless steel blades are most commonly used, are generally for single use and available as sterilized single units which can be attached to reusable handles made of stainless steel. They are also available loaded on plastic handles as ready to use disposable items. Diamond knives and blades are extremely sharp with excellent cutti ng qualities, but are expensive, need to be handledwith care and can be re-used after resterilization.

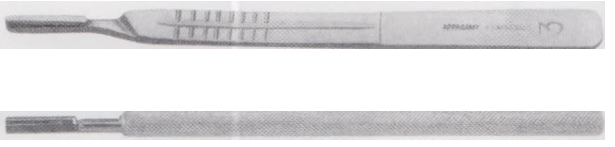
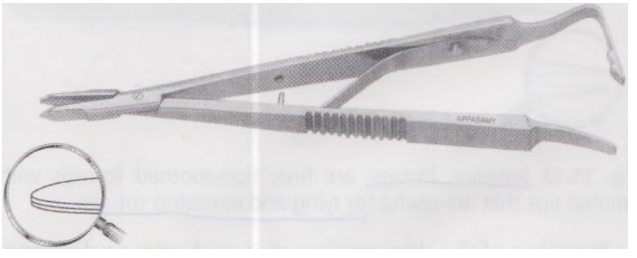


Fig. 35.20 Bard-Parker handle for disposable slot blades.



Fig. 35.21 Bard-Parker blades.



Fig, 35.22 Baixaquer blade breaker and holder, flat handle with spring lock. ' "

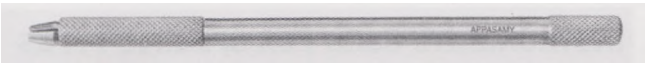


Fig. 35.23 Chuckjiandle for holding microblades.

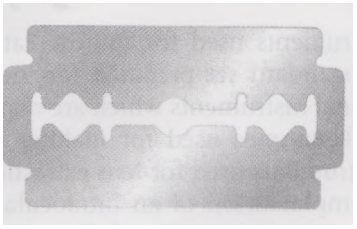


Fig. 35.24 Carbon razor blade.

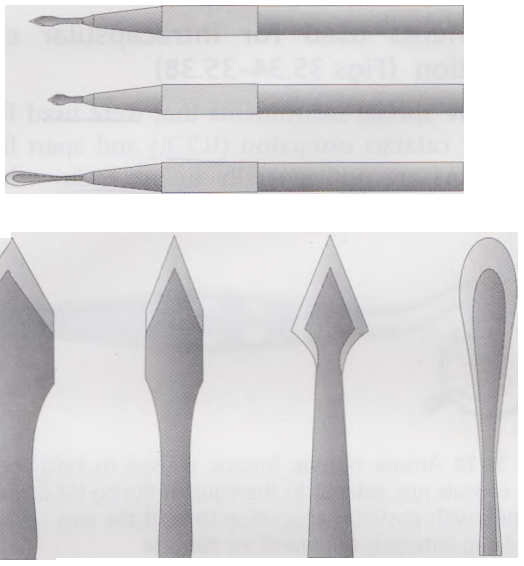


Fig. 35.25 Different design of disposable surgical blades. Precaliberated keratomes (lances) are available in different sizes with sharp cutting surfaces orTboth sides and sharp (lances) or rounded (crescent) cutting tips.

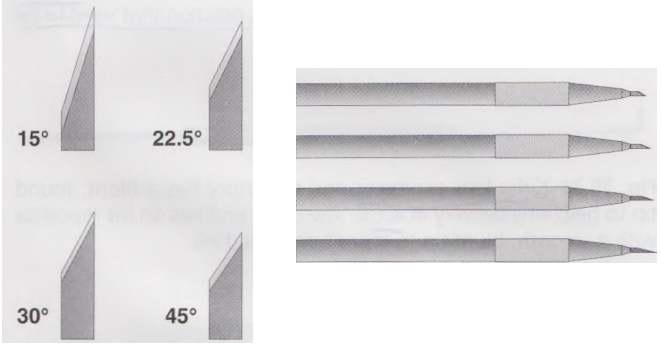


Fig. 35.26 Disposable stainless steel surgical blades are also available with only one cutting surface, available in various angles on a plastic handle.



Fig. 35.27 Stiletto or microvitreoretinal (MVR) blade.

Scissors (Figs 35.28-35.30)

there are various types of scissors used for different types of surgery. The blades can be straight, curved or angled. The size of the handle and the blades also vary in size depending on how strong or delicate the targeted tissues are. Special scissors encased in a sheath are available for insertion through microincisions (1.5-2.0 mm in width) which are used in surgery through the pars plana or anterior segment surgery in children.

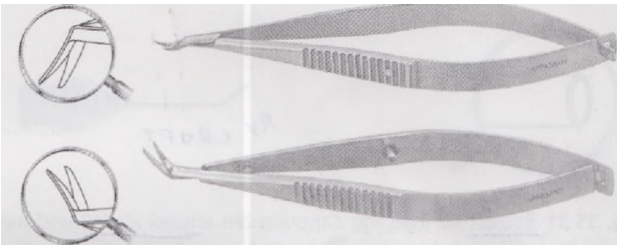


Fig. 35.28 Castroviejo corneoscleral scissors with right and left cutting blades are useful for dissecting the host button in keratoplasty.

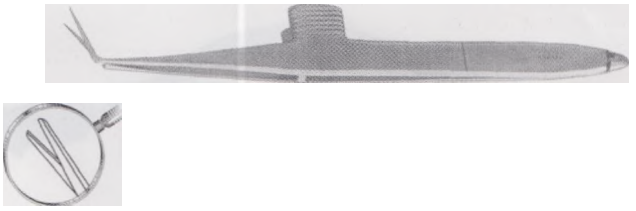


Fig. 35.29 De-Wecker's iris scissors are unique in having the blades at right angles to"the shaft and have a special quick-cutting spring action.

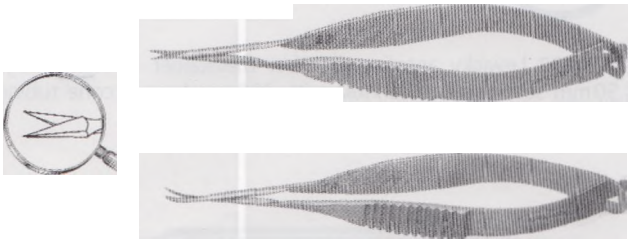


Fig. 35.30 Vannas_scissors are fine, multipurpose scissors which are useful for cutting the iris, lenTcapsule, fine sutures, lamellar corneal tissue, harvesting limbal stem cells, etc.

Miscellaneous

Cannulas are hollow, needle-like instruments with a blunt or rounded tip, that are fitted to an irrigation line or an aspiration mechanism such as a syringe or vacuum bulb, to either irrigate or aspirate fluids or soft material such as lens cortex (Fig. 35.31).

Anterior chamber maintainers are self-retaining, short, fine cannulas that are connected at one end to silicone tubing and an irrigation-infusion line while the tip is inserted into the anterior chamber. They ensure the anterior chamber is well infused with fluid to maintain the depth of the anterior chamber during surgery (Fig. 35.32).

Iris repositors are blunt tipped flat spatulated fine long handled instruments used to gently replace the iris inside the anterior chamber in case it prolapses out (Fig. 35.33).



Fig. 35.31 Rycroft air injection cannulas are angled at 45° and are available in different diameters. They are also useful for irrigating the anterior chamber with balanced salt solution, injecting intraocular preservative-free medications like pilocarpine, adrenaline, lignocaine and antibiotics.

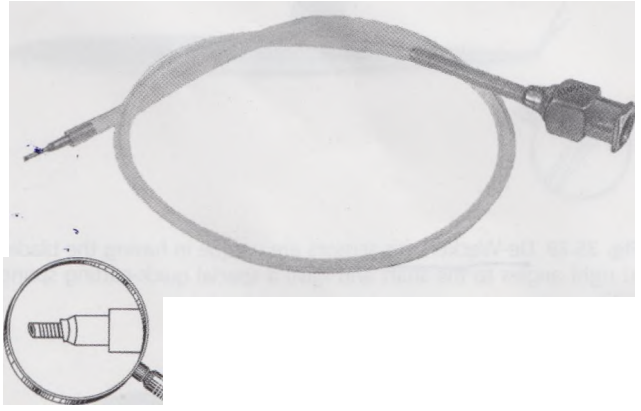


Fig. 35.32 Lewicky anterior chamber maintainer is a 20 gauge 3.50mm self-retaining cannula with 200 mm long silicone tubing and an adaptor.



Fig. 35.33 Iris repositor: smooth spatulated instrument with a rounded tip, useful for repositing iris.

INSTRUMENTS USED FOR SPECIFIC TYPES OF SURGERY

Instruments for cataract surgery

Surgical instruments used for routine cataract surgery include the standard set prepared for intraocular surgery. Additional instruments which are required include blades and keratomes used for making a self-sealing incision, instruments used for lens extraction and those needed for implantation of an intraocular lens (IOL). The exactxhoicE-af instruments varies according to the specific technique used and the individual preference of each surgeon.

Instruments used for intracapsular cataract extraction (Figs 35.34-35.38)

These are special instruments that were us^d for intracapsular cataract extraction (ICCE) and apart from few exceptions are not generally in use today with some exceptions.

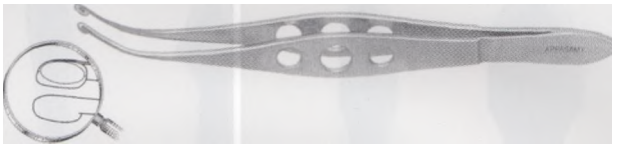


Fig. 35.34 Arruga capsule forceps is used to hold the anterior lens capsule just anterior to the equator during ICCE. The tips are cupped with posterior apposition to hold the lens capsule and a small gap anteriorly to prevent iris damage.



Fig. 35.35 von Graefe cataract knife has a sharp blade useful for making an *ab irtterno* incision at the cornea which is a 180° inside-outward incision from 3 to 9 o'clock position that used to be performed during ICCE



Fig. 35.36 J^jrby lens expressor and repository has a blunt, round tip to help lens delivery in n_Lt. The other end has an iris repositor with a smooth, blunt tip to reposit prolapsed iris.



Fig. 35.37 Smith lens expressor or lens hook is used to help lens delivery in ICCE or nucleus delivery in ECCE.

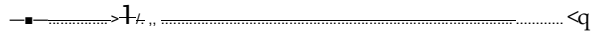


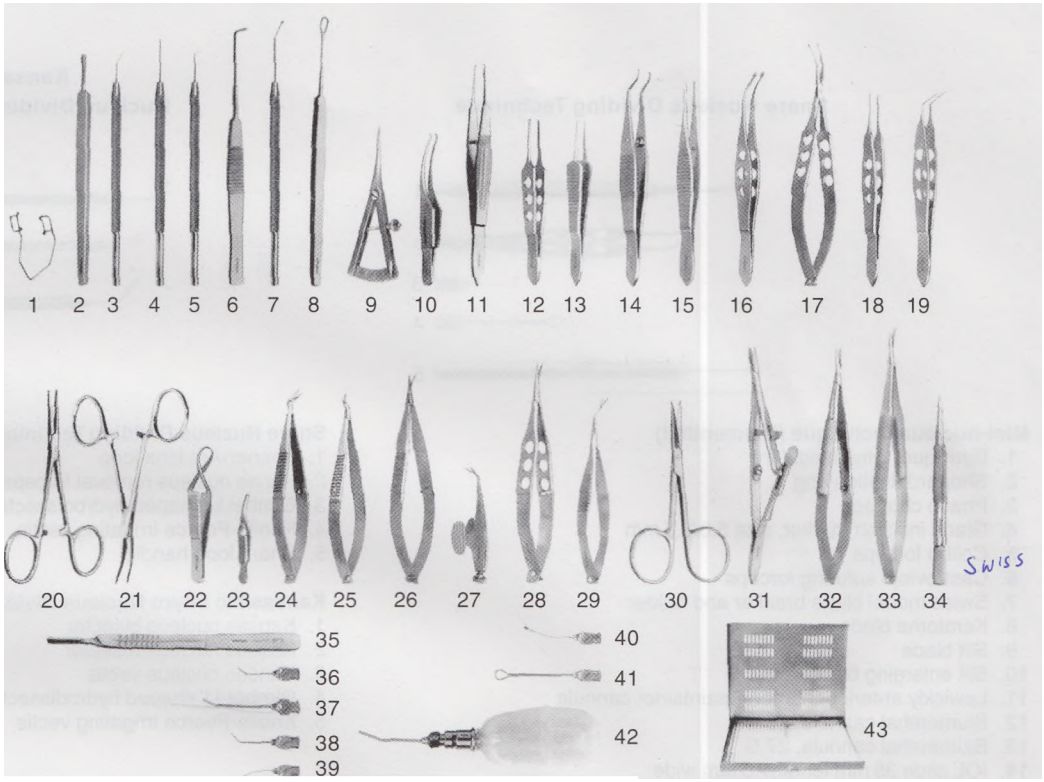
Fig. 35.38 Kirby lens expressor and vectis has a ring-shaped loop at one end which is useful in retrieving and delivering a subluxated lens or nucleus preventing it from falling back in the vitreous during cataract surgery complicated by a posterior capsular rent.

Instruments used for extracapsular cataract extraction (Figs 35.39 and 35.40)

Extracapsular cataract extraction (ECCE) can be performed through a conventional large incision (manual conventional ECCE) or by the manual small incision cataract surgery technique (manual small-incision cataract surgery).

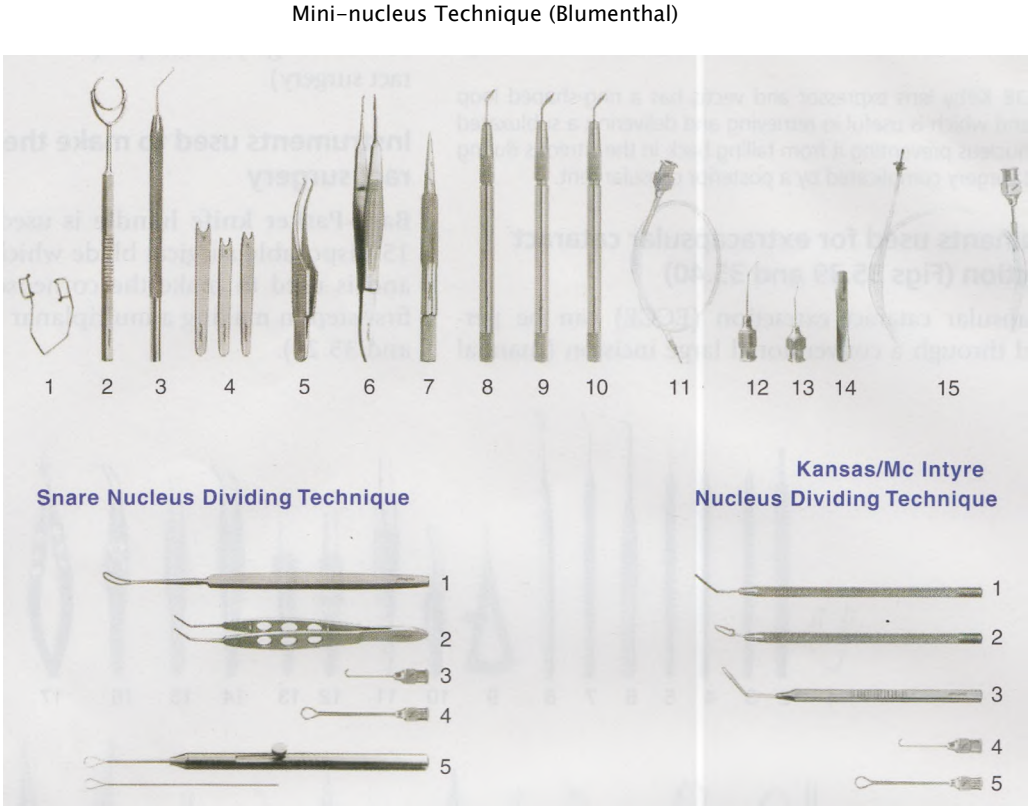
Instruments used to make the incision for cataract surgery

Bard-Parker knife handle is used to load a number 15 disposable surgical blade which has a rounded tip and is used to make the corneoscleral groove as the first step in making a multiplanar incision (Figs 35.20 and 35.21).



1. Barraquer wire speculum
2. Tooke corneal knife
3. Sinskey II lens manipulating hook
4. Kuglen iris hook
5. Barraquer iris spatula
6. Smith lens expressor
7. Nightingale capsule polisher
8. Lewis lens loop
9. Castrovieio calliper
10. Colibri forceps
11. Castroviejo suturing forceps
12. Bishop-Harmon tissue forceps
13. St. Martin suturing forceps
14. Superior rectus forceps
15. Wills hospital utility forceps
16. Arruga capsule forceps
17. Shepard IOL forceps
18. Me Pherson tying forceps
19. Me Pherson forceps
20. Hartman mosquito forceps
21. HartmSh mosquito forceps
22. Towel clamp
23. Serrefine small
24. Castroviejo corneoscleral scissors
25. Castroviejo corneoscleral scissors
26. Micro iris scissors
27. Barraquer iris scissors
28. Westcott tenotomy scissors
29. Vannas capsulotomy scissors
30. Iris scissors
31. Kalt needle holder
'32. Barraquer needle holder")
-33. Barraquer needle holderj
34. Swiss model blade breaker and holder
35. Bard-Parker handle #3
36. Rycroft air injection cannula, 16 G
37. Anterior chamber washout cannula, 16 G
38. Pearce hvdrodissection cannula, 35 anq, 25 G
39. Keilan nyaroaenneation, curved DtweriTp, 2§~G
40. Jensen capsule polisher, sand blast olive tip, 23 G
41. Knolle-Pearce irrigating vectis
42. Silicone bulb~with adapter "
43. Sterilization box with two silicone mats

Fig. 35.39 Extracapsular cataract extraction set (ECCE).



Mini-nucleus Technique (Blumenthal)
1. Barraquer wire speculum
2. Shepard fixation ring
3. Phaco chopper
4. Gland incision marker, size 3.0/3.5 mm
5. Colibri forceps
6. Castroviejo suturing forceps
7. Swiss model blade breaker and holder
8. Keratome blade
9. Slit blade
10. Slit enlarging blade, blunt
11. Lewickly anterior chamber maintainer cannula
12. Blumenthal cannula, 25 G
13. Blumenthal cannula, 27 G
14. IOL glide 35 mm lengthx5 mm wide
15. Infusion cannula

Snare Nucleus Dividing Technique
1. Keener-Arit lens loop
2. Kanas nucleus removal forceps
3. Gimbel U shaped hydrodissector, 25 G
4. Knolle-Pearce irrigating vectis
5. Snare loop handle

Kansas/Mc Intyre Nucleus Dividing Technique
1. Kansas nucleus bisector
2. Kansas nucleus trisector
3. Kansas nucleus vectis
4. .Gimbel 'U' shaped hydrodissector, 25 G
5. Knolle-Pearce irrigating vectis

Fig. 35.40 Microsurgery small incision non-phaco set.

Blade breaker: A blade breaker is used to hold the carbon razor blade, and is twisted to break off a fragment from the edge, which works as a microblade. This is relatively inexpensive and practically disposable. It can be used to make a corneoscleral groove as the initial step of making the incision for cataract surgery, a stab incision to enter the anterior chamber as in extracapsular cataract extraction (ECCE) or to make a side port opening into the anterior chamber during phacoemulsification surgery.

Pre-prepared disposable mini blades are available which can be held with chuck handle to function as a surgical knife.

Other varieties of blades/knives (Figs 35.41-35.42): Disposable knives mounted on plastic handles are also available with different angulations such as 15, 30 and 45° and in various widths such as 2.75, 3.2, 5.0 mm, etc. to make the corneoscleral groove and make a stab incision to enter the anterior chamber.

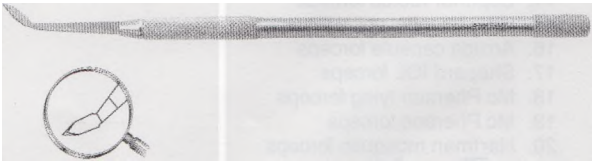


Fig. 35,41 There millimetres wide keratome with an angle of 45° for entry into the anterior chamber.



Fig. 35.42 Slit enlarging blade has a blunt tip and is 5 mm wide with cutting edges on both sides for extension of a keratome slit.

A Stiletto or MVR (microvitreoretinal) blade is available as a disposable lancet-shaped knife mounted on a plastic handle. The blade is designed to make a slit shaped, self-sealing incision which is a 20 gauge opening 0.9-1.0 mm wide at the limbus into the anterior chamber or in the sclera. A reusable stainless steel model is also available.

Instruments used for capsulotomy (Figs 35.43-35.46)

Instruments used for making an opening in the anterior capsule of the lens include an irrigating cystotome, ordinary cystotome or a bent 26 or 27 gauge needle. The capsulotomy can be completed with the bent needle or cystotome or by using capsulorhexis forceps.

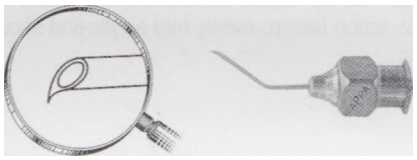


Fig. 35.43 Me Intyre cystotome 45° angled sharp tip.



Fig. 35.44 Irrigating cystotome made by bending 26 gauge disposable needle.



Fig. 35.45 Vitreous scissors (20 G, straight).



Fig. 35.46 Utrata capsulorhexis forceps have very delicate grasping tips and extremely thin long straight shanks. They are useful for holding the lens capsule after a flap has been raised with a cystotome or bent 26 gauge needle to perform a continuous curvilinear capsulotomy.



Fig. 35.47 Me Intyre irrigating vectis: Oval ring-shaped cannula with irrigating ports that allows fluid into the anterior chamber and behind the nucleus to help express the lens nucleus.

Instruments used for nucleus delivery or nudeotomy

Nucleus delivery

- Smith lens expressor or lens hook has a rounded tip with a gentle curve at the angulated elbow or knee to apply gentle pressure at the limbus inferiorly, facilitating delivery of the lens in ICCE and the lens nucleus in ECCE.
- Wire vectis or lens loop is used to apply pressure on the sclera superiorly, depressing the posterior lip of the wound to facilitate lens delivery by a tumbling or sliding technique for ICCE and nucleus delivery by the sliding technique for ECCE. An irrigating vectis (Fig. 35.47) has a hollow interior and multiple ports to allow egress of fluid from the leading edge or posterior surface of the vectis. This is attached to an infusion line to assist in hydraulic separation of the nucleus and facilitates easy nucleus delivery by providing additional hydrostatic pressure to push the nucleus out of the anterior chamber through the surgical incision.

Instruments used for aspiration of lens cortex (Figs 35.48-35.50)

Irrigation-aspiration cannulas: These are used for manual aspiration of the lens cortex and have the dual function of irrigation and aspiration. Such cannulas can also be used for aspiration of other material from the anterior chamber such as clearing of blood (hyphaema) or exudates. There are cannulas of different designs and dimensions, but the one which is most commonly used is the Simcoe cannula. This is available in two different designs. One is the original model also called the direct Simcoe where, aspiration is through the silicone tube and irrigation through the

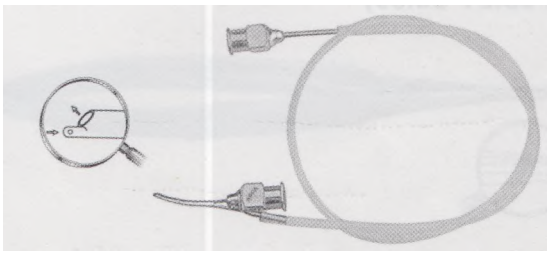


Fig. 35.48 Simco irrigating-aspiration cannula (original model).

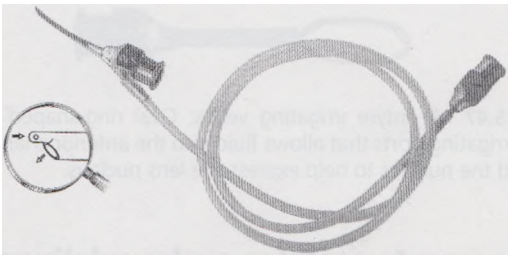


Fig. 35.49 Reverse Simcoe irrigation–aspiration cannula.



Fig. 35.52 dayman lens holding forceps are delicate with curved shanks.

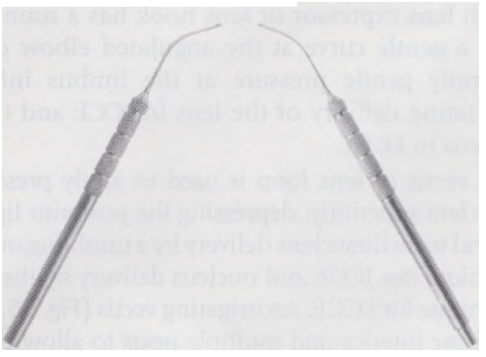


Fig. 35.50 Bimanual irrigation–aspiration cannula: a pair of cannulas which are used with the phacoemulsification machine for automated irrigation and aspiration of cortical matter.

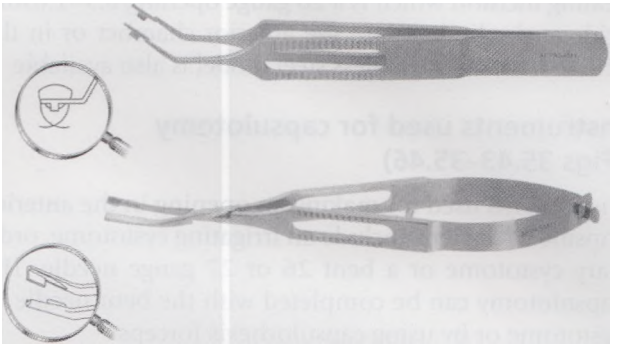


Fig. 35.53 Lens folding forceps for foldable intraocular lenses: Direct action or cross action forceps evenly fold acrylic and silicone lenses.

main hub. The surgeon holds the syringe attached to the silicone tubing which is used to generate suction for aspiration in his or her left hand and the irrigation line is attached to the main central hub. The second is the reverse Simcoe where irrigation is through the silicone tube and aspiration is through the main hub. The surgeon uses a syringe attached to the main hub to generate suction for aspiration of the lens cortex. The cannulas are available in different sizes, namely, 21, 22 and 23 gauge which have an aspiration port size of 0.5, 0.35 and 0.3 mm, respectively. The narrow bore ports are useful for aspiration of fine cortical fibres and get a better purchase on tissue, while the larger bore cannula is useful for faster aspiration of bulky lens cortex.



Fig. 35.54 Universal lens folding forceps: ideal for silicone and acrylic foldable lOLs. Box model jaws facilitate the folding of the lens precisely for transfer to the inserter.

Instruments used for intraocular lens insertion (Figs 35.51-35.59)

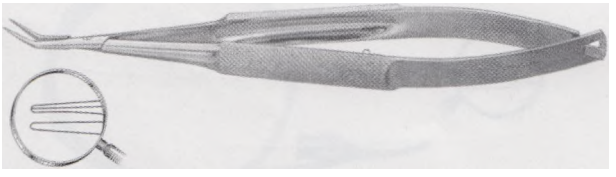


Fig. 35.51 Anis lens holding forceps have extra delicate long smooth jaws and a 45° angulation.

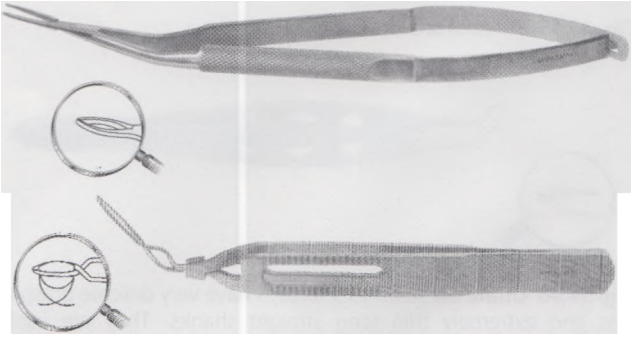
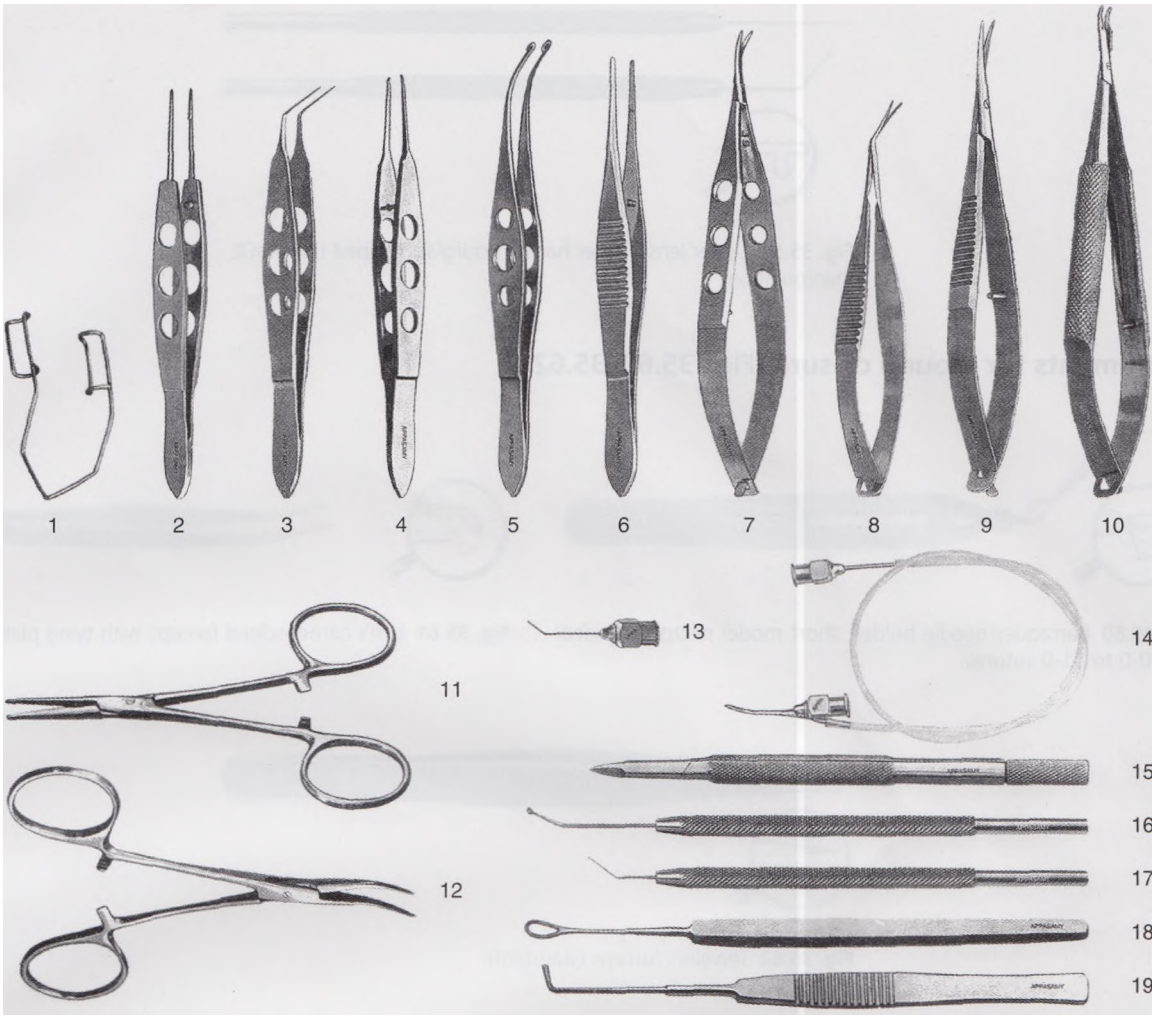


Fig. 35.55 Lens inserting forceps for foldable lens can be direct or cross action.



1 . Barraquer wire speculum, large
2. Jaffe tying forceps, straight
3. Me Pherson forceps, angled
4. Me Pherson corneal forceps, 1x2 teeth
5. Arruga capsule forceps
6. Wills hospital utility forceps
7. Castroviejo corneal scissors
8. Vannas capsulotomy scissors
9. Westcott stitch scissors
10. Barraquer needle micro jaws w/o lock
11. Hartman mosquito forceps, straight
12. Hartman mosquito forceps, curved
13. Rycroft air injection cannula
14. Simcoe I/A cannula, direct
15. Castroviejo blade breaker
16. Nightingale capsule polisher
17. Sinskey II lens manipulating hook
18. Lewis lens loop, small
19. Smith lens expressor

Fig. 35. 56 Microsurgery IOL set.

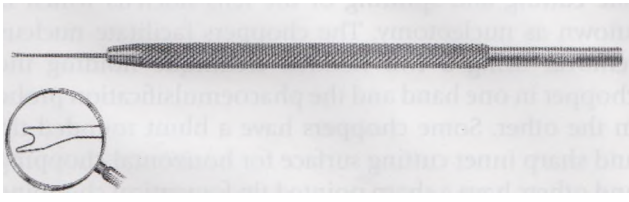


Fig. 35.57 Hessburg lenspusherhas a blunt, forked tip useful for manipulating IOL haptics of bothanteriorchamber and posterior chamber lenses.

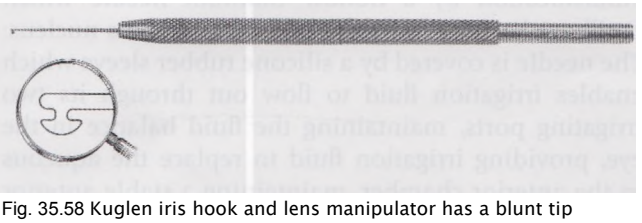


Fig. 35.58 Kuglen iris hook and lens manipulator has a blunt tip with a bulbous attachment just proximal to the tip. This is useful for dialling the IOL, manipulating the IOL haptic for insertion in the capsular bag, pushing back the iris gently, etc.



Fig, 35.59 Lester lens pusher has an hourglass shaped tip for IOL manipulation.

Instruments for wound closure (Figs 35.60-35.62)

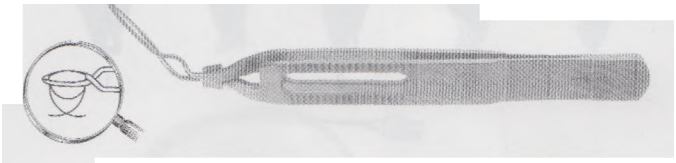


Fig. 35.60 Barraquer needle holder: short model micro jaws ideal for 10–0 to 11–0 sutures.



Fig. 35.61 Lim's corneoscleral forceps with tying platform,



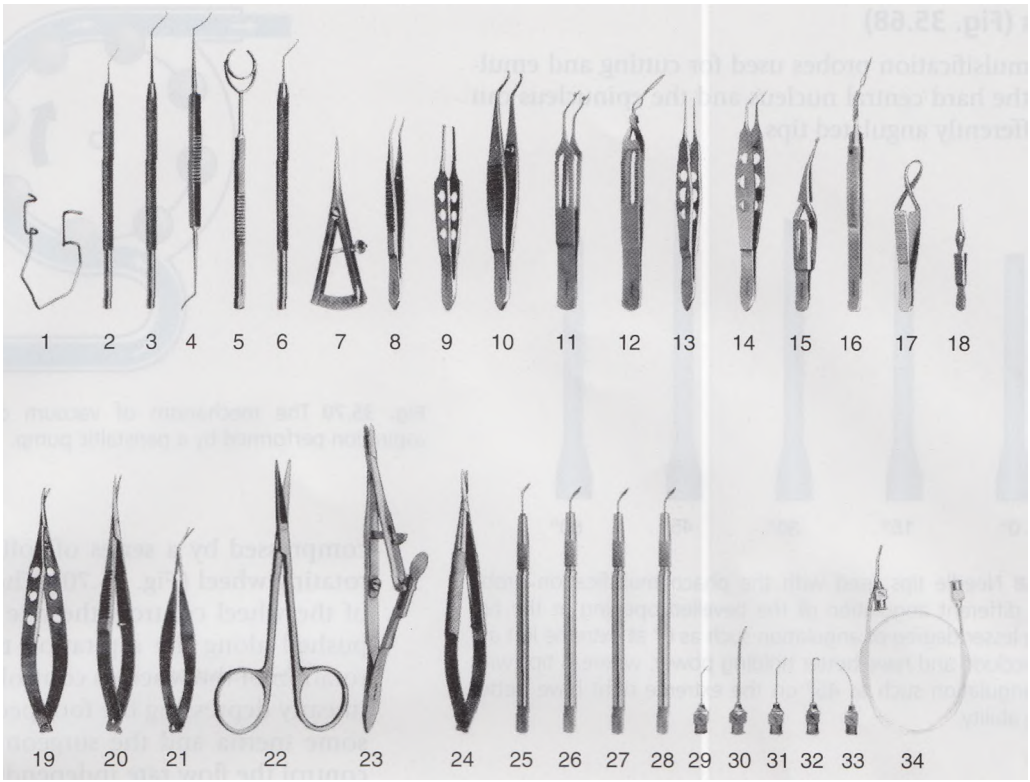
Fig. 35.62 Jewelers forceps (standard).

Equipment used for phacoemulsification (Figs 35.63-35.67)

Phacoemulsification is an automated technique of lens removal where the central nucleus is emulsified and then aspirated together with the residual lens cortex. Essential steps for phacoemulsification include a self-sealing incision, capsulorhexis, hydrodissection, nucleus removal, aspiration of lens cortex followed by implantation of a foldable IOL in the capsular bag.

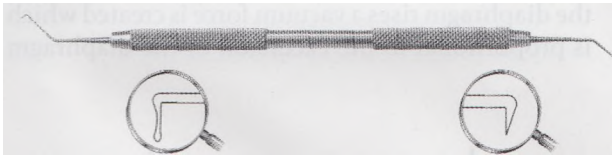
The machine used for phacoemulsification consists of a console with a digital display panel, a vacuum pump and a power source to provide energy for nucleus emulsification by a hollow titanium needle which oscillates back and forth to pulverise the lens nucleus. The needle is covered by a silicone rubber sleeve which enables irrigation fluid to flow out through its two irrigating ports, maintaining the fluid balance in the eye, providing irrigation fluid to replace the aqueous in the anterior chamber, maintaining a stable anterior chamber depth and also cooling the phacoemulsification tip to prevent corneal burns. The lens matter and irrigation fluid is aspirated out of the anterior chamber through the hollow phaco tip and the rate of egress is determined by the level of vacuum and the aspiration flow rate. The balance between the inflow and outflow of fluid and consequent mechanics involved is termed as fluidics. Different phacoemulsification machines have variations in these parameters to give different combinations of features. The aim is to have efficient phacoemulsification with a stable anterior chamber, minimum damage to the intraocular structures and a wide safety margin for complications such as wound burns, endothelial damage from excessive use of phaco power, etc.

Different designs of choppers are available to facilitate cutting and splitting of the lens nucleus which is known as nucleotomy. The choppers facilitate nucleus removal using a two handed technique holding the chopper in one hand and the phacoemulsification probe in the other. Some choppers have a blunt rounded tip and sharp inner cutting surface for horizontal chopping and others have a sharp pointed tip for vertical chopping and dividing or splitting the nucleus. This enables more efficient removal of the hard inner nucleus minimizing the use of phaco power.



1. Kratz Barraquer wire speculum
2. Sinskey II lens manipulating hook
3. Akahoshi nucleus sustainer
4. Castroviejo cyclodialysis spatula
5. Shepard fixation ring
6. Phaco chopper
7. Castroviejo calliper
8. Lim's corneoscleral forceps
9. Bishop-Harmon tissue forceps
10. Superior rectus forceps
11. Lens folder
12. Lens inserting forceps
13. Me Pherson tying forceps, long handle
14. Utrata capsulorhexis forceps, flat handle
15. Dodick nucleus cracker
16. Akahoshi prechop forceps, curved shanks
17. Towel clap
18. Serrefine small
19. Castroviejo corneal scissors
20. Vannas capsulotomy scissors
21. Vannas capsulotomy scissors
22. Eye scissors, straight
23. Kalt needle holder
24. Barraquer needle holder
25. Keratome blade
26. Slit blade
27. Slit enlarging blade
28. Super sharp blade
29. Rycroft air injection cannula, 23 G
30. Anterior chamber washout cannula, 16 G
31. Pearce hydrodissection cannula, 35 degree ang. 25 G
32. Gimbel 'U' shaped hydrodissector, 25 G
33. Kellan hydrodelineation, curved bevel tip, 25 G
34. Simcoe I/A cannula, 23 G, 'direct'

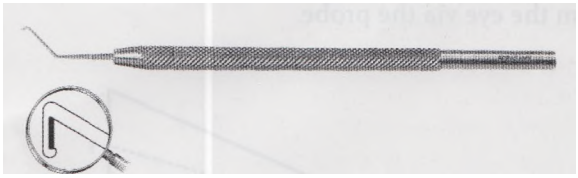
Fig. 35.63 Phacoemulsification set.



Fig, 35.64 Chop combo: this double ended instrument features a micro finger pointed 'quick chop' tip for chopping and dividing the nucleus and another tip for splitting the nucleus.



Fig. 35.65 Double ended phaco chopper and 'Y' rotator.



Fig, 35,66 Phaco chopper: 1.5 mm inner cutting edge and 0.25 mm blunt polished tip.

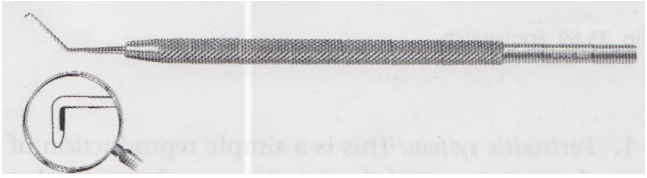
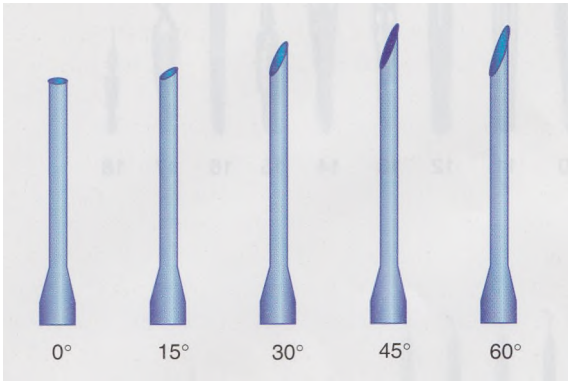


Fig. 35,67 Nagahara karate chopper: spear shaped for ease of insertion into the nucleus.

Probes (Fig. 35.68)

Phacoemulsification probes used for cutting and emulsifying the hard central nucleus and the epinucleus can have differently angulated tips.



Fig, 35.68 Needle tips used with the phacoemulsification probe showing different angulation of the bevelled opening at the tip. Tips with lesser degree of angulation such as 0° at extreme left are easy to occlude and have better holding power, whereas tips with greater angulation such as 45° on the extreme right have better sculpting ability.

The phacoemulsification machine footswitch depressed up to level 1 activates the irrigation, further pressure up to level 2 activates aspiration function and in position 3 all three functions, i.e. irrigation, aspiration and phacoemulsification are activated (Fig. 35.69). Aspiration pump principles for generating an aspiration force and removal of lens matter from the eye varies. There are three main types of machines based on the active pump mechanism. The force generated has two main purposes, namely, to generate a vacuum or negative pressure measured in mm Hg to produce a suction force to aspirate material and to create a flow which is strong enough to remove material from the eye via the probe.

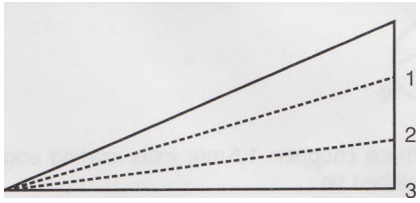


Fig. 35.69 Footswitch.

1. *Peristaltic system:* This is a simple reproduction of the movement of the intestines to shunt a bolus along its lumen. An elastic tube is circumferentially compressed by a series of rollers mounted on a rotating wheel (Fig. 35.70). The speed of rotation of the wheel controls the rate of flow as fluid is pushed along the aspiration tube. The speed of rotation of the wheel is controlled by the surgeon linearly depressing the foot pedal. This pump has some inertia and the surgeon has the ability to control the flow rate independent of the vacuum. There is therefore some lag between activation of the aspiration force and full generation of vacuum up to the limit set on the control panel. Moreover, full occlusion of the probe tip is required for full generation of the vacuum. Newer generation machines using the peristaltic system have modified wheel designs and connection systems to overcome the problem of slowness of the older machines and modern equipment can achieve maximum vacuum as rapidly as venturi pump systems.

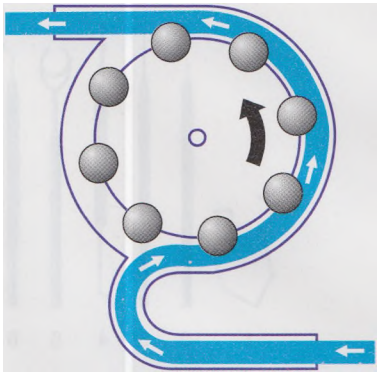


Fig. 35.70 The mechanism of vacuum creation and effective aspiration performed by a peristaltic pump.

2. *Diaphragmatic pump:* In machines operated by a diaphragmatic pump a piston connected to a diaphragm generates vacuum by moving up and down inside a closed container (Fig. 35.71). When the diaphragm rises a vacuum force is created which is proportional to the excursion of the diaphragm

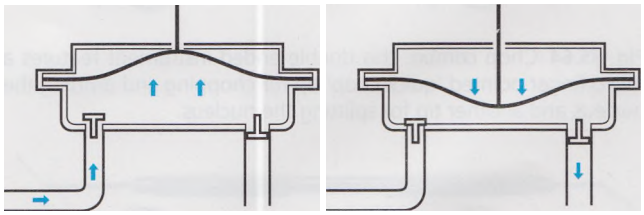


Fig. 35.71 A diaphragmatic pump has a moveable diaphragm which moves back and forth and creates a vacuum effect to facilitate aspiration through the phaco tip.

and causes a valve to open which transmits the suction force generated to the aspiration tip. As the diaphragm moves down the valve closes and the membrane returns to neutral position. There is an expansion reservoir where the aspirated fluids collect and this permits the vacuum level to remain constant. In this system the flow rate closely follows the level of vacuum attained so the surgeon has only one parameter, namely, vacuum level under his or her control. The response time of such pumps is almost immediate, although there are different models of newer machines that have the provision for selection of different response speeds, namely, fast, slow or medium. The main advantage of these pumps is the more powerful force and superior control over aspiration power. The rapidity of generation of vacuum can however be a disadvantage for inexperienced surgeons. Gradual filling of the expansion reservoir can affect the time lag in response and power of vacuum force.

3. *Venturi system:* In machines using this system, pressurized air flows along a tube past a valve which is connected to the aspiration line (Fig. 35.72). The difference in pressure generates a vacuum which is contained by a control valve and passes through a fluid collection cassette. In machines based on this pump mechanism, the surgeon sets the vacuum limit and adjusts the bottle height, but cannot independently set a flow rate. The latter is dependant on the set level of vacuum. This pump mechanism, operates faster than other pumps and does not require full occlusion of the tip for generation of the suction force. The surgeon must hence be careful to avoid inadvertent 'catching' of other delicate intraocular structures like the iris and lens capsule during surgery. A disadvantage of this system is that it requires a supply of compressed air which can be provided in an air cylinder, compressor or a piped wall supply calibrated according to the instructions of the manufacturer.

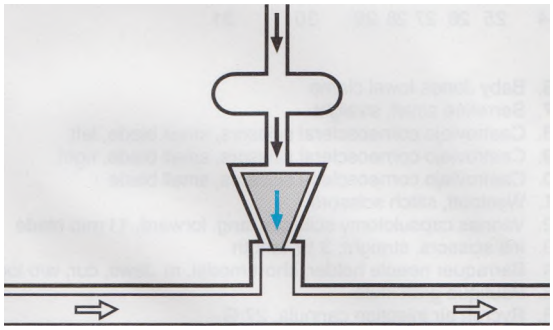
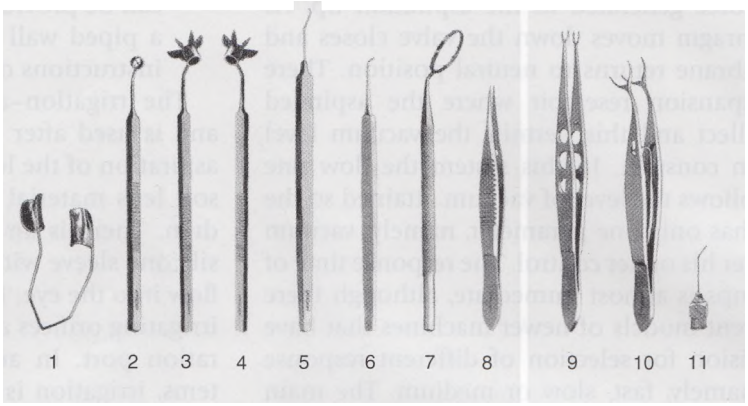


Fig. 35.72 A venturi based pump has a pneumatic mechanism for building up pressure and creating a vacuum for aspiration of the lens nucleus and cortical matter.

The irrigation-aspiration probe has a dual function and is used after phacoemulsification for automated aspiration of the lens cortex or aspiration of the entire soft lens material in developmental cataracts in children. There is an aspiration port near the tip and a silicone sleeve with two openings providing irrigation flow into the eye. The sleeve is oriented so that the two irrigating orifices are on either side of the central aspiration port. In automated irrigation-aspiration systems, irrigation is a passive function which is dependant on the force of gravity and maintains the chamber depth during the aspiration process by replacing the fluids aspirated with irrigating solution. The force of infusion is determined by gravity which is controlled by adjusting the height of the inverted irrigation fluid bottle with an attached infusion line, fitted with a drip chamber. The amount of irrigation fluid entering the eye will depend on the balance between the mechanical forces of gravity and the internal pressure within the eye. The irrigation probe is inserted into the eye through the incision and the system is activated by pressing the irrigation button on the panel and controlled with the foot pedal. The build up of positive pressure within the eye during irrigation is dependant on the balance of the height of the bottle above the eye and the size of the irrigation port. During the process of irrigation-aspiration it will be determined also, by the rate of flow out of the eye in comparison with the irrigation inflow. The generally recommended reference values for the height of the bottle above the eye, measured from the fluid level in the drip chamber, are 65 cm for phacoemulsification, 50 cm for automated extracapsular extraction and 40 cm for vitrectomy. The stand used for supporting the irrigation fluid bottle can be manually controlled or automatically regulated with a control panel or foot pedal. In case of the latter, the control panel and pump should be level with the patient's eye to avoid a negative effect on venting, which can occur with a lower position and a lower strength of vacuum in the aspiration tip that can occur with a higher position.

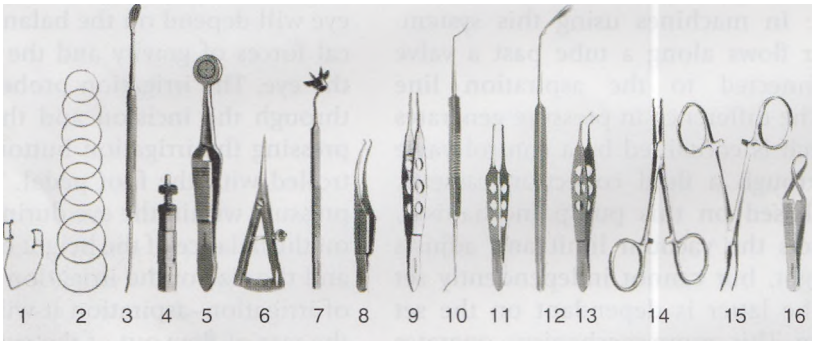
Bimanual aspiration systems have two single function probes one for irrigation and the other for aspiration. Each probe is connected to the irrigation or aspiration line of the phacoemulsification machine, respectively, and is designed to be of 20 gauge so that it can be inserted through the small side port. This maintains a stable anterior chamber, reduces astigmatism and enhanced manoeuvrability facilitates removal of residual subincisional cortical lens matter.

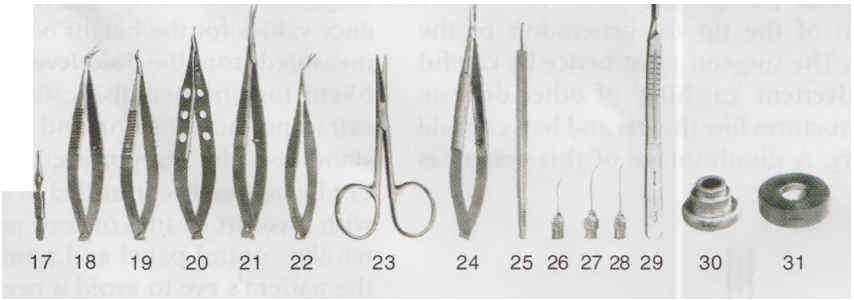
Instruments used for keratoplasty and corneal surgery (Figs 35.73-35.88)



1. Sold wire speculum, large
2. Optic zone marker (3 mm dia)
3. Radial marker (4 blades)
4. Radial marker (6 blades)
5. Visual axis marker
6. Incision depth gauge
7. Fixation ring
8. Corneal fixation forceps, straight
9. Incision spreading forceps
10. Corneal fixation forceps
11. Air injection cannula

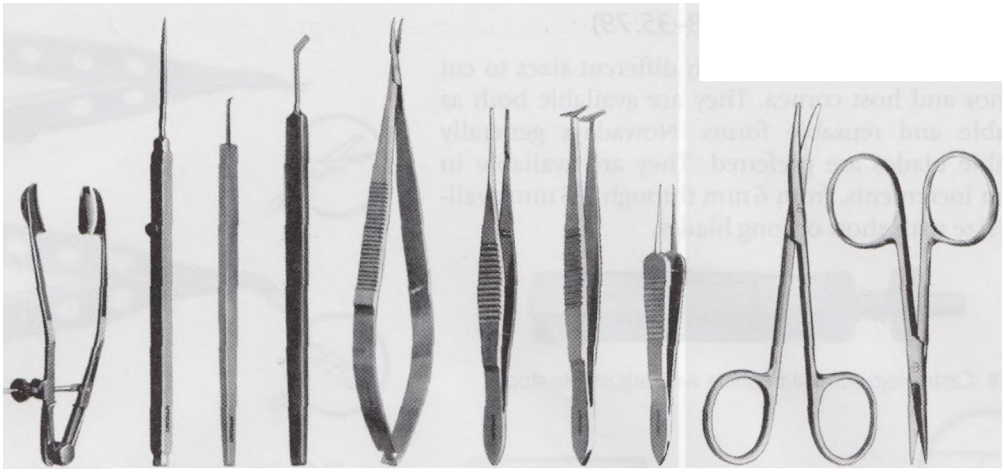
Fig, 35.73 Microsurgery radial keratotomy set.





1. Barraquer wire speculum, large
2. Flieringa scleral fixation ring (set of B sizes)
3. Paton spatula and spoon
4. Castroviejo corneal trephine, size 7.5 mm diameter
5. Dastoor corneal graft holding forceps
6. Castroviejo calliper, straight
7. Osher-Neumann radial marker, 8 blades
8. Colibri forceps, 1x2 teeth, 0.12 mm
9. Me Pherson corneal forceps, 1X2 teeth
10. Castroviejo cyclodialysis spatula
11. Bishop-Harmon tissue forceps, delicate, 0.8 mm
12. Dastoor keratoplasty spatula
13. Kelman-Mc Pherson forceps, long handle, 7.5 mm ang
14. Hartman mosquito forceps, straight
15. Hartman mosquito forceps, curved
16. Baby Jones towel clamp
17. Serrefine small, straight
18. Castroviejo corneoscleral scissors, small blade, left
19. Castroviejo corneoscleral scissors, small blade, right
20. Castroviejo corneoscleral scissors, small blade
21. Westcott, stitch scissors
22. Vannas capsulotomy scissors, ang. forward, 11 mm blade
23. Iris scissors, straight, $3^1/_2$" length
24. Barraquer needle holder, short model, m. Jaws, cur, w/o lock
25. Paufique graft knife
26. Rycroft air injection cannula, 27 G
27. Bracken anterior chamber cannula, curved, 19 G
28. Knolle anterior chamber irrigating, 23 G
29. Bard-Parker handle #3
30. Tudor Thomas corneal graft stand
31. Lieberman Teflon block

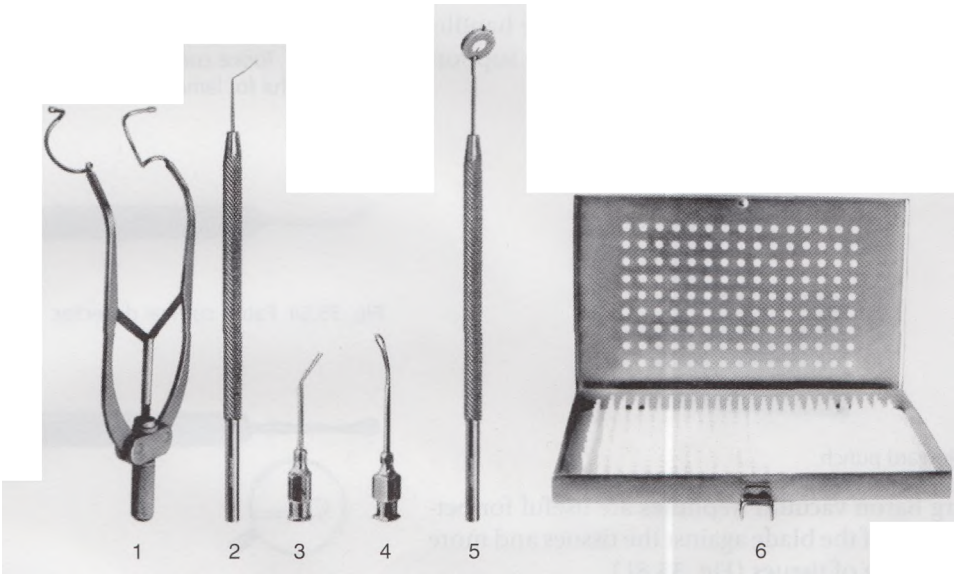
Fig. 35.74 Corneal transplant set.



6 7 8 9 10

1. Eye speculum
2. Cataract knife
3. Paufique graft knife
4. Paton corneal dissector
5. Castroviejo needle holder
6. Utility forceps
7. Fixation forceps, 10 mm wide jaws
8. St. Martin forceps
9. Scissors, curved
10. Scissors, straight

Fig, 35.75 Pterygium set.



1 2 3 4 5 6

1. LASIK speculum
2. Spatula
3. Flap irrigator
4. Irrigating cannula
5. Marker
6. Sterilization box

Fig. 35.76 LASIK set.



Flieringa ring

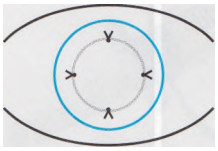


Fig. 35.77 Flieringa ring. Used for scleral support to prevent globe collapse in eyes with low scleral rigidity such as young children, high myopes and aphakes.

Corneal trephines (Figs 35.78-35.79)

Corneal trephines are available in different sizes to cut the donor and host cornea. They are available both as disposable and reusable forms. Nowadays generally disposable blades are preferred. They are available in 0.25 mm increments, from 6 mm through 9.5 mm available in size with short or long blades.



Fig. 35.78 Castroviejo corneal trephine with adjustable stop.



Fig. 35.79 Corneal trephine see through.

Howard punch (Fig. 35.80)

Used with the Howard Universal Trephine Handle:
The Howard punch has a self-aligning mechanism for easy insertion of the Howard universal trephine handle. The base plug is a Teflon block which is used to support the donor corneoscleral rim.

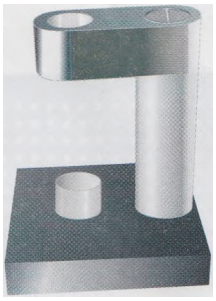


Fig. 35.80 Howard punch.

Hessburg Baron vacuum trephines are useful for better stabilization of the blade against the tissues and more controlled cutting of tissues (Fig. 35.81).

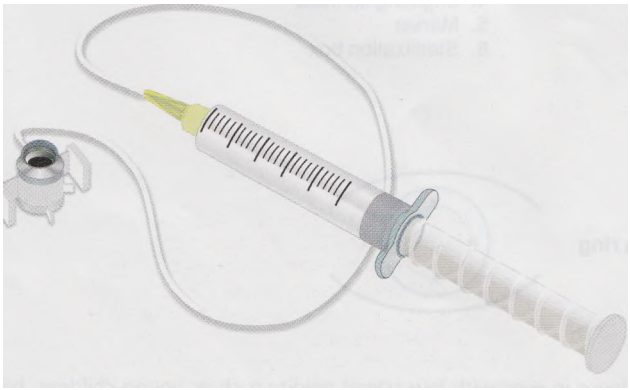


Fig. 35.81 Hessburg Baron vacuum trephines.



Fig. 35.82 Troutman-Katzin corneal transplant scissors: strong curve 6 mm long blades.



Fig. 35.83 Tooke corneal knife: straight blade with curved cutting edge. Useful for lamellar dissection of the cornea.



Fig. 35.84 Paton corneal dissector.



Fig. 35.85 Gill corneal knife: curved cutting edge. Useful for lamellar dissection of the cornea in lamellar keratoplasty, dermoid excision, etc.



Fig. 35.86 Paufique graft knife: angled tip, curved cutting edge. Useful for lamellar dissection for lamellar keratoplasty, removal of corneal or limbal dermoid, corneal tumours or carcinoma-in situ, pterygium excision, etc.

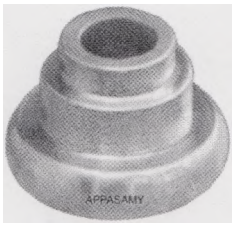


Fig. 35,87 Tudor Thomas stand: used for fixing the globe to trephine the donor cornea for transplantation. Using this technique the cornea is trephine from the epithelial side.

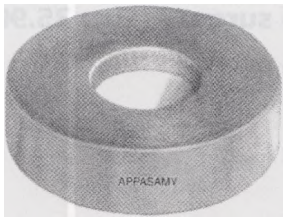


Fig. 35,88 Lieberman Teflon block for corneal cutting: used for supporting the excited donor corneoscleral button. Donor graft of the desired diameter is then trephined from the endothelial side before transplantation.

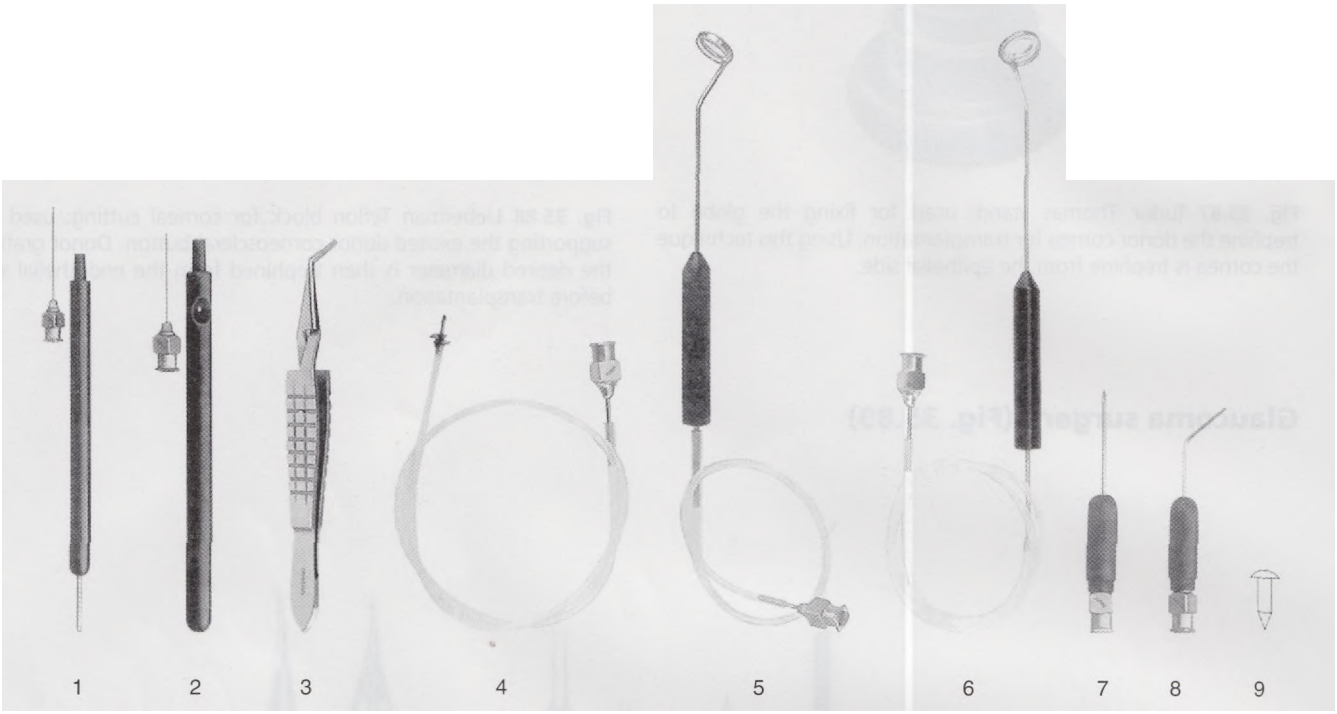
Glaucoma surgery (Fig. 35.89)



1. Wire speculum
2. Spatula, double ended
3. Castroviejo calliper, straight
4. Colibri forceps, 1 x 2 teeth, 0.12 mm
5. Tying forceps, curved
6. Towel clamp
7. Castroviejo corneal scissors
8. Westcott scissors
9. Vannas scissors, curved
10. Tenotomy scissors, curved
11. Bard-Parker handle # 3
12. Kelly Descemet's membrane punch
13. Harms trabeculotomy probe, right
14. Harms trabeculotomy probe, left
15. Rycroft air injection cannula, 27 G
16. Anterior chamber washout cannula, 16 G
17. St. Martin forceps
18. Me Pherson tying forceps, angled 11 mm

Fig. 35.89 Glaucoma set.

Vitreoretinal surgery (Figs 35.90 and 35.91)



1. Tapered extrusion needle
2. Charles flute needle
3. Scleral plug
4. Infusion cannula
5. 45 Diopter irrigating contact lens
6. 90 Diopter irrigating contact lens
7. Membrane peeler
8. 30 Degree bent needle
9. Scleral plugs (set of 3)

Fig. 35.90 Vitreoretinal posterior segment set.

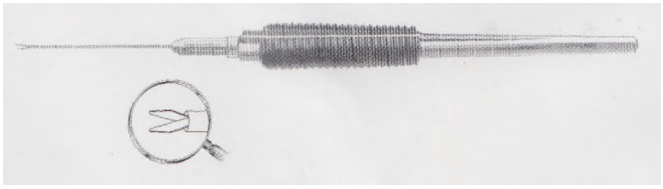


Fig. 35.91 Vitreous forceps: can have smooth or serrated jaws.

Lids and lacrimal sac surgery (Figs 35.92-35.100)

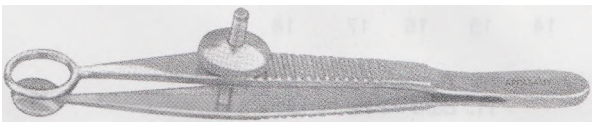


Fig. 35.92 Chalazion clamp: This is used for holding the lid during incision and curettage of a chalazion and achieving haemostasis during surgery. Excessive tightening can lead to pressure necrosis. The solid blade is placed externally on the skin and the ring-shaped blade on the inner conjunctival surface. After aligning the position to enclose the chalazion in the ring, the clamp is tightened and fixed.

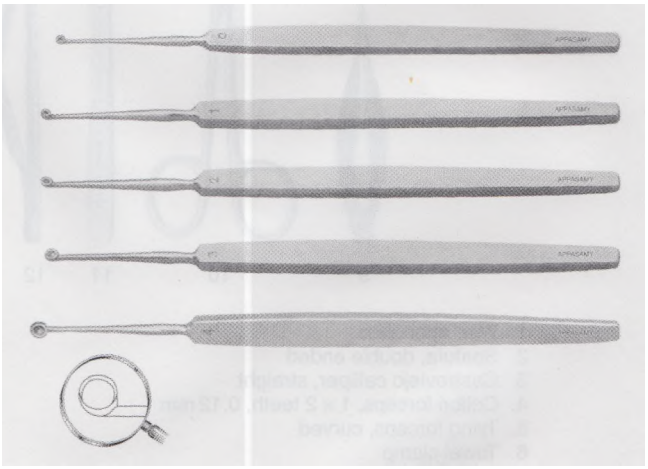
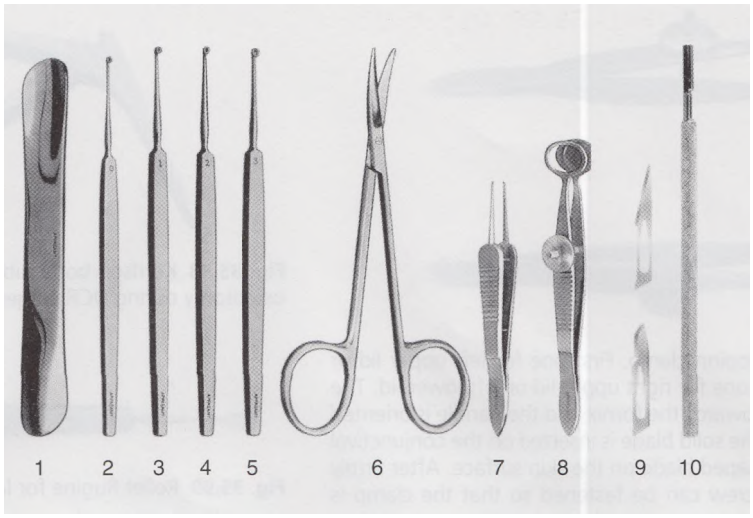
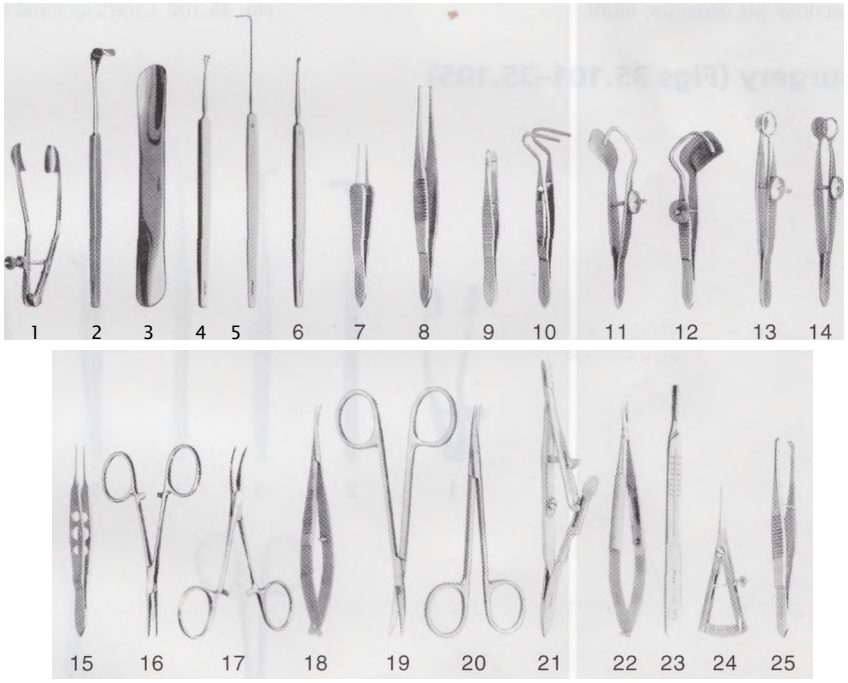


Fig. 35.93 Chalazion curette: round cup-shaped tip. Edge of the cupped tip is slightly sharp. Used to scoop out the contents of the chalazion and curette the base after making a vertical incision opening up the wall of the chalazion from its palpebral surface.



1. Jaeger lid plage
2–5. Chalazion curette of different sizes
6. Scissors, straight
7. St. Martin forceps
8. Chalazion forceps
9. Bard-Parker blade
10. Bard-Parker handle

Fig, 35.94 Chalazion set.



1. Eye speculum
2. Desmarres lid retractor
3. Lid plate
4. Fixation hook
5. Graefe muscle hook
6. Chalazion curette
7. St. Martin forceps, 1X2 teeth
8. Fixation forceps
9. Cilia epilation forceps
10. Ptosis forceps
11. Entropion forceps, left, small
12. Entropion forceps, right, small
13. Chalazion forceps
14. Chalazion forceps
15. Me Pherson forceps
16. Hartman mosquito forceps
17. Hartman mosquito forceps, curved
18. Westcott tenotomy scissors
19. Scissors
20. Tenotomy scissors
21. Needle holder
22. Barraquer needle holder
23. Bard-Parker handle
24. Castroviejo calliper, straight
25. Fixation forceps

Fig. 35.95 Lid set.

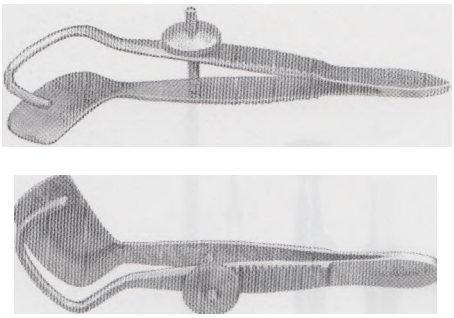


Fig. 35.96 Snellen entropion clamp. First one for left upper lid or right lower lid. Second one for right upper lid or left lower lid. The convex side is aligned towards the fornix and the handle is oriented on the temporal side. The solid blade is inserted on the conjunctival surface and the wire-shaped blade on the skin surface. After firmly clamping the lid the screw can be fastened so that the clamp is self-retaining.



Fig. 35.97 Lacrimal sac dissector, blunt.

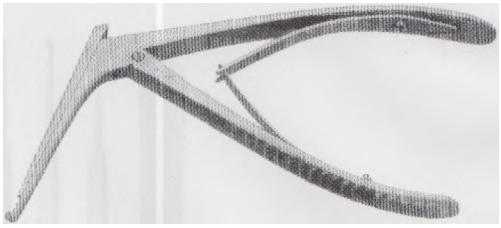


Fig. 35.98 Kerrison bone nibbling rongeur: useful for making the osteotomy during DCR surgery.

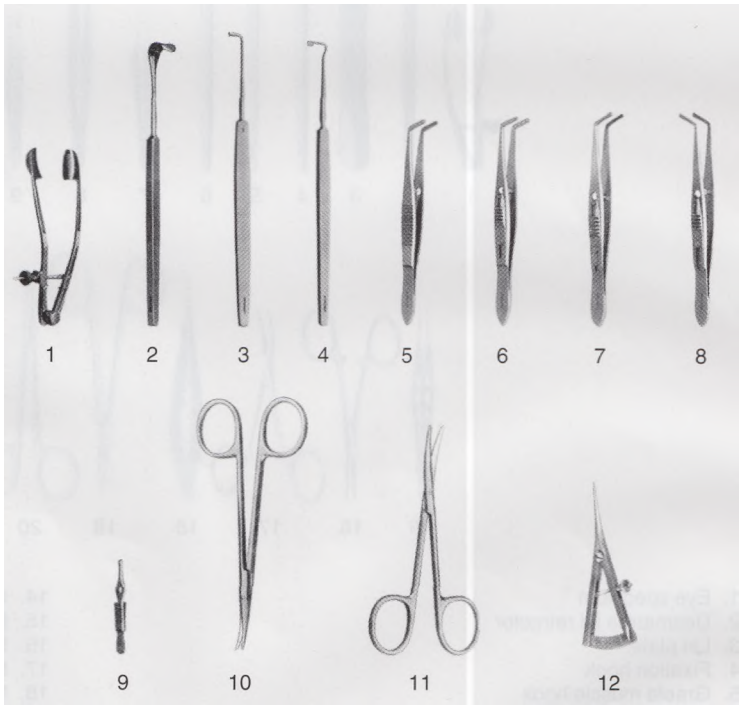


Fig. 35.99 Rollet Rugine for lacrimal sac.



Fig. 35.100 Lang's lacrimal sac dissector, sharp.

Squint surgery (Figs 35.101-35.105)



1. Lancaster eye speculum
2. Desmarres lid retractor, size 0
3. Graefe muscle hook size 1
4. Jameson muscle hook, large
5. Jameson muscle forceps, left
6. Jameson muscle forceps, right
7. Worth advancement forceps
8. Worth advancement forceps
9. Serrefine
10. Stevens tenotomy scissors
11. Knapp strabismus scissors
12. Castroviejo calliper

Fig. 35.101 Squint surgery set.

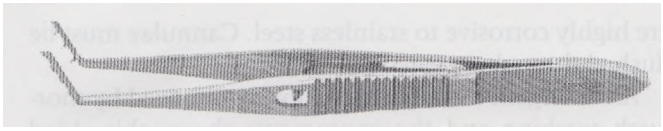


Fig. 35.102 Prince advancement forceps.

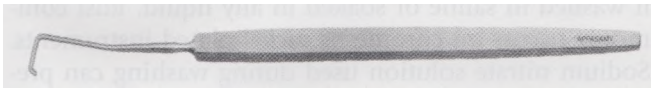


Fig. 35.103 Green muscle hook: useful for hooking and holding the muscle. The tip is placed underneath the belly of the muscle and drawn up to the insertion. Also useful when isolating the extraocular muscles during retinal detachment surgery.

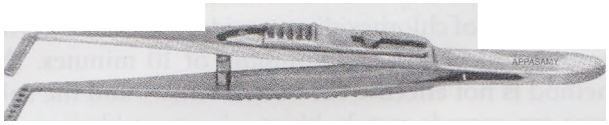


Fig. 35.104 Jameson muscle forceps with side lock.



Fig. 35.105 Chavasse's muscle hook.

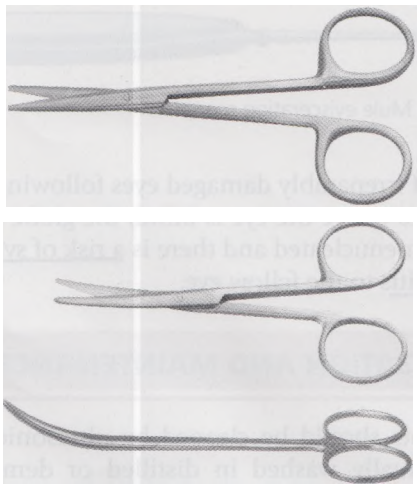


Fig. 35.106 Enucleation scissors ring handle.



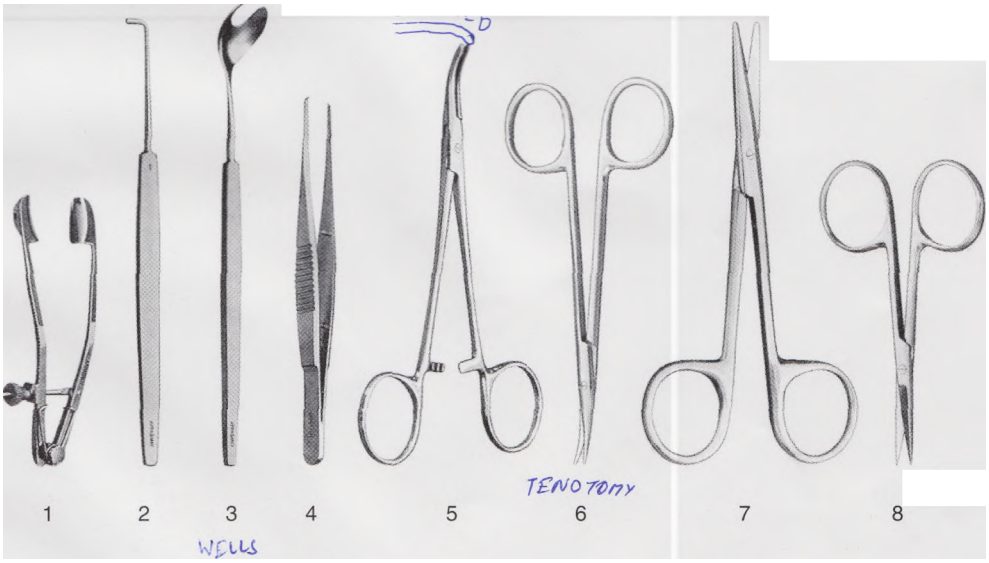
Fig. 35.107 Wells enucleation spoon.

Instruments for enucleation (Figs 35.106-35.108)

These instruments are used for enucleation or removal of the whole eyeball as is required for ocular tumours, severe trauma with irretrievably damaged blind eyes, and painful blind eyes. The same instruments are also used for harvesting donor eyes after death.

Instruments for evisceration (Fig. 35.109)

The instruments for evisceration are used for removing all the contents of the eyeball and leaving only the sclera behind in cases of severe suppurative panophthalmitis which is not responding to therapy and at risk of progressing to orbital cellulitis or cavernous sinus thrombosis. Evisceration may also sometimes be undertaken



1. Eye speculum
2. Muscle hook
3. Wells enucleation spoon
4. Fixation forceps
5. Halsted mosquito forceps, curved
6. Tenotomy scissors, curved
7. Enucleation scissors, straight
8. Small scissors, straight

Fig. 35.108 Enucleation set.



Fig. 35.109 Mule evisceration scoop.

in cases of irreparably damaged eyes following perforating injuries where the eye is blind, the globe cannot be repaired or enucleated and there is a risk of sympathetic ophthalmitis to the fellow eye.

STERILIZATION AND MAINTENANCE

Instruments should be cleaned by ultrasonic cleaning or individually washed in distilled or demineralized water immediately after use to prevent blood and other debris from drying on to the surface. Blood causes a stain which is difficult to remove, and saline solutions are highly corrosive to stainless steel. Cannulae must be flushed through repeatedly.

All detergent must be meticulously removed by thorough washing and the instruments thoroughly dried with a clean, absorbent cloth. Stainless steel can corrode if washed in saline or soaked in any liquid. Rust commonly occurs on chrome or nickel-plated instruments. Sodium nitrate solution used during washing can prevent rusting.

Instruments can be sterilized, to kill bacteria, spores, fungi and viruses by a number of methods outlined in Table 35.1.

Instruments may also be disinfected by soaking them in solutions of chlorhexidine, povidone iodine and 70% isopropyl alcohol for a minimum of 10 minutes. This method is not effective for certain viruses and the solutions can corrode metals, blunt scissors and knives, and stain instruments.

Table 35.1 Various methods used for sterilizing instruments

Sterilization method	Utility	Advantages	Drawbacks
Autoclave	Metallic instruments, toughened plastic, glass and cloth	Cheap	Instruments have to be dried
Hot air oven	Metallic instruments, toughened plastic and glass	Instruments are dry	Instruments need to cool
Ethylene oxide	All instruments, plastic and tubing	Large quantities and delicate items	Expensive, explosive and carcinogenic
Formalin	Metallic instruments, toughened plastic, glass and tubing	Low cost and delicate items	Irritant—all items have to be well rinsed
Ionising gamma radiation	Needles, syringes and sutures	Large quantities of delicate items	Only commercial use

Appendices

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III. IOL Designs and Materials 585

I. Local Anaesthesia in Ophthalmology

Local or regional anaesthesia is being employed with increasing frequency in ophthalmology in preference to general anaesthesia. Its major advantages are that surgery can be undertaken as a day-care procedure, it does not require sophisticated equipment and the anaesthesia can be used to reduce the intraocular pressure and vitreous volume when necessary. However, it cannot be used in uncooperative patients or children.

Local anaesthetics are used clinically to produce a temporary loss of sensation, analgesia and/or function, usually akinesia, in a restricted area of the body. It is thought that the local anaesthetic receptors are protein-bound receptors located near the sodium channel. Anaesthesia causes a decreased depolarization of the nerve membrane, so that impulses are not conducted along the nerve. Drugs commonly used for local anaesthesia are either ester agents such as procaine or amides such as lignocaine and bupivacaine. Esters may cause more allergies and have largely been replaced by the amides.

Local anaesthesia in ophthalmology consists of topical applications to the conjunctiva, and local injections in the subcutaneous or submuscular plane in surgeries of the lid. However, intraocular surgeries require specific nerve blockade for anaesthesia and akinesia. Propofal and midazolam are given to reduce anxiety and produce amnesia, and an intravenous cannula should be placed for any possible emergency.

To avoid any toxicity a dose of lignocaine above 3 mg/kg should not be used; for bupivacaine the safe dose is 2 mg/kg. Adjuvant adrenaline in doses of 1:200,000 is utilized to prolong the duration of anaesthesia and reduce bleeding during surgery. It is contraindicated in hypertensive patients and those with cardiovascular problems.

Accidental intravascular or intrathecal injection, or the injection of a large dose of the local anaesthetic can cause central nervous system and cardiovascular toxicity. The patient will complain of dizziness and circumoral paraesthesia, progressing to visual dysfunction and tinnitus and, ultimately, generalized convulsions. The cardiovascular symptoms of toxicity are sinus bradycardia and depressed cardiac contractility.

The sensory nerve supply to the eye is from the ophthalmic branch of the trigeminal nerve, which divides into further branches. The lacrimal nerve is responsible for the innervation of the conjunctiva. The anterior segment of the eye—cornea, sclera, iris and ciliary body—is supplied by the nasociliary nerve. Parasympathetic function is through the parasympathetic fibres that travel with the oculomotor nerve. They then leave to synapse in the ciliary ganglion situated just medial to the lateral rectus muscle. The postsynaptic fibres travel in the short ciliary nerves and supply the sphincter pupillae and ciliary muscle.

LOCAL ANAESTHESIA IN OPHTHALMOLOGY

Topical anaesthesia

Topical anaesthesia is used for most manipulations of the superficial cornea or conjunctiva, phacoemulsification in cooperative patients and prior to regional blocks

Local anaesthetic	Onset of action	Duration of action	Use (concentration)
Benoxinate	6–20 seconds	15 minutes	Topical (0.4%)
Proparacaine	15–30 seconds	15–20 minutes	Topical (0.5%)
Amethocaine	10–25 seconds	10–20 minutes	Topical (0.5–1 %)
Lignocaine			
	10–35 seconds	15–20 minutes	Topical (4%)
	5–10 minutes	30–60 minutes	Infiltration (0.5–1 %)
Bupivacaine	Moderate	75–90 minutes	Infiltration (0.25–0.75%)
Ropivacaine	Moderate	116-6 hours	Infiltration (1 %)

for intraocular surgery. Commonly used topical anaesthetics include lignocaine 4%, paracaine, benoxinate 0.4% and cocaine. Oxybuprocaine or benoxinate also has bactericidal properties and is available mixed with fluorescein for applanation pressure recordings.

Regional anaesthesia

This may be achieved by (i) nerve blocks or (ii) local infiltration.

Nerve blocks

These are of various types:

- Peribulbar block
- Retrobulbar block
- Parabulbar or sub-Tenon block
- Intracameral anaesthesia
- Facial block
- Frontal block

Peribulbar block: Peribulbar blocks are employed for intraocular anaesthesia and analgesia, and have now almost replaced retrobulbar block. They are considered to cause less optic nerve damage, but the akinesia produced is not as good as in retrobulbar block. As two injections are given the likelihood of vascular damage persists. In a 10 ml syringe 5 ml bupivacaine 0.75%, 5 ml lignocaine 2% with 1:200 000 adrenaline and 75 units of hyaluronidase are mixed. The lignocaine provides an early onset of action, bupivacaine prolonged efficacy and hyaluronidase permits diffusion into the orbit. A 25 gauge 2.5 cm disposable needle is attached to the syringe. Topical anaesthesia is instilled into the conjunctival sac. The patient is placed in the supine position and asked to look steadily straight ahead. The needle is inserted transconjunctivally or transcutaneously at the junction of the middle two-thirds and lateral one-third of the lower lid adjacent and parallel to the orbital floor for about 2.5 cm (Figs 1 and 2). Gentle aspiration of the syringe is performed to alleviate possible entry of the needle into a blood vessel and then 5 ml of the mixture is injected into the lateral adipose tissue of the orbit. Pressure is applied to the site for a couple of minutes. Subsequently, just medial to the middle canthus the same needle is inserted to a depth of 2.5 cm and a further 3 ml of anaesthetic mixture is injected. Pressure is again applied to the site for a couple of minutes. The second injection may also be given just inferomedial to the supraorbital notch, but is likely to cause more complications. A Honan pressure cuff is applied for about 15 minutes. Anaesthesia and analgesia begin in about 5 minutes, but in most patients it takes about 15 minutes. Supplemental injections may be necessary inferiorly for persisting inferolateral movements, and superiorly to

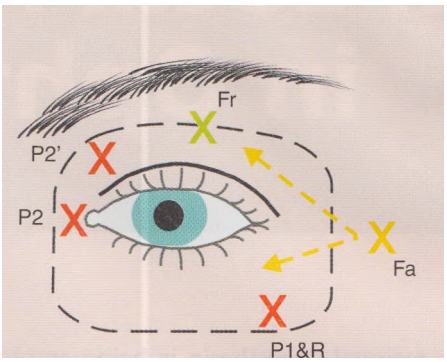


Fig. 1 Red crosses (P1, P2, P2') indicate the sites of injection for peribulbar block. The yellow cross (Fa) indicates the site of insertion of the needle for facial block by the van Lint technique. Yellow arrows indicate the direction of injection. The green cross (Fr) indicates the site of insertion of the needle for a frontal block. R is the site of retrobulbar block.

block any residual superior or medial movements. Such a block is used for cataract, glaucoma, keratoplasty, vitreoretinal and strabismus surgeries.

Retrobulbar block: A 22 gauge 3.5 cm long needle is used to enter transcutaneously at the junction of the middle and lateral thirds of the lower orbital margin. The needle is inserted directly backwards for about 15 mm and is then angled upwards and medially towards the apex of the orbit (Figs 1 and 2). As the needle pierces the intermuscular septum between the lateral and inferior rectus muscles the 'feel' is altered. After aspiration,

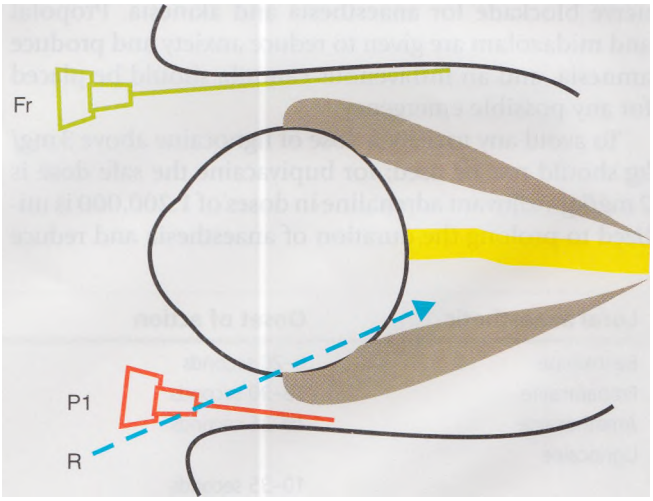


Fig. 2 Sagittal section of the orbit showing the sites of insertion of the needles for retrobulbar (blue, R), peribulbar (red, P1) and frontal (green, Fr) blocks.

2-4 ml of the anaesthetic is injected. This is indicated in all intraocular surgeries as in peribulbar anaesthesia, but needs an additional facial block.

Parabulbar or sub-Tenon block: A conjunctival incision 2-3 mm in size, is made halfway between the inferior limbus and fornix to open into the sub-Tenon space. A blunt cannula or needle is used to inject anaesthetic into the posterior sub-Tenon space, bathing the nerves and muscles within the cone. This is thought to completely avoid vascular and optic nerve injury, requires lower volumes of anaesthetic and provides better anaesthesia to the iris and anterior segment, but causes more postoperative morbidity. This can also be used in all intraocular surgeries.

Complications of peribulbar, retrobulbar and parabulbar anaesthesia include chemosis, retrobulbar haemorrhage, penetration of the globe, inadvertent intravascular or intrathecal injection and optic nerve damage, directly or by vascular occlusion. All needles used in orbital anaesthetic injections should have their bevel facing the globe and be tangential to the sclera. Penetration of the globe is more common in myopes with larger eyes and staphylomas.

Intracameral anaesthesia: Intracameral anaesthesia—lignocaine 1% without preservative or adrenaline, has been used for phacoemulsification.

Facial block: Facial block is not required in most cases when a peribulbar block has been given. It becomes necessary if a retrobulbar block is planned. A number of techniques have been described; the most popular are the van Lint and O'Brien techniques.

1. van Lint technique: A 22 gauge 3.5 cm long needle is inserted subcutaneously outside the lateral canthus and advanced upwards towards the brow, and downwards towards the infraorbital foramen, injecting along both paths.
2. O'Brien technique: A needle is placed just posterior to the condyloid process of the mandible and local anaesthetic is injected around it to block the facial nerve and its branches.

Frontal block: The frontal nerve has two branches—the supraorbital and supratrochlear nerves—supplying the upper eyelid. A frontal block is therefore useful while doing a surgical procedure such as ptosis surgery, on the upper lid of patients unfit for general anaesthesia. A long 4 cm needle is used to enter the orbit transcutaneously, just below the midpoint of the supraorbital margin. The needle is directed towards the roof of the orbit and follows its contour for a distance of 4 cm. At this point the plunger is aspirated to ensure that the tip of the needle is not in a blood vessel and about 2 ml of anaesthetic is injected.

II. Lasers in Ophthalmology

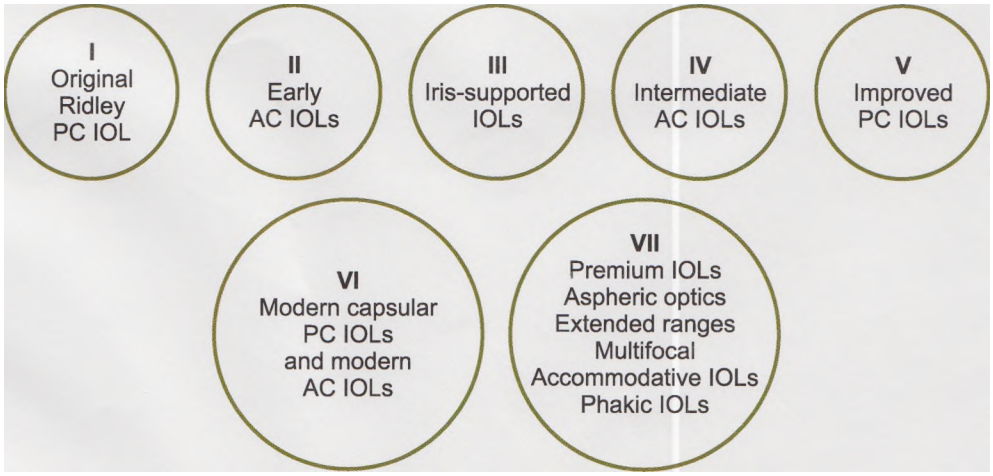
Lasers used in ophthalmology

Laser	Wavelength (nanometer)	Clinical applications
Nd:YAG (Neodymium-Yttrium-Aluminium-Garnet)	1064	Posterior capsulotomy, iridotomy, vitreolysis
Frequency-doubled Nd:YAG	532	Retinal photocoagulation, cyclophotocoagulation
Argon green	514	Trabeculoplasty, iridoplasty, pupillomydriasis, retinal photocoagulation*
Diode laser	800	Retinal photocoagulation
Krypton red	714	Retinal photocoagulation
Excimer (argon fluoride)	193	Photorefractive keratectomy (PRK), phototherapeutic keratectomy (PTK), LASIK, LASEK
Femtosecond laser (neodymium-glass)	1053	Femtosecond laser assisted refractive surgery, lamellar and full thickness corneal transplants

'Retinal photocoagulation includes treatment for diabetic retinopathy, other causes of retinal neovascularization or retinal oedema, retinal breaks, central serous retinochoroidopathy, subretinal neovascular membranes, small retinal tumours, angiomas, etc. Argon green laser is the most widely used but other lasers are increasingly being used as substitutes in certain situations.

III. IOL Designs and Materials





Fig, 1 Diagrammatic representation of history of evolution of IOLs (PC = posterior chamber, AC = anterior chamber).

1. Based on location or site of implantation

- Anterior chamber Angle fixated
  Iris fixated
- Posterior chamber Supported within capsular bag
  Sulcus fixated anterior to anterior lens capsule
  Iris fixated
  Scleral fixated

2. **Based on shape and size**

- Optic size
  - Large optic 6-6.5 mm
  - Small 5-5.25 mm
- Overall diameter including optic and haptic
  - 12-14 mm
- Overall shape
  - Central optic with haptic
    - Single piece
    - Multipiece
    - Angulated haptics
  - Plate haptic
- Optic shape
  - Posterior square edge
  - Biconvex
  - Aspheric optic

3. Based on optical correction

- Monofocal
- Multifocal
  - Refractive
  - Diffractive
- Accommodative IOLs
- Phakic IOLs designed to correct high-refractive errors in the presence of the crystalline lens, e.g. high myopic > 12 D

4. Based on physical flexibility/incision by

- Foldable
- Non-foldable rigid IOLs

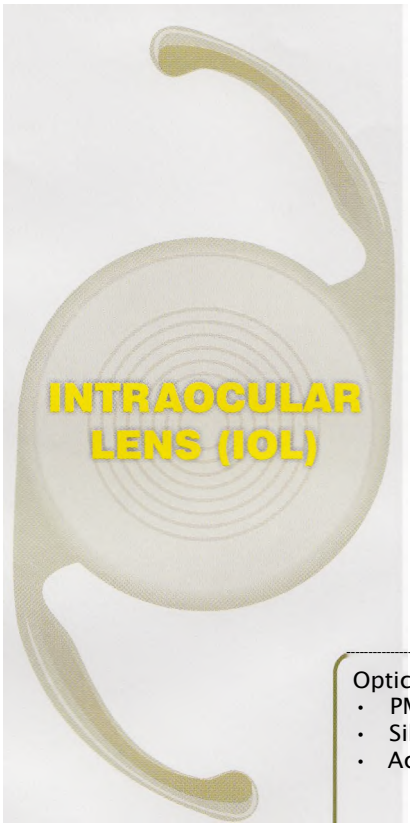
5. Based on UV absorption

6. Based on IOL materials

- Rigid
  - Polymethylmethacrylate (PMMA)
    - with PMMA haptic (single-piece design)
    - with polypropylene haptic (multipiece design)
- Soft or foldable
  - Acrylic Hydroxyethyl methacrylate (HEMA)
    - Hydrophobic (non-hydrogel)
    - Hydrophilic (hydrogel)
  - Silicone Polysiloxane
  - Collamer Combination of collagen, a UV-absorbing chromophore
- Adjustable
  - Light adjustable IOLs
  - Smart IOLs

III. IOL Designs and Materials

Optic Designs
- Size 5.5 or 6.0 mm
- With or without positioning holes
- Biconvex or aspheric
- Unifocal or multifocal (refractive or diffractive)
- Light adjustable



Overall Shape and Size
- Overall diameter 12–14 mm
- Single piece or multipiece
- Accommodative
- Adjustable

Haptic Materials
- PMMA
- Polypropylene
- Silicone
- Acrylic
  - Hydrophilic
  - Hydrophobic

Haptic Designs
- Loop haptic
  - Open
    - C shaped
    - J shaped
  - Closed
- Plate haptic

Optic Materials
- PMMA
- Silicone
- Acrylic
  - Hydrophilic
  - Hydrophobic
- UV absorbing blue light filtering

Fig. 2 IOL designs and materials.

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