

6

The Corene

William T Green

Malcolm G Kerr Muir

THE NORMAL CORNEA

The cornea has three primary functions:

- # Light transmission which must be achieved with the minimum of distortion and absorption of light.
- # Refraction; the main refractive interface is between air and the precorneal tear film. This surface must be free of imperfections to avoid disturbance of the visual image.
- # Protection of the anterior globe without compromising the optical requirements.

Achieving these functions in a biological tissue has resulted in the evolution of an avascular structure whose metabolic requirements are mainly supplied posteriorly by the aqueous. Aqueous glucose is utilized by corneal cells for energy. Carbon dioxide can either freely diffuse away through cell membranes or be converted to bicarbonate which is pumped into the aqueous by the endothelial cells with the help of carbonic anhydrase. Lactate cannot escape so readily, particularly through the epithelial barrier, and must diffuse posteriorly

into the aqueous; hypoxia leads to lactate accumulation and local acidosis in the cornea which contributes to oedema. Oxygen is present in the aqueous but the main supply is provided by atmospheric oxygen dissolved in the tear film anteriorly with a small contribution from the limbal vessels peripherally.

The embryonic cornea is derived from surface ectoderm after invagination of the lens vesicle. At this stage the corneal stroma is represented by a layer of loose collagen fibrils between the ectoderm and the lens vesicle. Mesenchymal cells from the perilimbal cell mass begin to form endothelium and the stroma is invaded by perilimbal fibroblasts (future keratocytes) at about six weeks of gestation. The origin of these perilimbal cells is now thought to be neural crest rather than mesoderm. The cornea is large at birth relative to the rest of the globe and adult size is attained by about the age of two years.

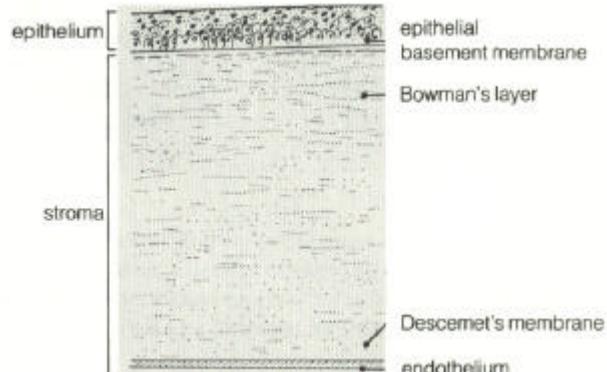
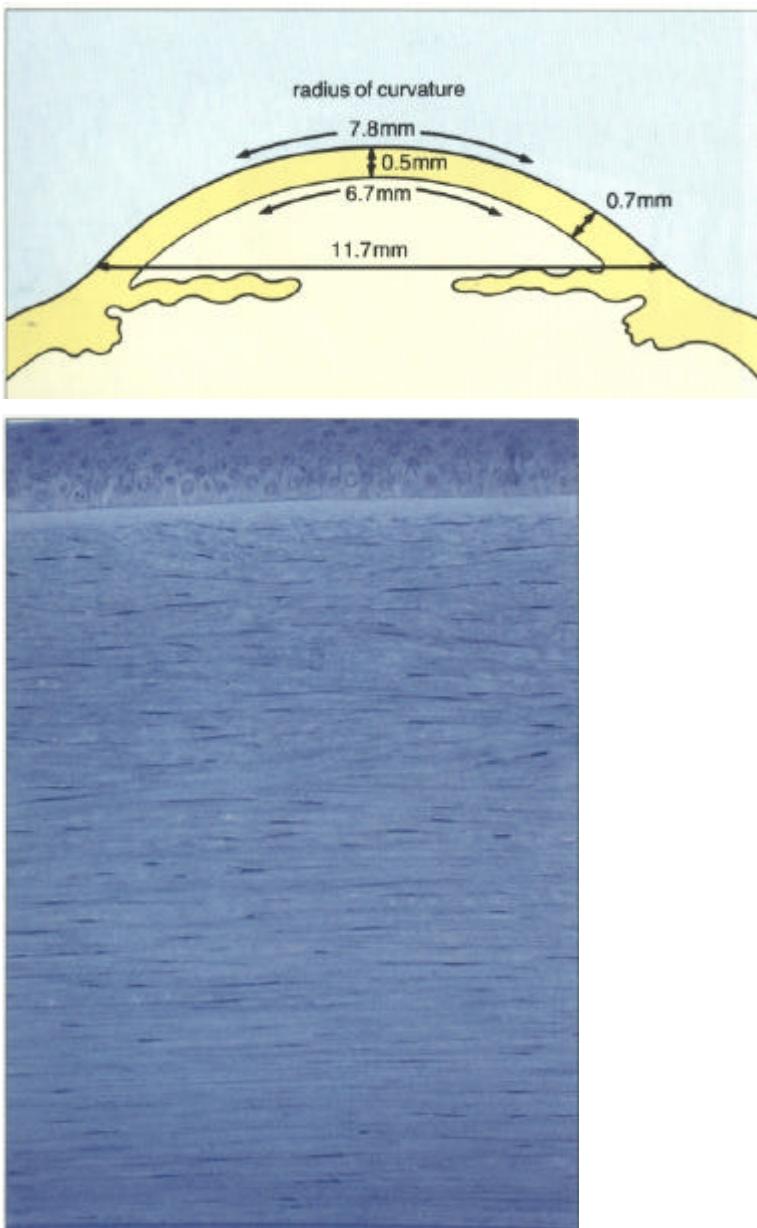


Fig. 6.1 The cornea has a horizontal diameter of 11.7mm and somewhat less than this in the vertical meridian due to encroachment by the limbus. The corneal apex has an anterior radius of curvature of 7.8mm (normal range 6.75-9.25mm) and 6.6mm on its posterior aspect. The central corneal thickness is 0.5mm (normal range 0.49-0.56mm), increasing to 0.7mm peripherally, with an axial refractive power of approximately 43 dioptres.

There are five distinct histological layers. The epithelium consists of basal columnar cells attached to their basement membrane, intermediate wing cells and elongated superficial cells with flattened nuclei beneath the tear film. Bowman's layer is an acellular condensation of superficial stroma approximately 10-20gm thick which lies immediately beneath the epithelial basement membrane. The stroma forms over 90 per cent of the corneal thickness and consists of collagen lamellae (layers) in a proteoglycan matrix interspersed with keratocytes. Descemet's membrane is composed of a lattice-work of collagen fibrils which is 3gm thick at birth, when the entire layer appears striated or 'banded'. A posterior 'nonbanded' layer is continuously laid down by the endothelium throughout life so that Descemet's membrane increases in thickness with age. The endothelium consists of a monolayer of hexagonal cells which do not divide during life but are able to enlarge and spread to fill defects in the cell layer. By courtesy of Prof J Marshall.

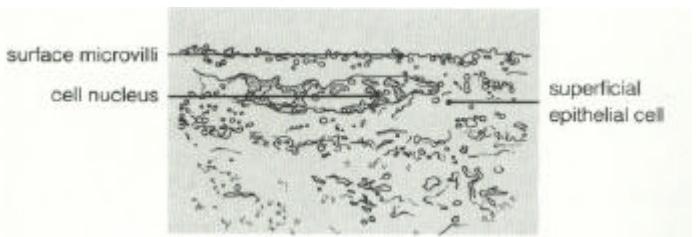
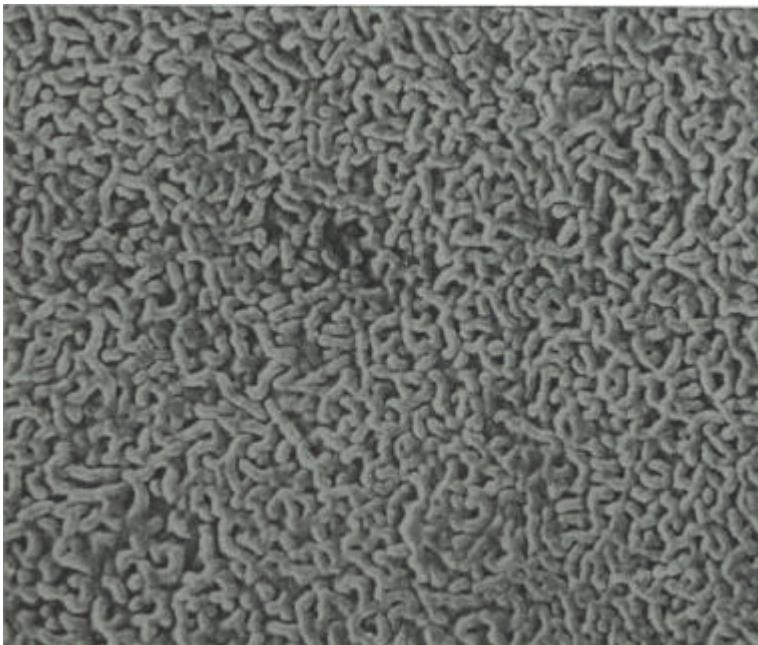
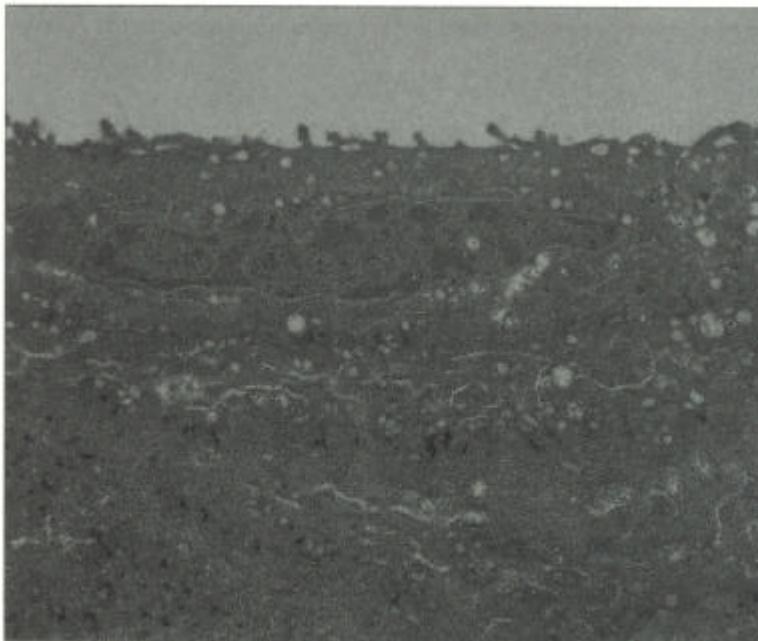


Fig. 6.2 The precomeal tear film must be supremely smooth and stable for regular refraction. It covers the epithelial surface which is thrown into multiple folds (microvilli and microplicae). These evaginations elaborate a glycocalyx (a branching mucoprotein layer) which renders the surface hydrophilic. The continuous mitotic activity of the basal epithelium accounts for the rapid cellular turnover of the epithelium (one week) and numerous tonofilaments indicate the potential for movement of basal cells to fill epithelial defects. The precorneal tear film is 40 micro m thick and composed predominantly of mucus derived from the conjunctival epithelial and goblet cells, an aqueous component secreted by the lacrimal glands and a superficial lipid layer from the meibomian glands. Maintenance of corneal transparency depends on a healthy epithelium with an adequate supply of atmospheric oxygen dissolved in the tear film (partial pressure of oxygen is 160mmHg with the lids open and 55mmHg when closed). By courtesy of Prof J Marshall.

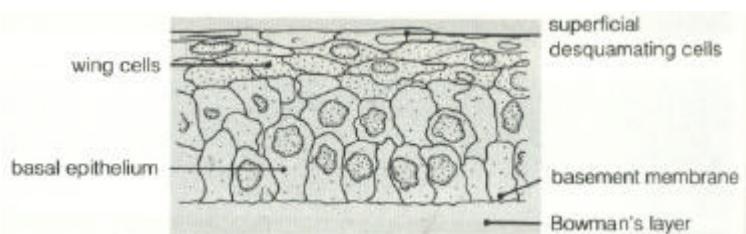
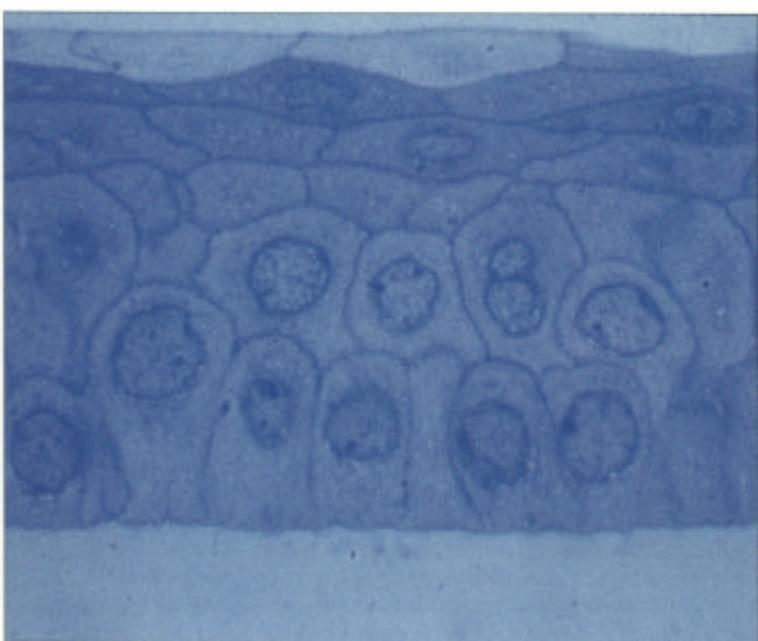


Fig. 6.3 The nonkeratinized, stratified, squamous epithelium can be seen as a layer of about five cells in thickness separated from Bowman's layer by the epithelial basement membrane. Only the basal cells divide. The morphology of the daughter cells changes as they migrate anteriorly during maturation to finally desquamate from the surface. By courtesy of Prof J Marshall.

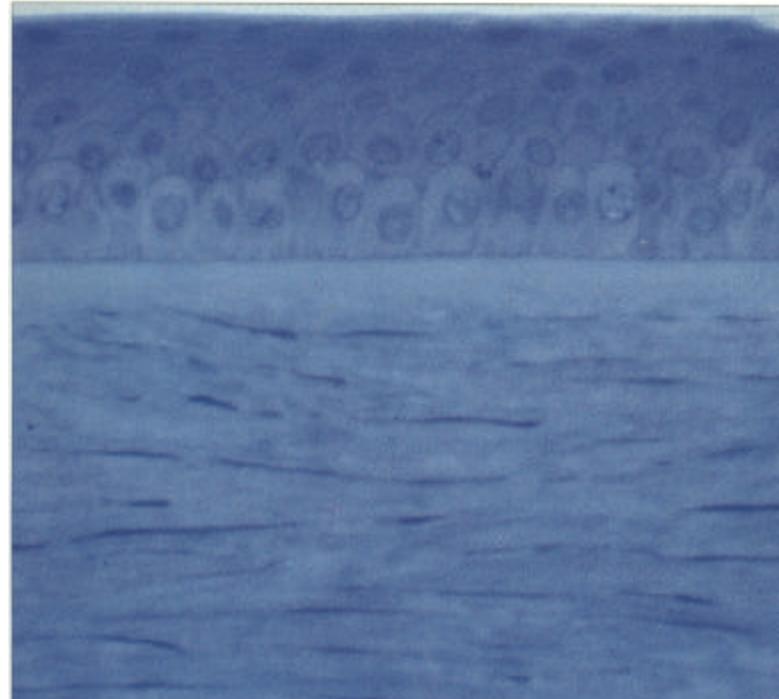
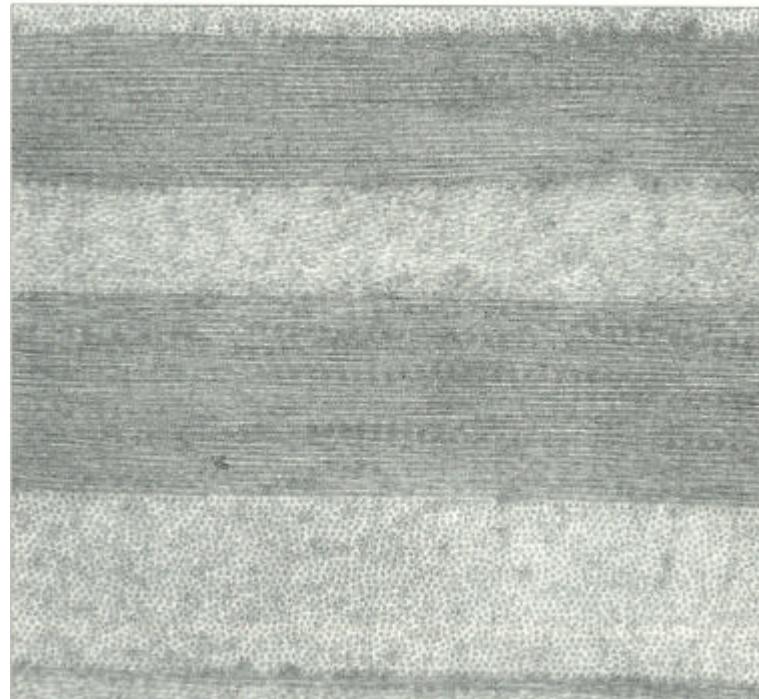


Fig. 6.4 The mechanical strength of the cornea is provided by the stroma with its dense aggregations of interwoven collagen fibrils (mainly Type 1 collagen) maintained in a proteoglycan matrix seen here by light and electron microscopy. The fibrils are continuous from limbus to limbus and are arranged into about 200 layers or 'lamellae' with a small degree of interdigititation between them. In Bowman's layer the collagen fibrils are finer and more densely packed. Transmission of light depends on the highly ordered



disposition of the collagen fibrils with small changes of refractive index over short distances and relative dehydration of the stromal proteoglycans. Light transmission is maximal at 700nm (98 per cent) and decreases to 80 per cent at 400nm. Ultraviolet light with a wavelength below 310nm is strongly absorbed by the stroma. By contrast, the cornea readily transmits infrared radiation (70 per cent is transmitted up to 2400nm). By courtesy of Prof J Marshall.

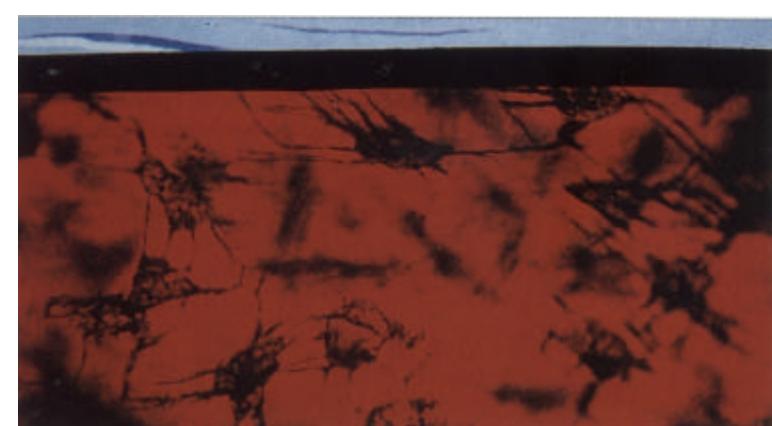


Fig. 6.5 Keratocytes with multiple processes lie between the lamellae in a syncytial arrangement (appearing dark with this silver stain). They are nonphagocytic but can transform to fibroblasts and migrate to areas of damage (e.g. the bed of excimer laser ablations). By courtesy of Prof J Marshall.

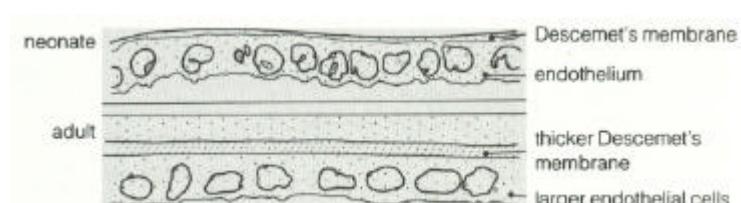
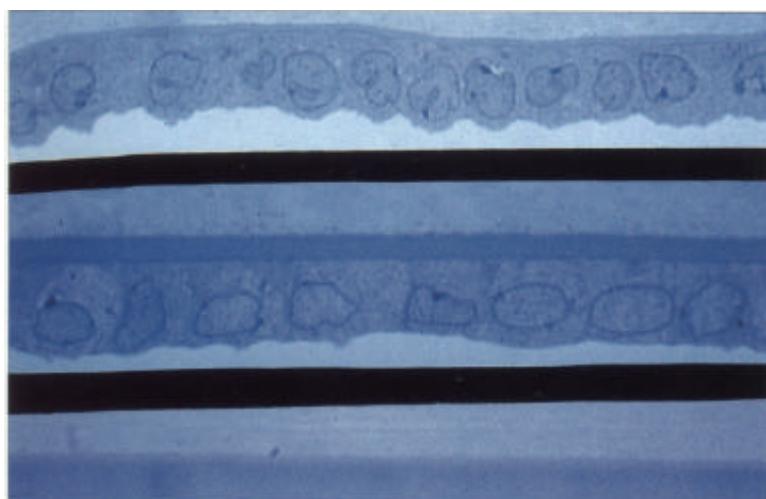


Fig. 6.6 Descemet's membrane which consists of type IV collagen is secreted by the endothelium, a monolayer derived from neural crest. It is elastic, permeable to water and solutes and increases in thickness throughout life. The strong epithelial and moderate endothelial cellular physical barriers combined with normal endothelial cell function counteract the aqueous influx into the corneal stroma from the intraocular pressure and the osmotic pressure of the glycosaminoglycans in the cellular stromal matrix (the stromal swelling pressure). By courtesy of Prof J Marshall.

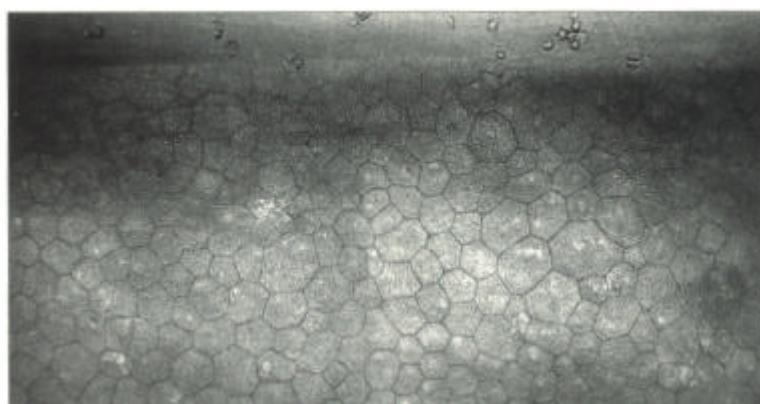
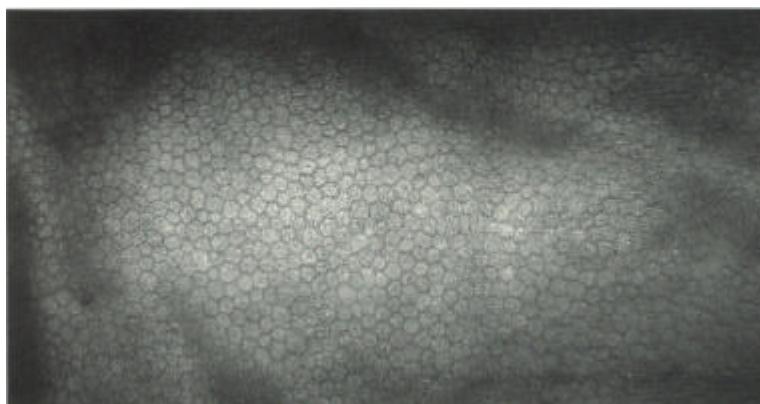
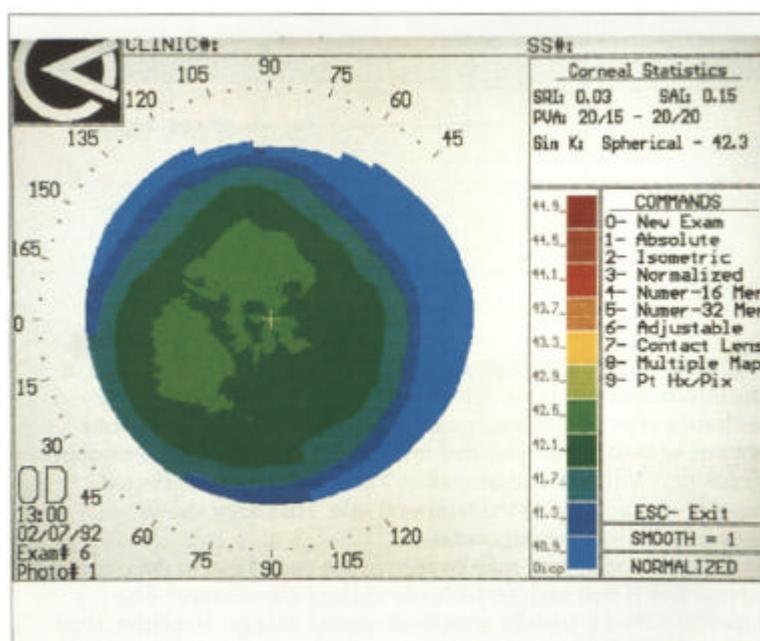


Fig. 6.7 The corneal endothelium can be assessed by specular microscopy (see Chapter 1). The endothelial monolayer does not replicate in vivo. Normal cell counts are $3500-4000/\text{mm}^2$ at birth and gradually decrease to approximately $1500-2000/\text{mm}^2$ in the adult cornea. Decompensation with corneal oedema becomes increasingly likely with cell counts of less than $500/\text{mm}^2$. Cell density alone, however, is a poor guide to function which is better assessed by a combination of cell density, cell area and variation in cell size and morphology (polymegathism and polymorphism). These specular photographs show the endothelium of an 18-month-old infant (top), and a normal 74-year-old man (middle). Notice the decreasing cell count and larger cell size with age. Larger and variable cell size with variation in morphology is seen in the endothelium of a patient with Fuchs' endothelial dystrophy (bottom).



NORMAL CORNEAL TOPOGRAPHY

The central 3mm of the corneal surface is spherical with progressive flattening towards the periphery. Keratometry (see Chapter 1) measures the average curvature of the central 3mm. along the two main meridia.

Fig. 6.8 In keratoscopy a series of concentric rings is projected onto the corneal surface. Their disposition indicates corneal curvature from the visual axis to the periphery. In its simplest form this is done with a Placido's disc but these images can now be analyzed by computer systems which display the contours of the corneal surface as dioptric powers and cover virtually all of the corneal area. The results are usually presented as a colour-coded topographical map in which colours towards the red end of the spectrum represent increasingly steep dioptric powers. A small range of dioptric powers can be seen on this normal cornea which therefore has few colours.

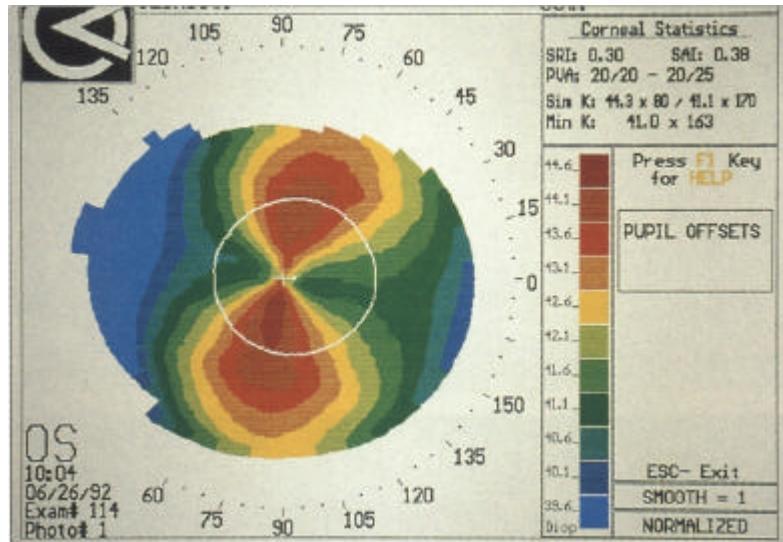
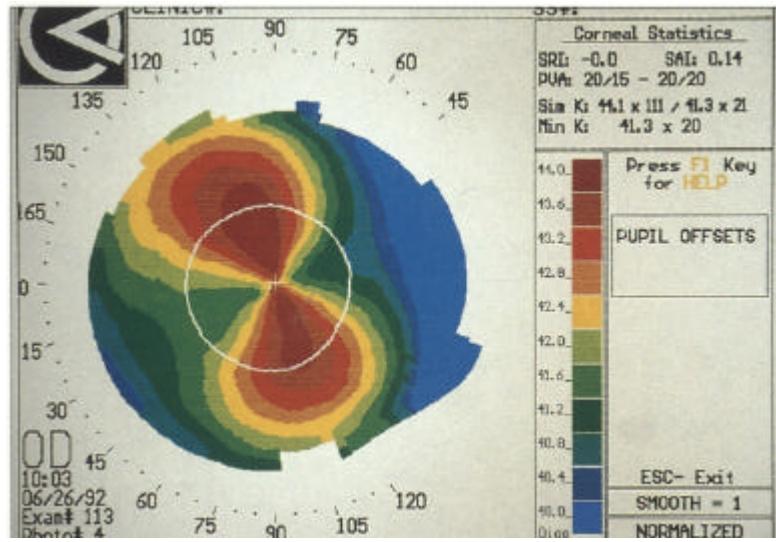
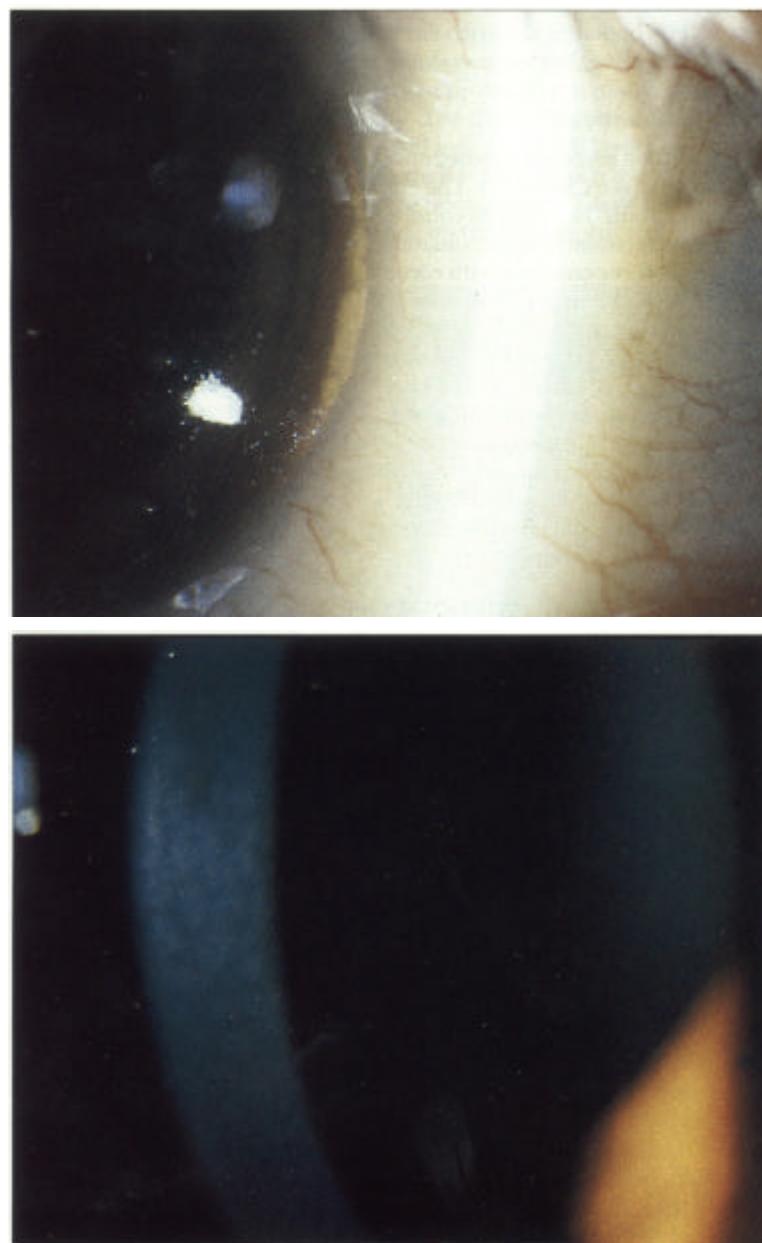


Fig. 6.9 Astigmatism is seen on keratoscopy as a distortion of the circular projections into concentric oval reflections. Colour-coded topographic representation of regular astigmatism appears as a image symmetry between the two eyes.



NORMAL CORNEAL VARIANTS

Variations in the normal corneal architecture or changes associated with age must be distinguished from, and may influence, the signs of superimposed pathology.

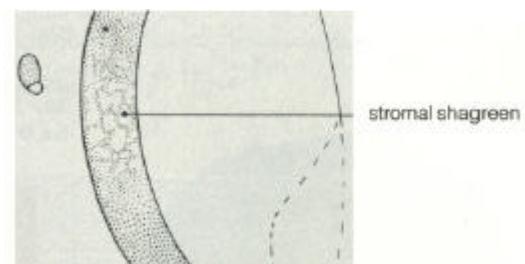
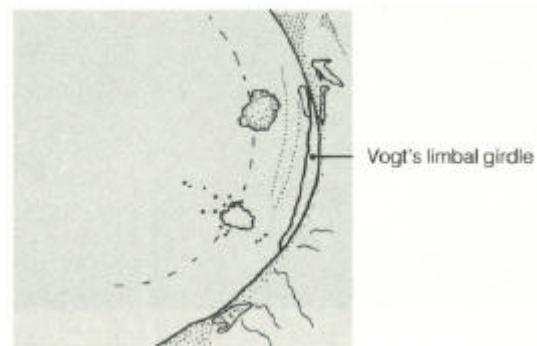


Fig. 6.10 Vogt's limbal girdle (top) is a common ageing change of the interpalpebral limbus which appears as a semilunar opacity without a clear separation from the limbus, best seen by sclerotic scatter, as in this example, and must be distinguished from calcium deposition with band keratopathy. The nasal cornea is affected nearly twice as often as the temporal side. Histology shows subepithelial hyaline degeneration.

'Crocodile' shagreen may be seen in the superficial or deep corneal stroma and is best seen by wide-slit oblique illumination. The superficial type is usually seen as an ageing change, but either type may be familial and neither produce visual symptoms (bottom).

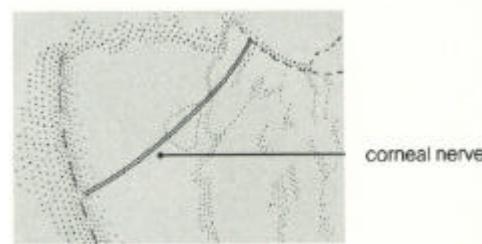


Fig. 6.11 Corneal nerves are not usually visible but maybe incidentally noted in the peripheral or central cornea and single nerves may be prominent for some distance as seen here. The axon terminals lie in the corneal epithelium. In certain disorders such as keratoconus the nerves are more easily seen and some infections (e.g. leprosy and acanthamoeba keratitis) may also make the nerves more visible.

CONGENITAL CORNEAL ANOMALIES

Anterior segment dysgenesis produces a wide clinical spectrum of anomalies. The affected structures are derived from neural crest rather than mesoderm as previously thought. The spectrum includes Axenfeld's, Reiger's, and Peter's anomalies,

posterior keratoconus and posterior embryotoxon. This group of ocular abnormalities can be associated with systemic defects such as dental and cranial anomalies and malformations of the upper limbs and spine.

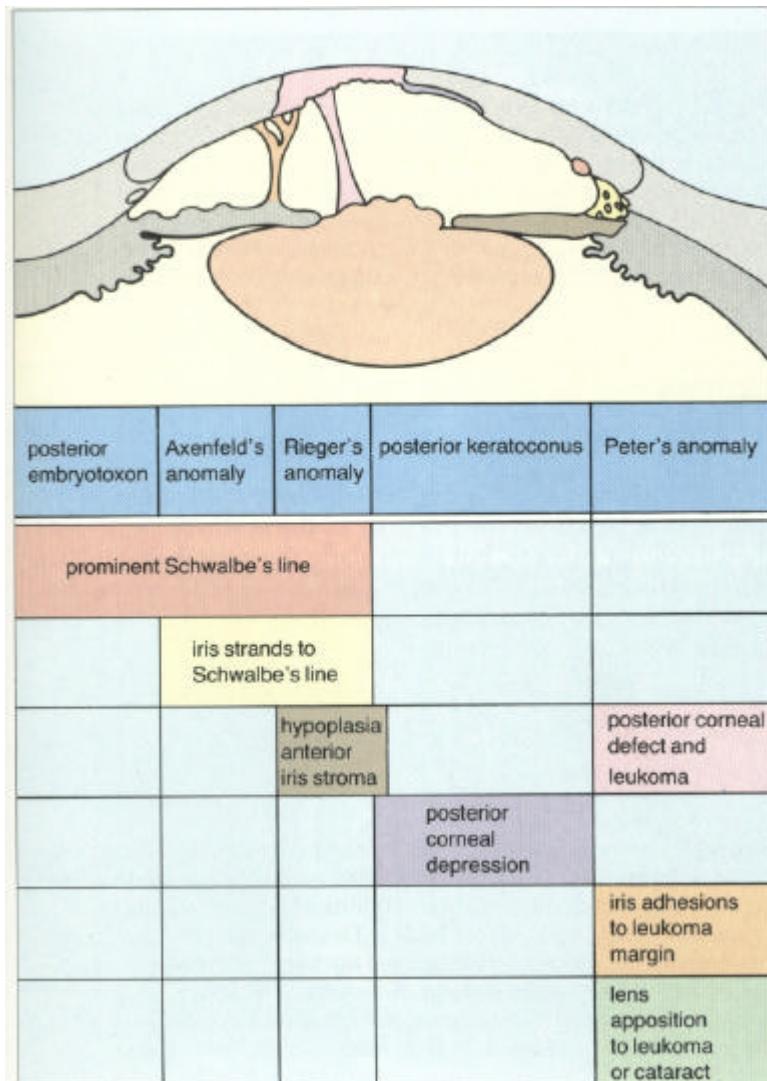


Fig. 6.12 The spectrum of anterior segment dysgenesis is illustrated by this diagram. Adapted from Survey of *Ophthalmology* (1987) Volume 31(4), 262-6.

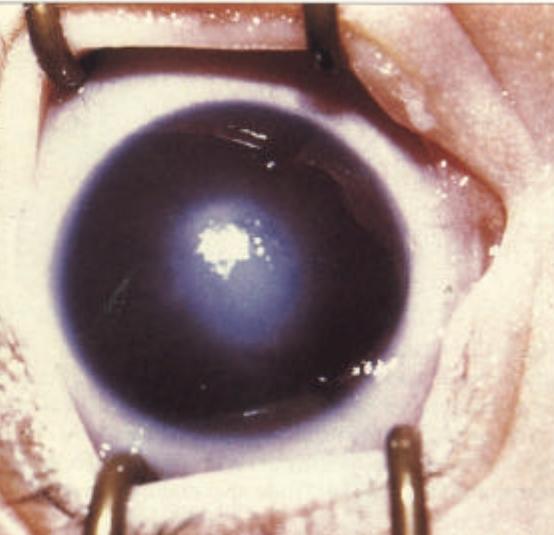
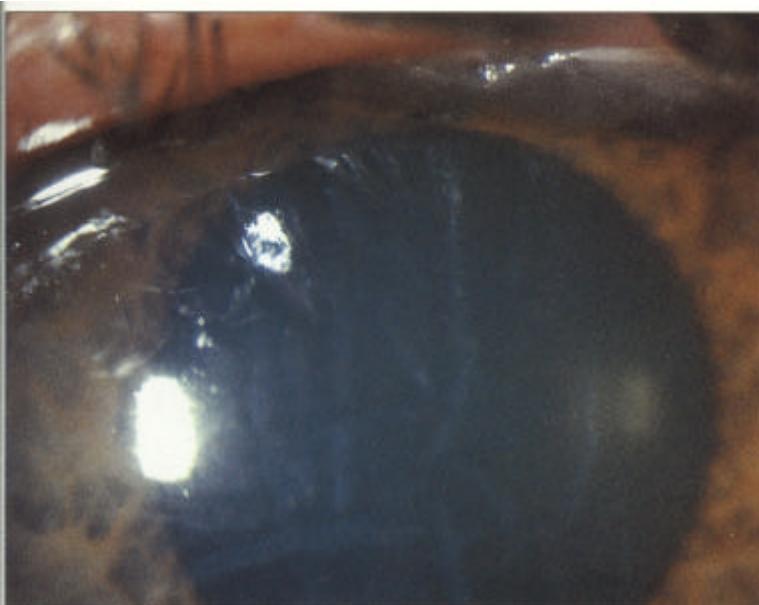


Fig. 6.13 Peter's anomaly is characterized by a central corneal white scar (leukoma) with posterior stromal, Descemet's and endothelial defects with adhesions to the iris collarette. Associated ocular features commonly include glaucoma and lens opacity, but skeletal abnormalities (including craniofacial dysplasia) and cardiac defects may also occur. The condition is usually bilateral with a sporadic incidence although inherited cases occur. By courtesy of Mr P Khaw.



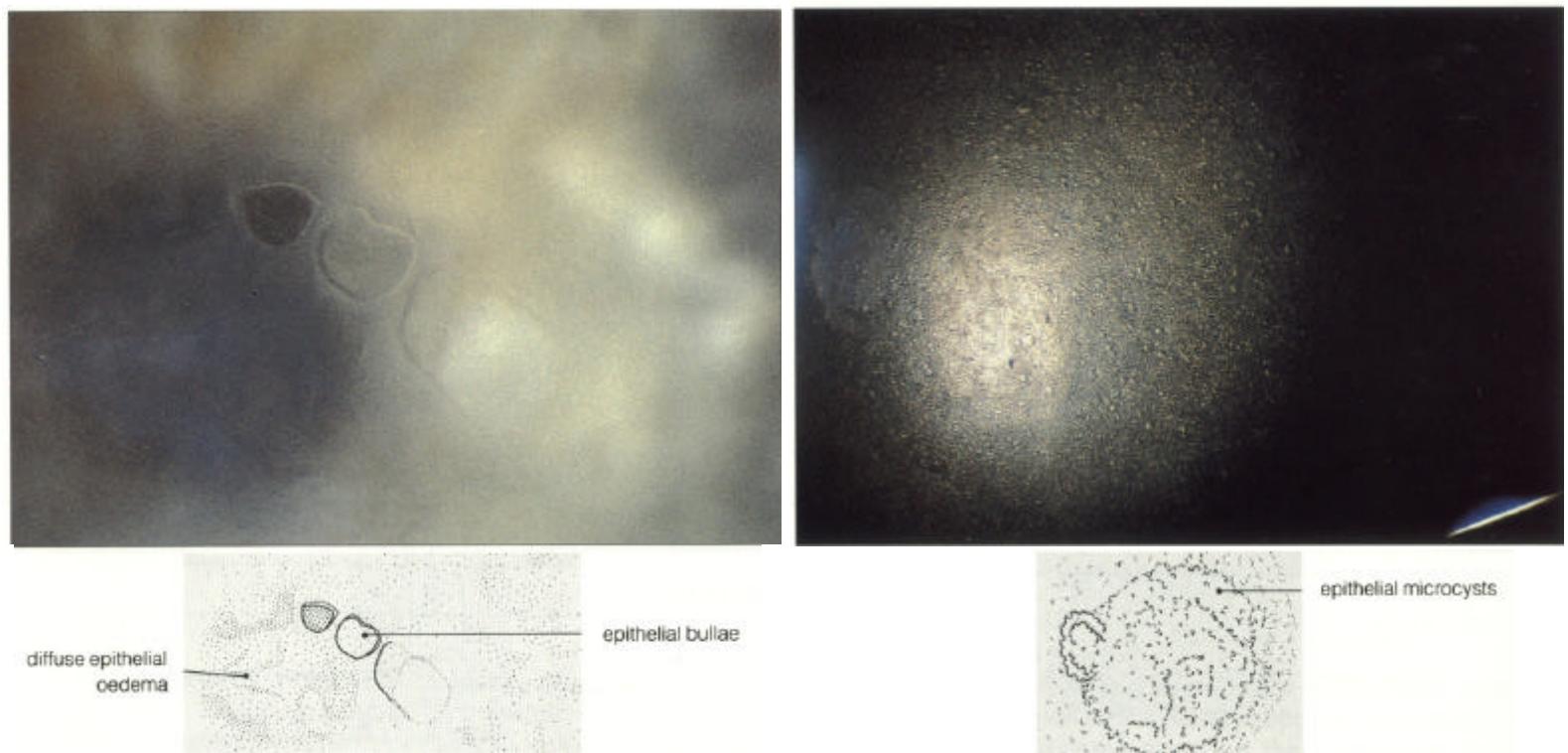
Fig. 6.14 Sclerocornea is a diffuse or predominantly peripheral corneal opacity due to disorganization of the stromal collagen fibrils similar to those of normal sclera. There is also a much reduced corneal curvature, suggesting a failure of limbal development. The condition is bilateral with equal sex incidence and is usually sporadic, although dominantly inherited forms have been described. Abnormalities of the angle with secondary glaucoma are common.

CORNEAL OEDEMA



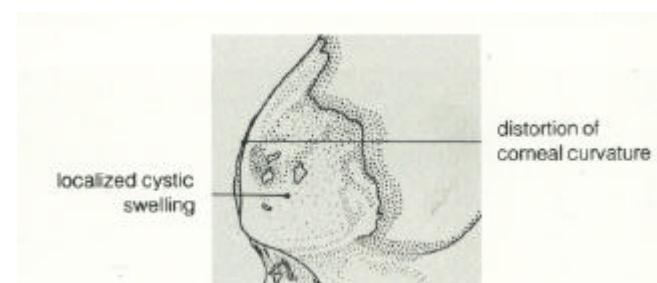
The normal cornea is 78 per cent hydrated. Maintenance at this level depends on the integrity of the epithelial and endothelial cellular barriers, but particularly the endothelial cellular pump which constantly works against the stromal swelling pressure and the intraocular pressure to transfer fluid from cornea to the anterior chamber.

Fig. 6.15 Accumulation of stromal interfibrillar fluid increases corneal thickness without a change in the anterior corneal curvature. It is accommodated posteriorly and inferred by the wrinkling of Descemet's membrane. These folds in Descemet's membrane ('striate keratopathy') indicate corneal stromal thickening. Note the normal transparency despite the oedema. Severe stromal oedema is usually associated with epithelial oedema, but intercellular epithelial oedema may occur in isolation (e.g. from contact lens induced hypoxia).



*Fig. 6.16*An accumulation of intercellular fluid beneath an intact anterior epithelial barrier is seen as bullae (left) and microcysts (right) in the epithelium, seen in the specular reflection here. The

brilliant air-tear interface becomes disrupted and vision deteriorates. Rupture of bullae can be extremely painful. Subepithelial scarring is often present in longstanding cases.



*Fig. 6.17*An acute tear in Descemet's membrane results in a rapid influx of aqueous into the stroma (hydrops) and is most commonly seen in keratoconus. The condition is painful but resolves without specific treatment as endothelial cell migration and elaboration of new Descemet's membrane occurs over a period of months, although visual improvement is often limited by subsequent scarring.

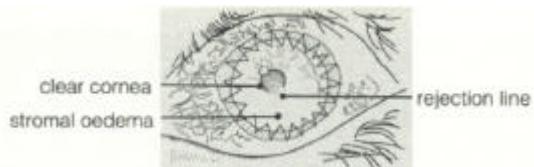
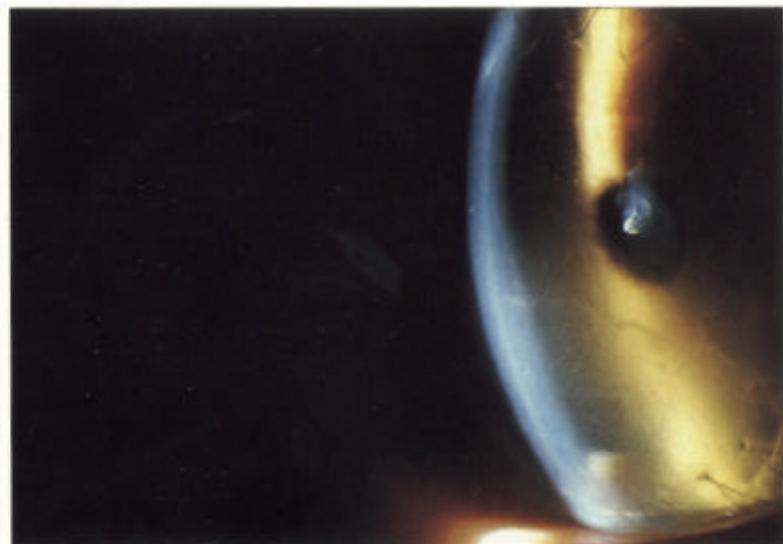
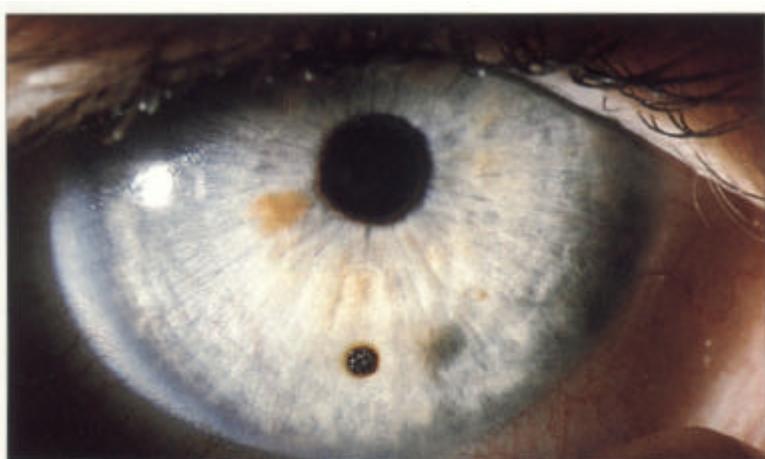


Fig. 6.18 Discrete damage to the corneal endothelium interferes with both its barrier and cellular pump functions resulting in focal oedema. This is a feature of herpes simplex or zoster disciform



keratitis, and is also seen in this example of corneal allograft rejection. Note the aggregations of lymphocytic keratic precipitates on the endothelium along the rejection (Khodadoust) line.

CORNEAL TRAUMA



The inherent strength of the corneal stroma is demonstrated by its resistance to physical penetration.



Fig. 6.19 Impaction of a ferrous foreign body on the cornea is a very common injury, frequently associated with drilling or grinding steel without protective goggles. These particles normally have insufficient penetrating power to pass through the entire cornea and frequently lodge superficially. Within a few days they become surrounded by a ring of rust which can be lifted off the cornea with a sharp needle under topical anaesthesia. If confined to the epithelium, distortion or scarring will not occur, but involvement of Bowman's membrane and the stroma leads to localized opacity.

Fig. 6.20 Corneal blood staining is associated with large hyphaemas (blood filling more than half of the anterior chamber), a high intraocular pressure and corneal oedema. The earliest changes are in the deep stroma with a dark brown discolouration from haemoglobin and haemosiderin which progresses to involve the full stromal thickness, but leaves the peripheral cornea clear. Blood staining will clear but may take years to resolve completely. It can also occur in a vascularized cornea from intrastromal bleeding, as in this example in which the overlying central stroma has also become necrotic. By courtesy of Mr MG Falcon.

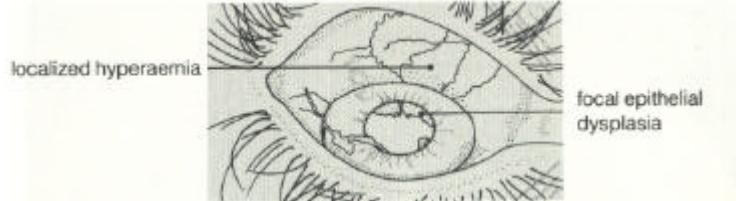
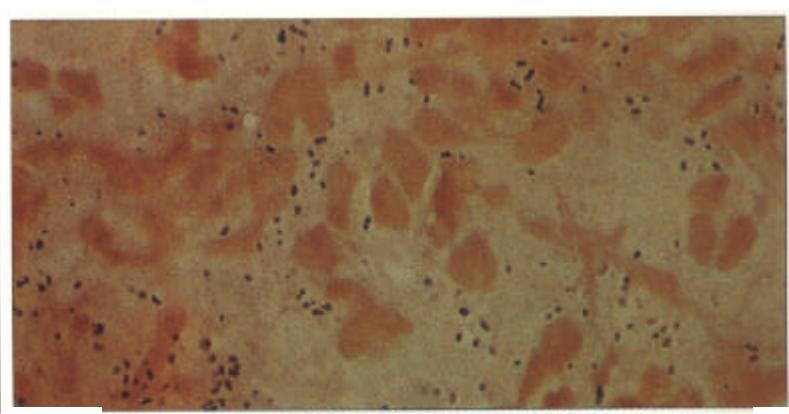
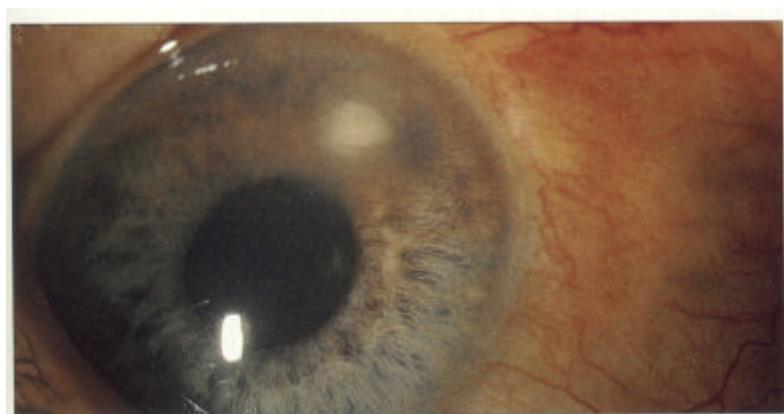


Fig. 6.21 Epithelial chemical injury may occur from long-term instillation of topical medications or their preservatives and is particularly important in patients with tear deficiency or compromised corneas where it results in a diffuse epithelial keratopathy. Thiomersal is commonly used as a preservative in many soft contact lens solutions and toxicity can develop after many years of uneventful treatment. It is seen here as dysplasia of the surface epithelium manifested as a non-wetting area of the superior cornea. By courtesy of Mr I Mackie.

INFECTIVE KERATITIS

Bacterial infections present with pain, photophobia and blurred vision and represent an ophthalmic emergency, as delay in appropriate treatment can lead to loss of the eye from corneal perforation or endophthalmitis. Clinical assessment is directed towards factors in the history and the physical signs which may indicate a predisposing cause, and identification of the causative organism. A hypopyon confirms the serious nature of an infection, but any anterior chamber activity is significant. Immediate management involves scraping the cornea (particularly the edge of the affected area) with a scalpel blade or disposable needle to obtain exudate and tissue to place on a dry, clean microscope slide for Gram staining and also on blood and chocolate agar for bacterial culture, and Sabaroud's medium for fungal culture. The first sample from an infected cornea is the one most likely to produce the causative organism and must therefore be obtained before topical antibiotics have been started using topical unpreserved anaesthetic. There is no benefit in tapping the anterior chamber or hypopyon as this reflects the effect of chemoattractant factors

recruiting polymorphs and is invariably sterile. After adequate specimens have been obtained, appropriate antibiotic therapy is immediately instigated based on the Gram stain findings, the clinical history and signs and is later modified when bacterial cultures and antibiotic sensitivities become available. Intensive topical treatment is the most effective route for corneal infections. Cultures of contact lens solutions, their containers or bottles of eye drops are frequently also helpful in identifying the causative bacteria. In the absence of bacteria being identified on the Gram stain, a broad spectrum treatment with an aminoglycoside and a cephalosporin half-hourly day and night is commenced until cultures and sensitivities become available. Topical atropine helps to reduce painful miosis. Topical steroids may be required to suppress inflammation but must be used with caution as they can potentiate uncontrolled infection or induce corneal thinning. Corneal biopsy for histology and culture is sometimes helpful in those patients with negative cultures who fail to respond to treatment.



hyperaemia

stromal infiltrate



Gram-positive cocci

polymorphs

Fig. 6.22 In the early stages corneal infiltrates may appear trivial, but must be managed as potentially serious ocular infections. Commensal organisms from the lids and conjunctiva may become pathogens if the corneal epithelium is breached, or there is compromise of the ocular surface defenses and gram positive cocci are therefore common causes of microbial keratitis, seen in Gram stain here. By courtesy of Dr S Eykyn.

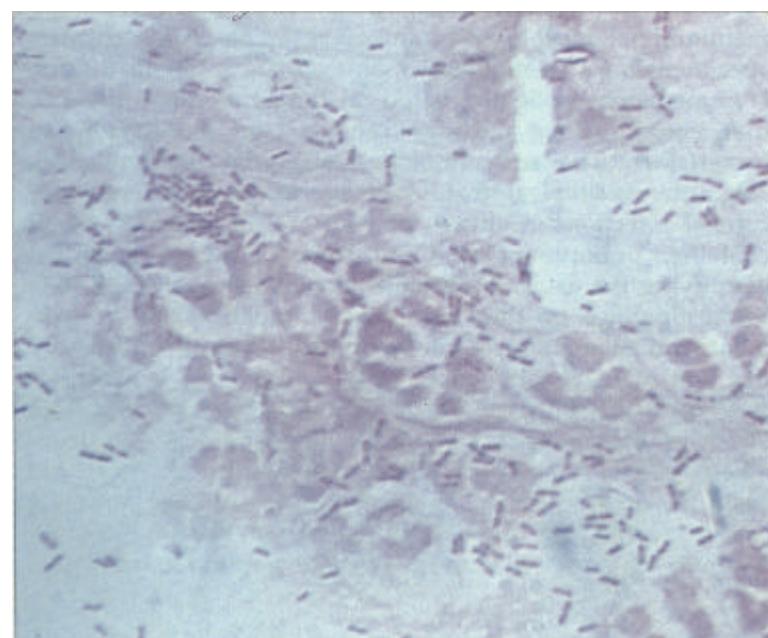
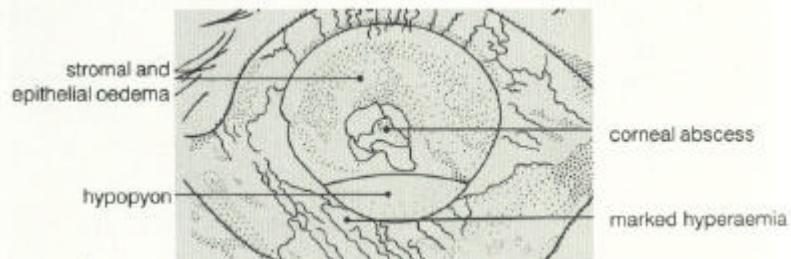
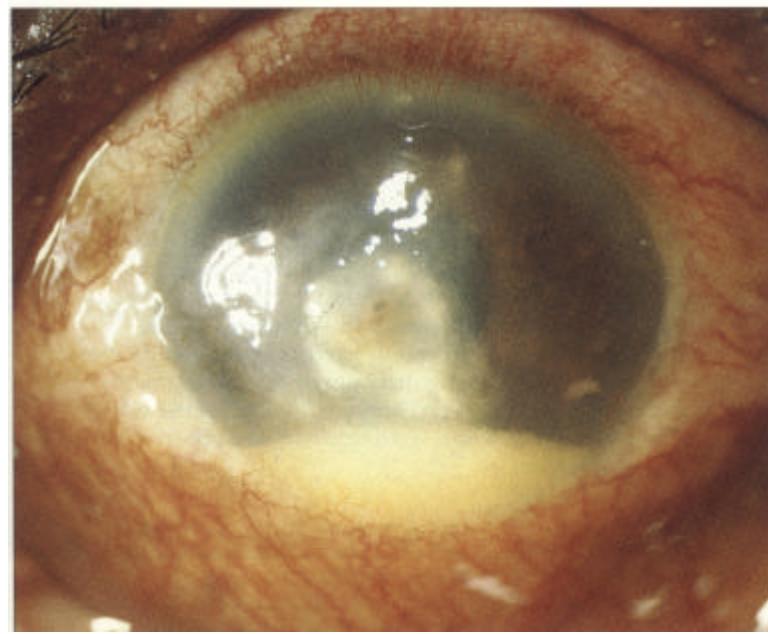


Fig. 6.23 Soft contact lens wear (especially any type of extended wear lens) predisposes to microbial keratitis despite the large numbers of wearers who never suffer any problem. *Pseudomonas* species are able to penetrate intact corneal epithelium and produce rapid and extensive local destruction of the corneal stroma which may lead to perforation. Since this organism is more common in soft contact lens wearers and the effects of infection are so devastating it is sensible to start intensive treatment with gentamicin or another aminoglycoside in suspected cases in this group of patients as soon as appropriate bacteriological specimens have been obtained. Gram negative rods are seen in this Gram-stained specimen of a corneal scrape. By courtesy of Dr S Eykyn.

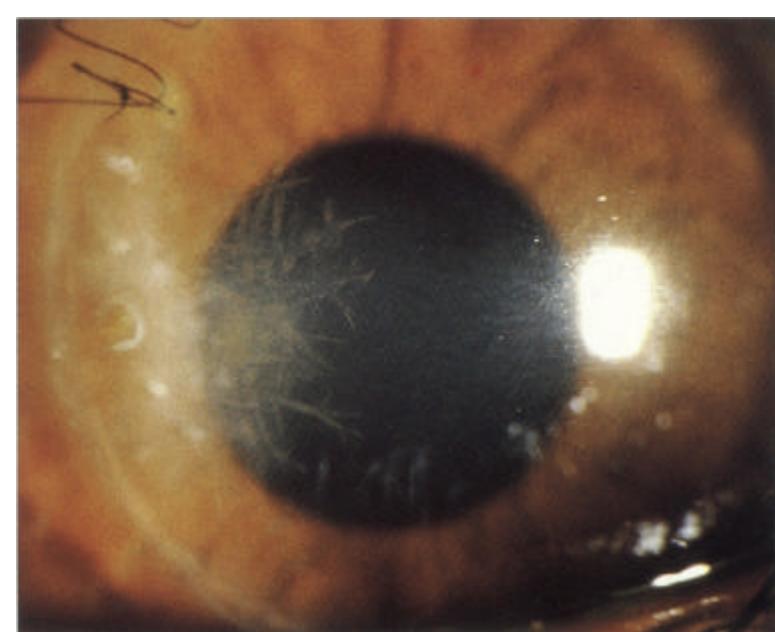


Fig. 6.24 This extraordinary appearance of crystalline keratopathy is characteristic of streptococcal bacterial infection, in this case occurring at the margin of a corneal graft. Despite the stellate edge it is important not to confuse this with fungal keratitis (the filaments are much too large to be fungal hyphae). By courtesy of Mr MG Falcon.

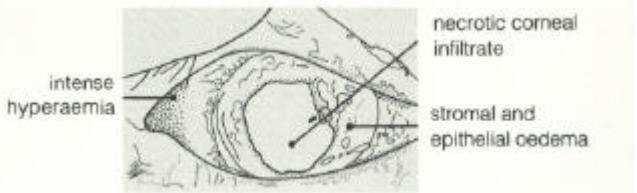


Fig. 6.25 Keratomycosis is more common in countries with a warm humid climate where it is often the result of agricultural ocular injury, being particularly common in paddy field workers who have a high risk of getting a corneal abrasion from the ends of rice stalks. Fungal infections may also occur as a secondary infection in a compromised cornea. A wide range of fungi have been reported to cause ocular infection; the most common are filamentous moulds such as *Aspergillus* and *Fusarium* or yeasts such as *Candida*. Treatment is with topical antifungal agents such as the imidazoles (e.g. econazole) or the polyenes (e.g. natamycin). This example shows a *Fusarium* infection which required an emergency corneal graft following perforation.

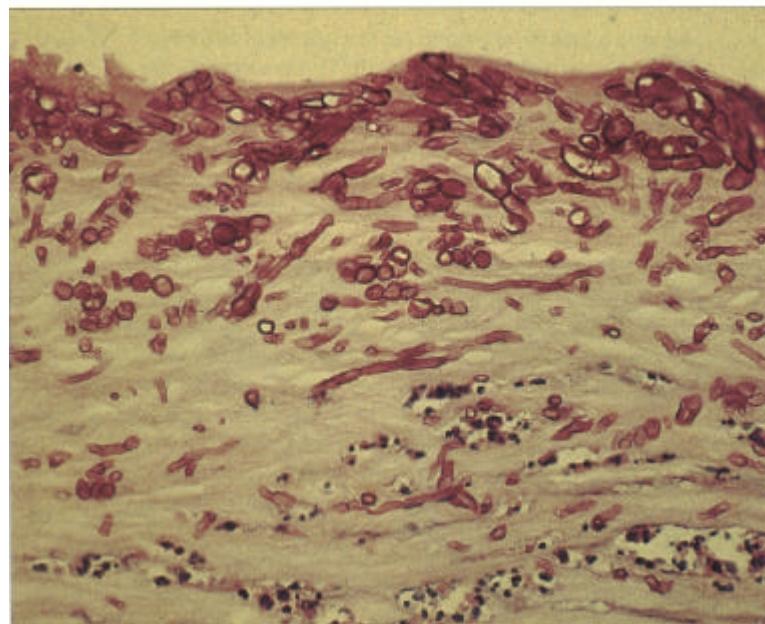


Fig. 6.26 Histology of the removed corneal button shows hyphae through all levels of the cornea with destruction of the stromal lamellae and ulceration of the epithelium. By courtesy of Dr ACE McCartney (PAS stain).

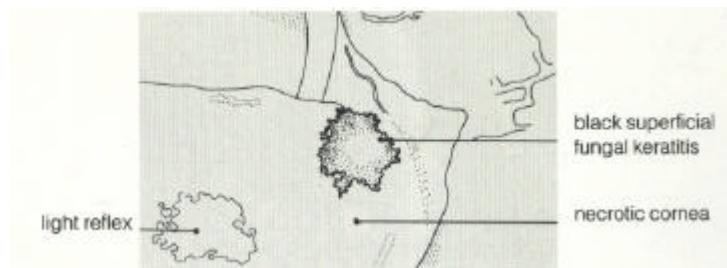
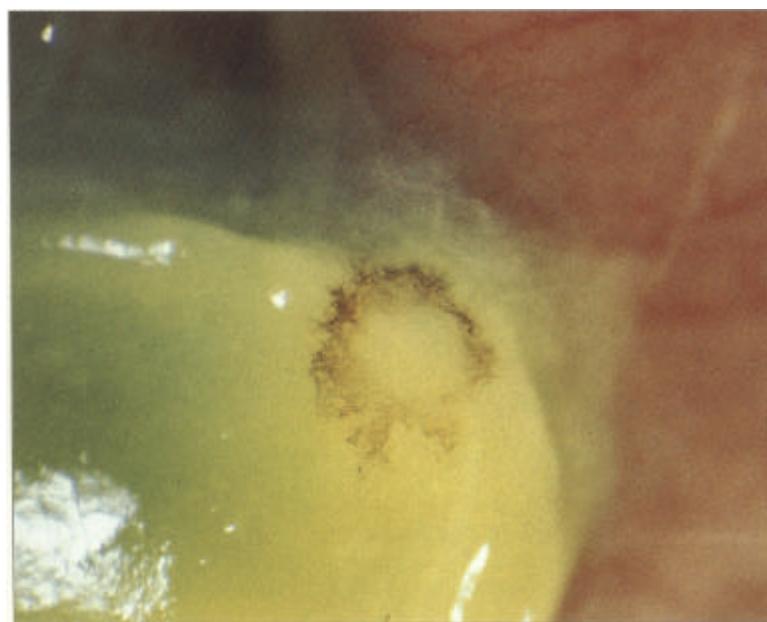


Fig. 6.27 This example of keratomycosis shows a pigmented stellate superficial fungal infection (*Curvularia* species) occurring on a cornea grossly compromised by exposure from proptosis secondary to an orbital tumour.

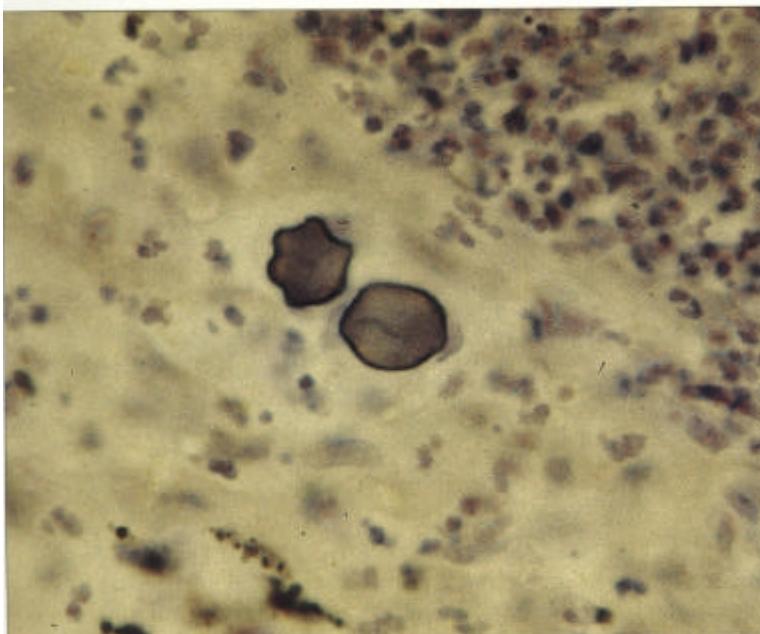
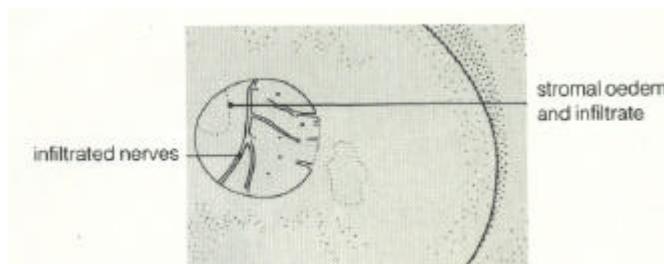
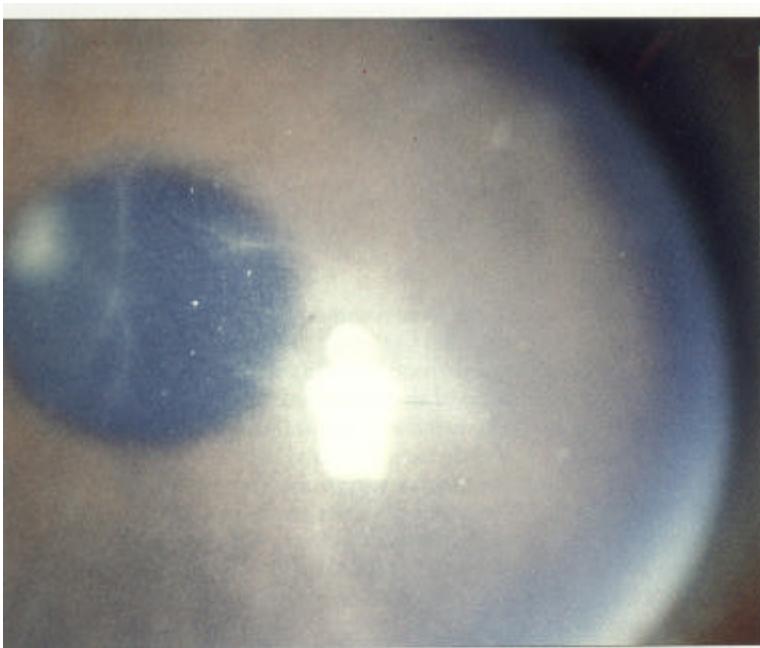


Fig. 6.28 Acanthamoebae are free-living organisms which have only recently been implicated as a rare cause of infective keratitis, particularly in disposable soft contact lens wearers with inadequate lens cleaning regimes. Pain is often a feature. The corneal nerves may be seen to be infiltrated by the neurotrophic amoebae, as in this example. Diagnosis is made by appropriate cultures on E. coli-seeded blood agar medium or by finding the organism in a corneal biopsy specimen. Treatment is limited to amoebicidal agents (e.g. brolene, neomycin, polyhexamethylbiguanide [PHMB]). By courtesy of Dr ACE McCartney.

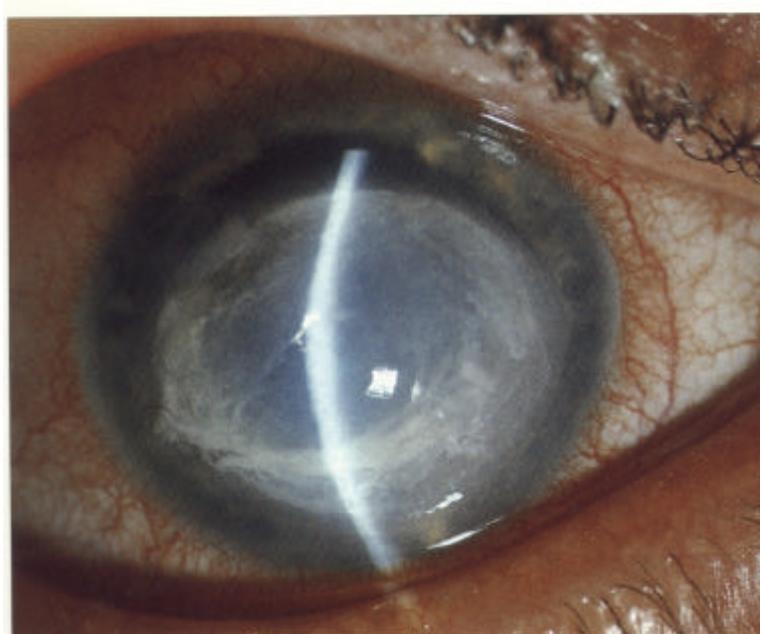


Fig. 6.29 An example of the destructive nature of this infection is seen in this case with an expanded necrotic central corneal stroma. Amoebae readily encyst and can be seen histologically at all levels within the stroma in severe cases but may be confined to the epithelium in early infections.

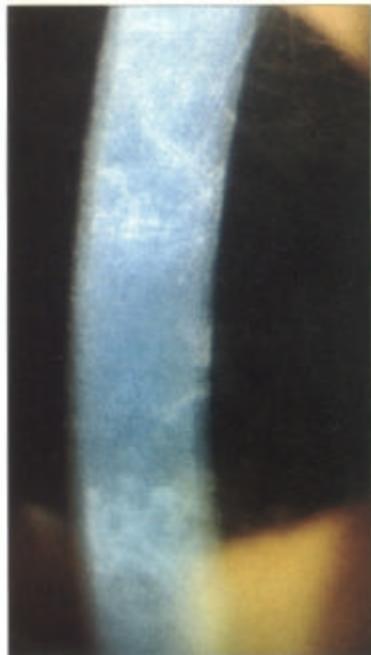


Fig. 6.30 Interstitial keratitis due to congenital syphilis may be associated with the systemic features of neural deafness, Hutchinson's teeth and a collapsed nasal bridge. The active phase of corneal inflammation occurs during the first two decades of life with an intense corneal stromal vascularization and photophobia which is now rarely seen and which resolves over months if untreated to leave faint stromal scarring and empty stromal 'ghost' vessels which

characteristically lie deeply in the stroma just above Descemet's membrane. Patients may also have signs of a retinopathy (see Chapter 10) and frequently develop cataracts in later life. Interstitial keratitis is also a feature of Cogan's syndrome (interstitial keratitis with severe neural deafness in young adults in the absence of syphilis), although most cases now seen are idiopathic.

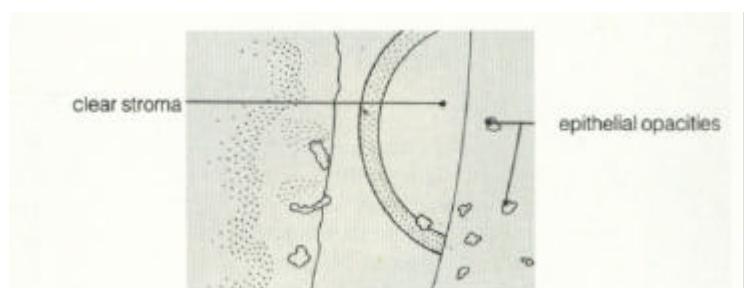
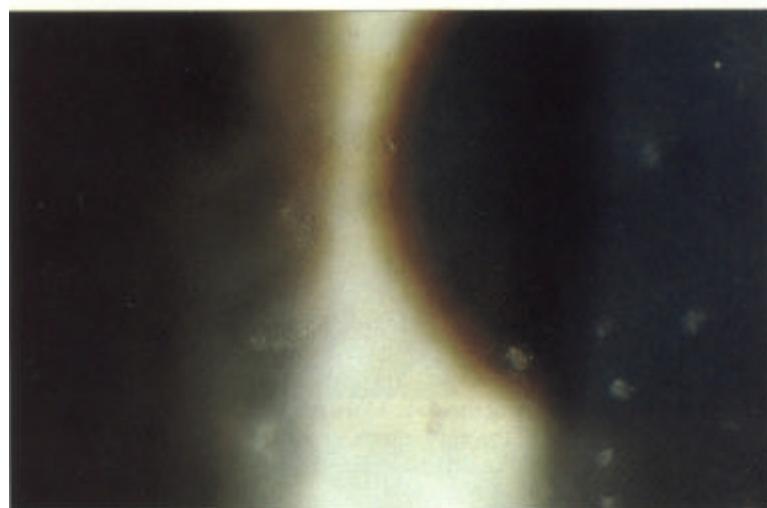


Fig. 6.31 The cause of Thygeson's superficial punctate keratitis is unknown. It is an uncommon, noncontagious and usually bilateral keratitis with episodes of recurrent discomfort occurring over several years. Discrete chalk-dust opacities occur in the epithelium without stromal involvement and protrude into the tear film. New and resolving deposits occur simultaneously. There is no conjunctival hyperaemia, follicular response or lymphadenopathy. Discomfort is usually rapidly reduced with a very short course of topical corticosteroids, but occasionally bandage contact lenses are required.

CORNEAL DYSTROPHIES

Corneal dystrophies can be classified both by their mode of inheritance and their anatomical site within the cornea. Many are extremely rare and only the more common types are illustrated here. Dystrophies which predominantly involve the epithelium and anterior stroma tend to present with recurrent

epithelial erosions and worsening vision from subsequent scarring; those involving the deeper cornea present with loss of acuity. Early or subclinical cases may be found on routine examination or by examination of other family members.

EPITHELIAL DYSTROPHIES

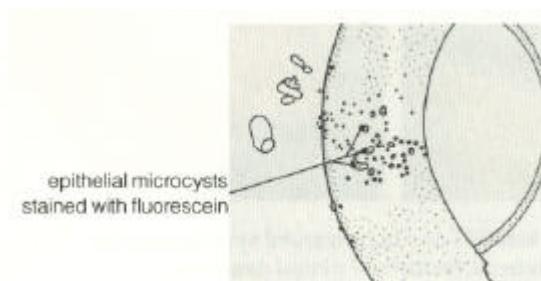
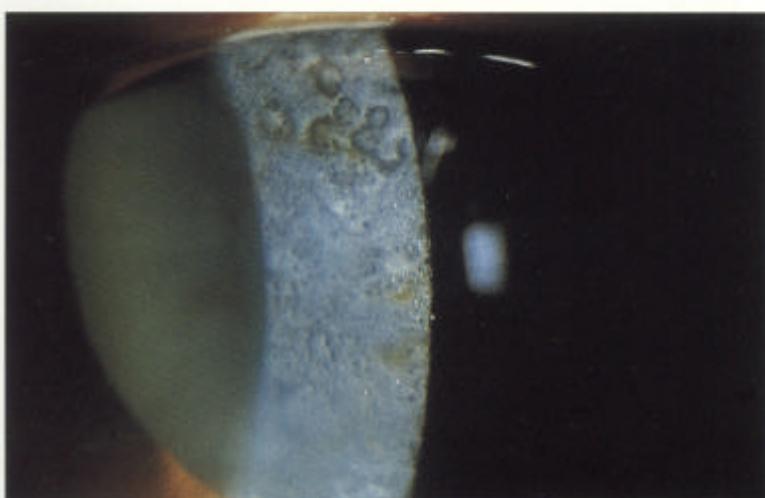
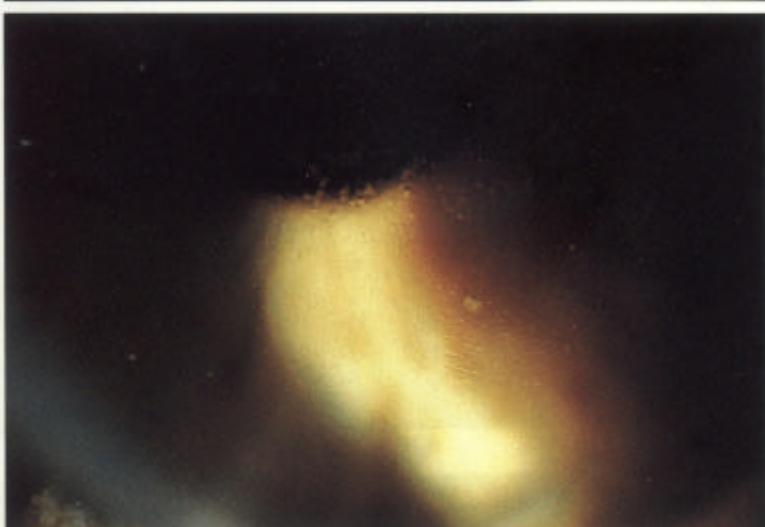
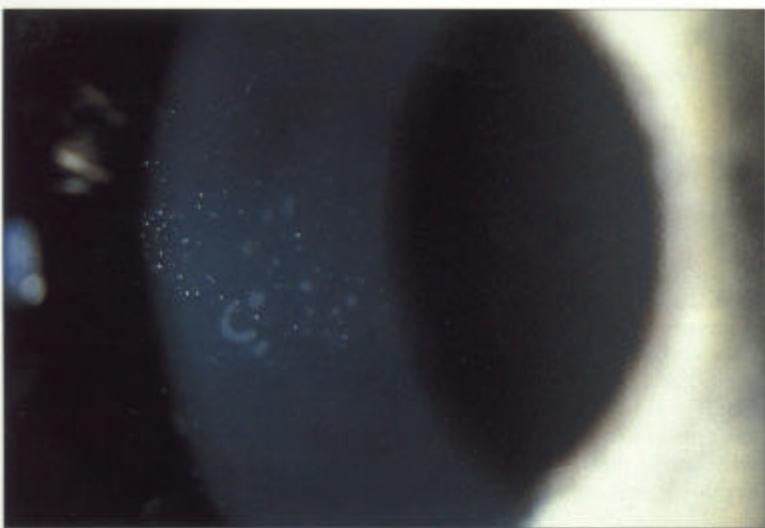


Fig. 6.32 Nontraumatic recurrent epithelial erosions are common and known as Cogan's epithelial dystrophy. This usually presents in young adults and is characterized by lines and dots in the corneal epithelium (hence it is also known as 'map, dot and fingerprint' dystrophy). Most patients remain asymptomatic, but recurrent erosions may occur, causing intense pain. A common trigger in susceptible patients is minor trauma. Symptoms are especially common on waking in the morning, improving over the next few hours. Many patients can obtain prophylactic relief by using a lubricating ointment on going to bed with additional lubrication with artificial tears during the day. More frequent and severe cases require debridement of the epithelium, sometimes with puncture of Bowman's membrane. Superficial keratectomy with the excimer laser has recently been used with success.

Fig. 6.33 Reis-Bucklers' dystrophy involves the epithelium, Bowman's layer and the superficial stroma in a bilateral and symmetrical pattern with the central cornea being mainly affected. Patients usually present during the first or second decade of life with recurrent erosions and are found to have a honeycomb appearance of the central corneal epithelium and anterior stroma. Lamellar or penetrating keratoplasty (and more recently excimer laser keratectomy) is sometimes required for visual improvement if scarring is sufficiently severe or the recurrent erosions incapacitating. The condition is dominantly inherited.

STROMAL DYSTROPHIES

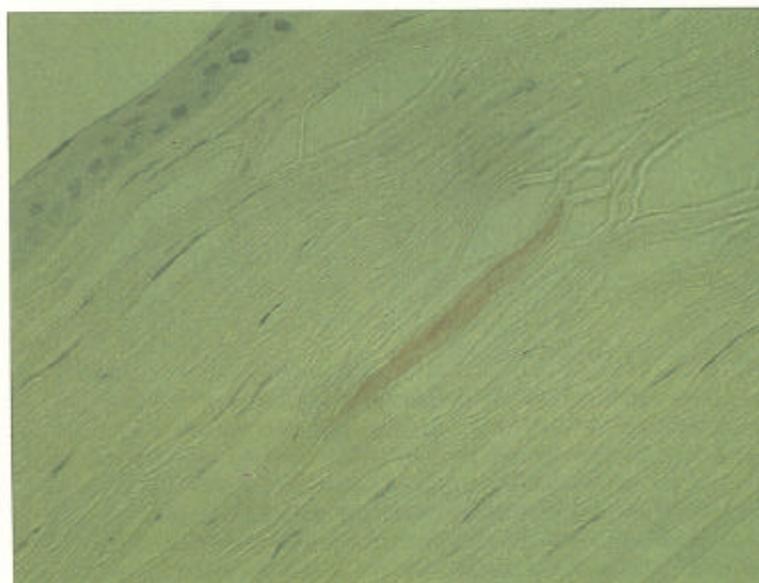
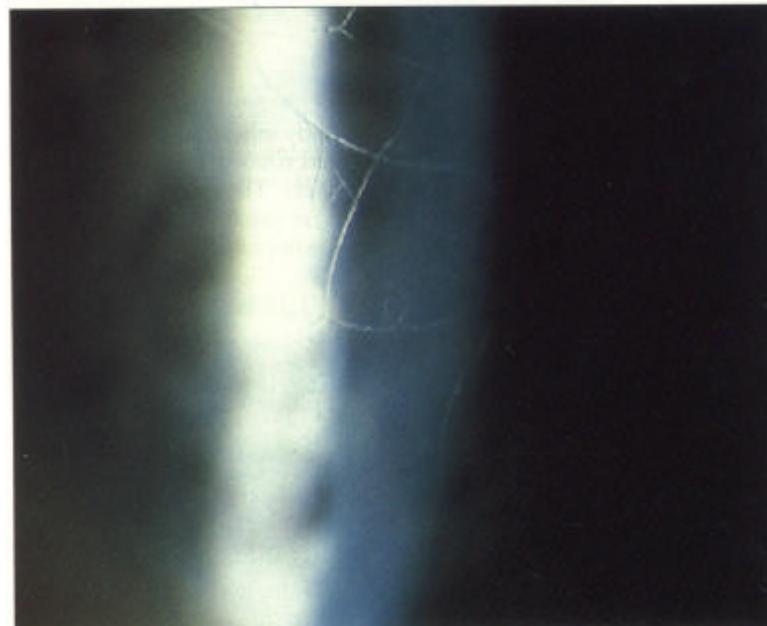


Fig. 6.34 Lattice dystrophy is dominantly inherited. Presentation is usually in the first decade of life with recurrent erosions. Vision deteriorates slowly and corneal grafting is often necessary in the third or fourth decade. The central cornea is predominantly affected with interlacing filaments which are present through all levels of the stroma (but absent from the periphery).

Fig. 6.35 The lesions stain with congo red and have birefringence when viewed with crossed polarizing filters. The condition is considered to represent a form of localized amyloid deposition.

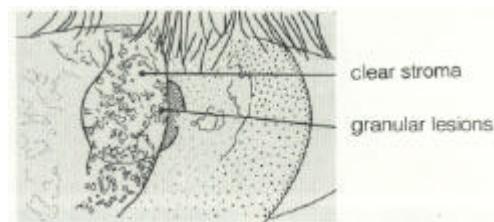
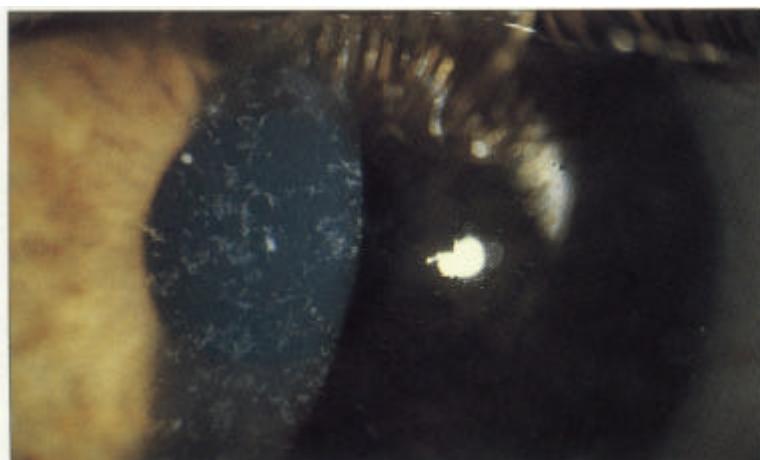
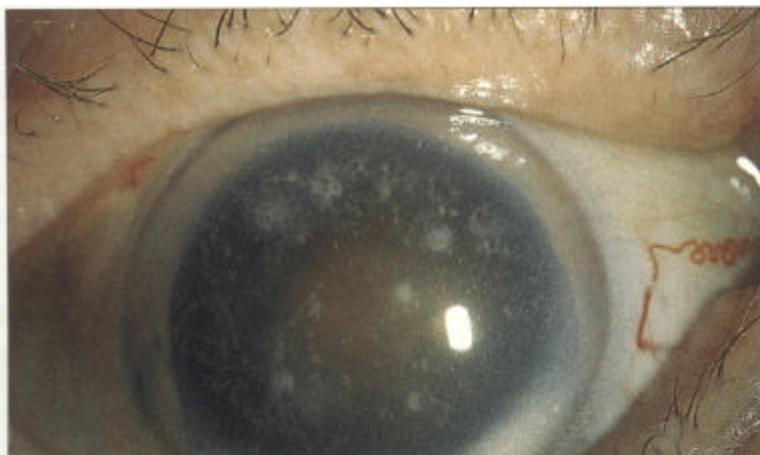


Fig. 6.36 Granular dystrophy is dominantly inherited. It presents in the first decade of life with well demarcated white-grey lesions at all levels of the stroma but sparing the periphery. The stroma adjacent to the lesions also remains clear. Symptoms are usually limited to glare from light scattering and corneal grafting is not usually required.

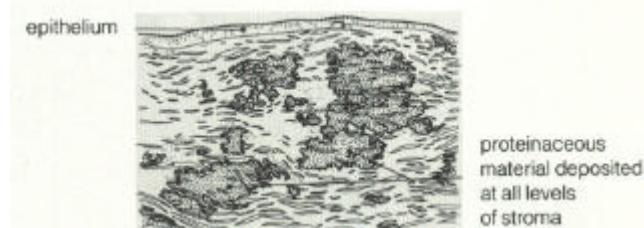
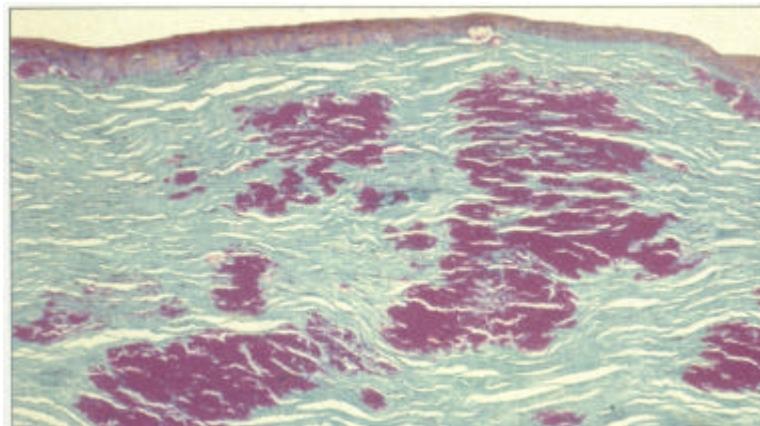


Fig. 6.37 Histologically these amorphous proteinaceous lesions stain red with Masson's trichrome stain.

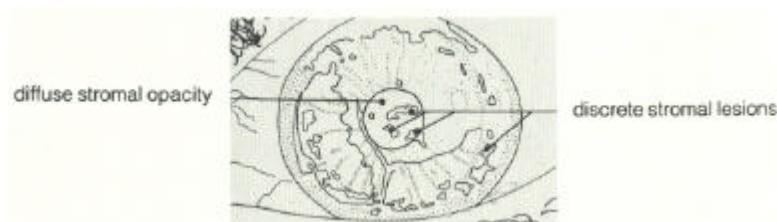


Fig. 6.38 Macular stromal dystrophy is inherited as an autosomal recessive condition. Poorly defined grey lesions appear in the superficial central corneal stroma during the first decade of life and gradually spread to the more peripheral and deeper stroma and up to the limbus. In contrast to granular dystrophy, there is diffuse stromal opacity between the lesions. In addition to impaired vision, recurrent corneal erosions may occur. Corneal grafting is often required, although the condition may recur in the graft. By courtesy of Mr MG Falcon.

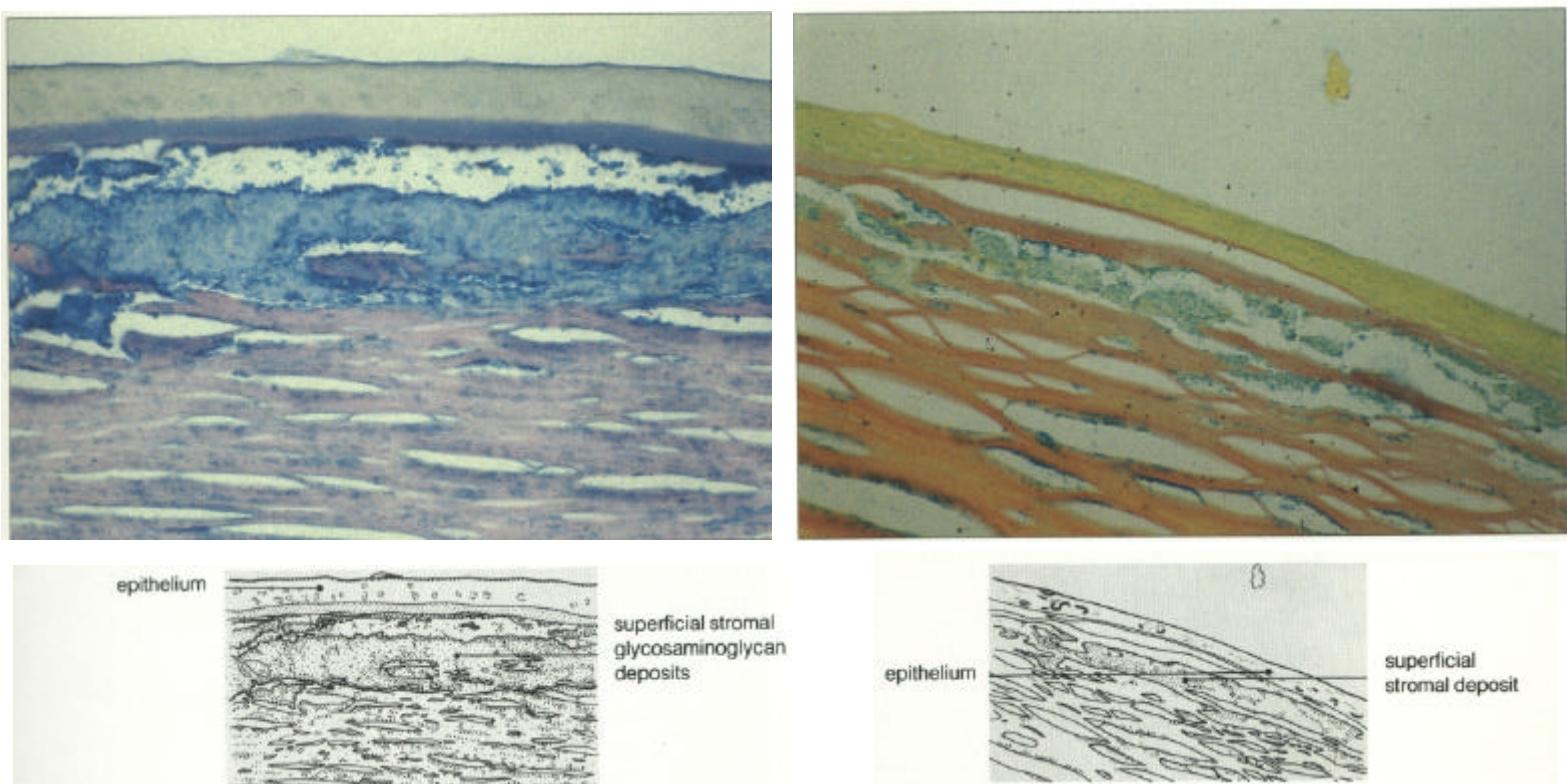


Fig. 6.39 Keratocytes accumulate an abnormal glycosaminoglycan beneath the epithelium and between the stromal lamellae which is evident on Alcian blue (left) and colloidal iron staining (right). By courtesy of Dr ACE McCartney.

POSTERIOR CORNEAL DYSTROPHIES

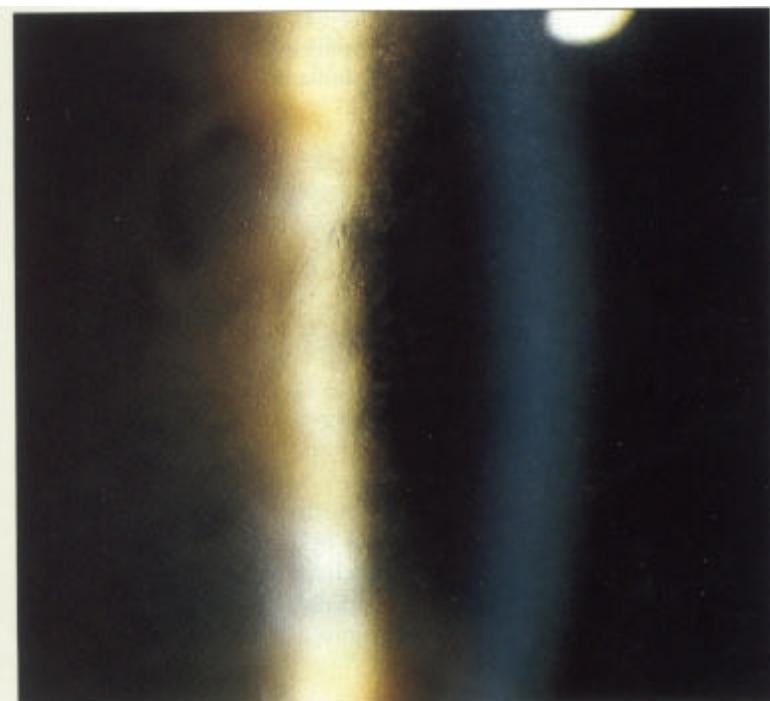


Fig. 6.40 Guttata are excrescences of Descemet's membrane due to deposition of excessive local collagen and become more common with age. This may represent one end of a clinical spectrum with Fuchs' dystrophy at the other in which large numbers of guttata occur centrally together with a decreased endothelial cell density. Endothelial decompensation leads to stromal hydration and later to epithelial oedema with microcysts and bullae (see Figs 6.15 and 6.16). Should these rupture, then pain, watering and photophobia ensue.

Visual acuity may fluctuate in the early stages from corneal oedema, often being worse in the morning, but chronic oedema with corneal stromal thickening eventually markedly impairs vision which may require penetrating keratoplasty. Visual loss is, however, often due to cataract in these elderly patients and surgery, when indicated, requires great care to minimize further endothelial cell loss and corneal decompensation. By courtesy of Mr S Hardman Lea.

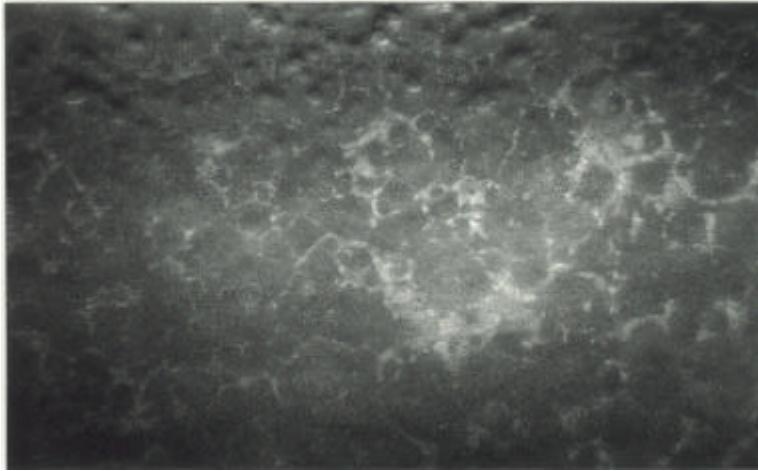


Fig. 6.41 Specular microscopy of the endothelium from a patient with moderately advanced disease shows numerous guttata which appear as dark areas due to interference with the specular reflection from the endothelial mosaic (see also Fig. 6.7).

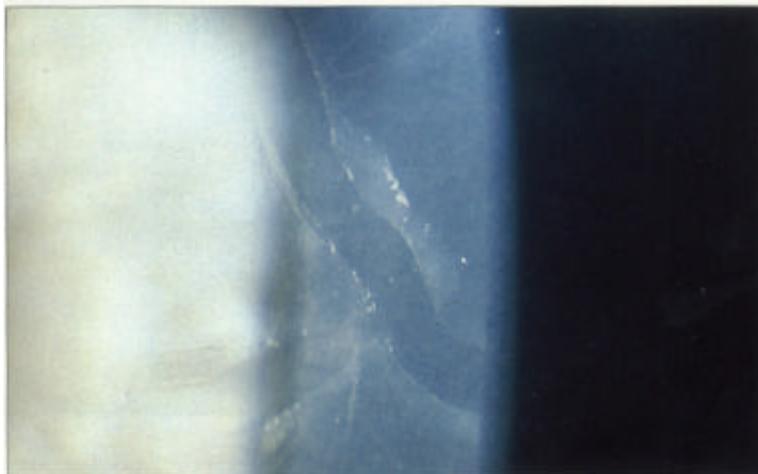


Fig. 6.42 Posterior polymorphous dystrophy may be noted coincidentally as geographic, 'vesicular' or linear areas of abnormality at the level of Descemet's membrane which are diagnostic. Geographic changes rarely cause visual loss, and the condition is nonprogressive.

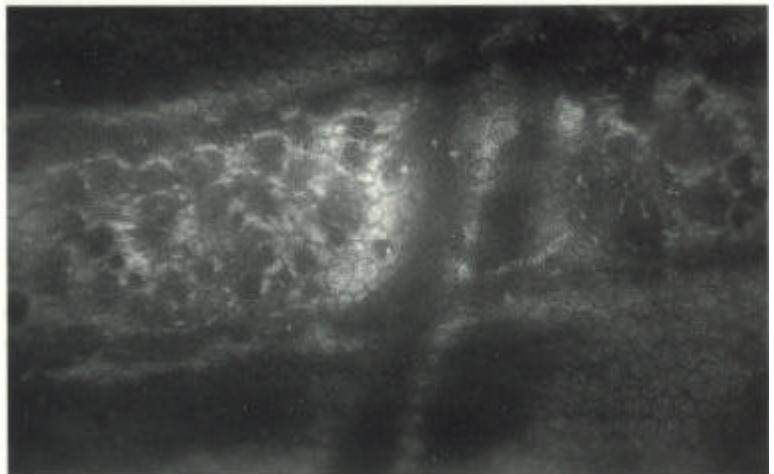
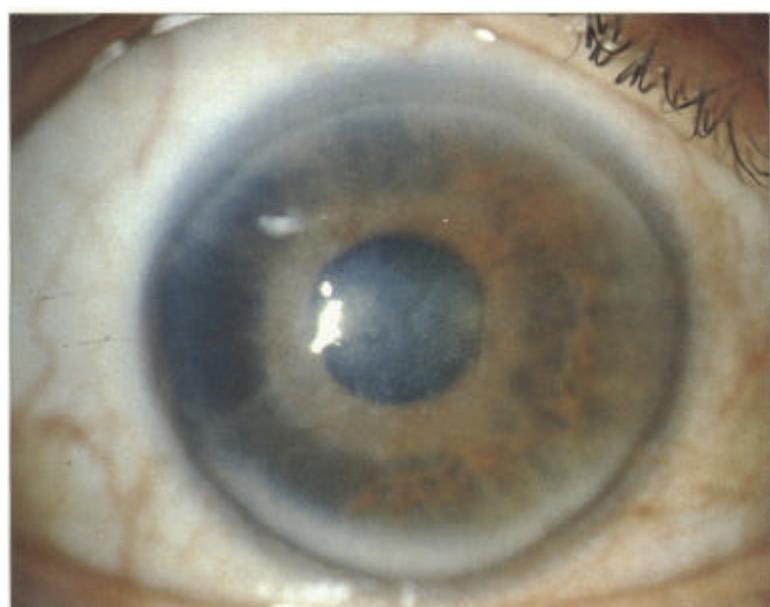


Fig. 6.43 Endothelial cell density is decreased as confirmed by endothelial specular microscopy. The splits in Descemet's membrane seen in buphthalmos can appear very similar to the linear form of this condition.

THE IRIDOCORNEAL ENDOTHELIAL SYNDROME



The iridocorneal endothelial (ICE) syndrome (previously known as essential iris atrophy, the Cogan-Reese syndrome or Chandler's syndrome; see Chapter 8) is characterized by an abnormal endothelium which may be accompanied by iris atrophy, ectropion uveae, pseudonodules on the iris and broad-based anterior peripheral synechiae. Visual loss is commonly due to glaucoma or corneal oedema. The aetiology is unknown and the condition is subdivided on the basis of the endothelial cell findings into disseminated, total, subtotal plus (with increased cell density), and subtotal minus (with fewer, larger cells) morphological forms.



Fig. 6.44 ICE syndrome with corneal oedema, iris atrophy and slightly displaced pupil.

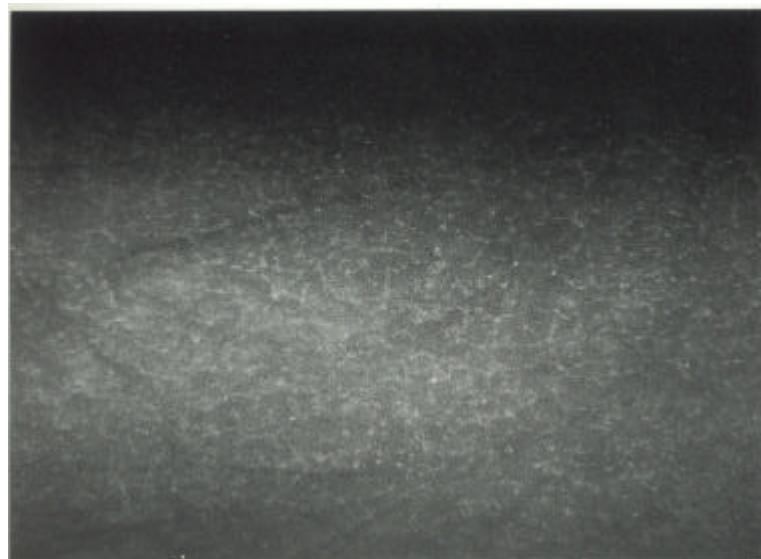


Fig. 6.45 Endothelial specular micrograph from a case of total ICE syndrome.

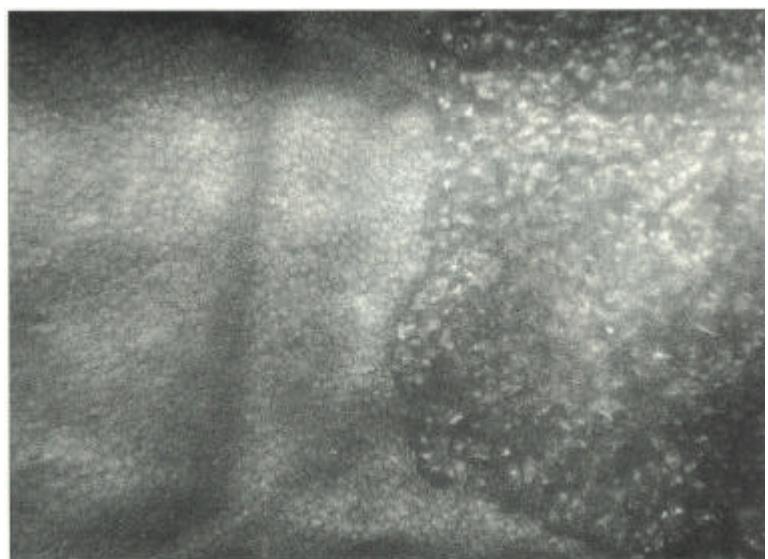


Fig. 6.46 Endothelial specular micrograph from a case of subtotal ICE syndrome with increased cell density.

CORNEAL ECTASIA

Keratoconus is characterized by thinning and distortion of the inferior and central cornea with an increasingly steep apex (conical cornea). It usually presents during the second or third decade as a slow deterioration of vision from progressively increasing myopia and astigmatism or as contact lens intolerance but can become stationary at any time. The incidence is equal in males and females and the condition is bilateral in 80 per cent of patients although ocular involvement is often markedly asymmetrical. Most patients do not have a family

history but studies using corneal topography indicate that subclinical changes may be found in the eyes of asymptomatic relatives. Clinical signs include a characteristic swirling reflex with a dark centre on retinoscopy due to irregular myopic astigmatism which can be confirmed on keratometry by finding distorted mires. The majority of patients can be managed by hard contact lenses to correct the irregular astigmatism when spectacles do not provide adequate vision, and a minority require penetrating keratoplasty for contact lens intolerance or apical scarring.



Fig. 6.47 The abnormally steep corneal apex can be seen on lateral view of this patient with gross keratoconus and may indent the lower lid on downgaze (Munson's sign). Systemic associations include Down's, Marfan's and Ehlers-Danlos syndromes. Affected patients have a high incidence of atopy. By courtesy of Mr MG Falcon.



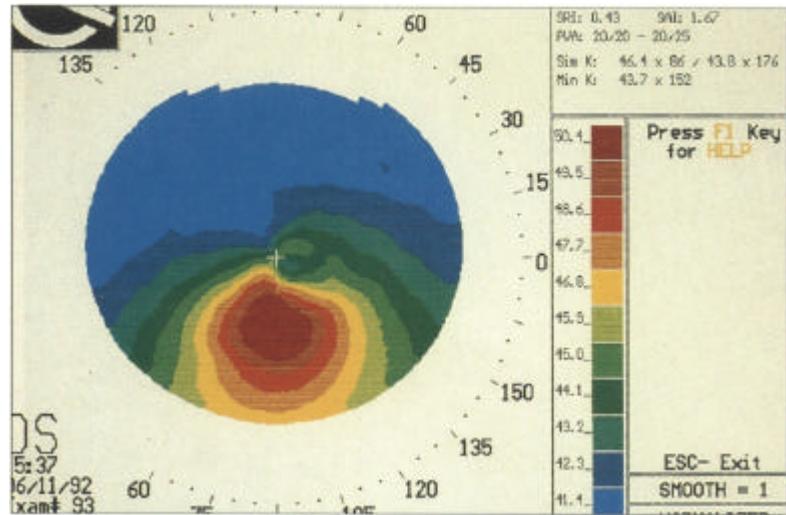
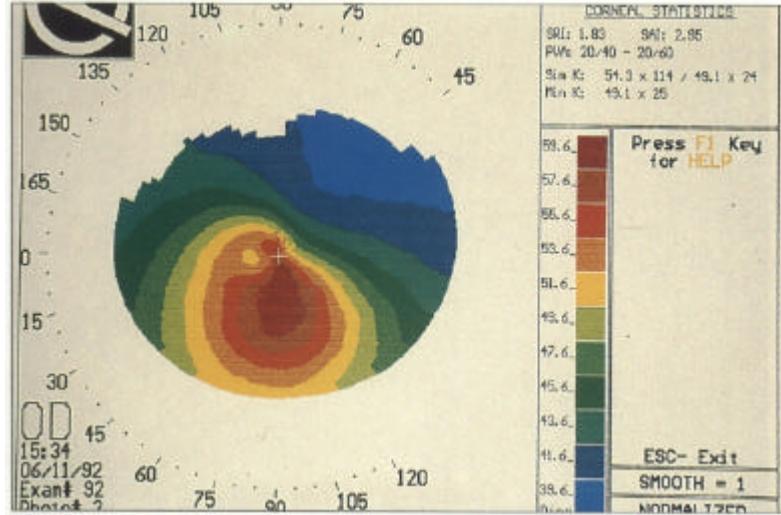


Fig. 6.48 Corneal topography demonstrates the steep irregular astigmatism of the cone with its peak in the inferior cornea below fixation. This patient retains a small central area of normal curvature in the right eye which allows vision of 20/30. In the left eye, however, the cone is completely eccentric and acuity is reduced to 20/200.

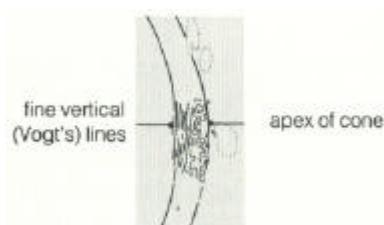
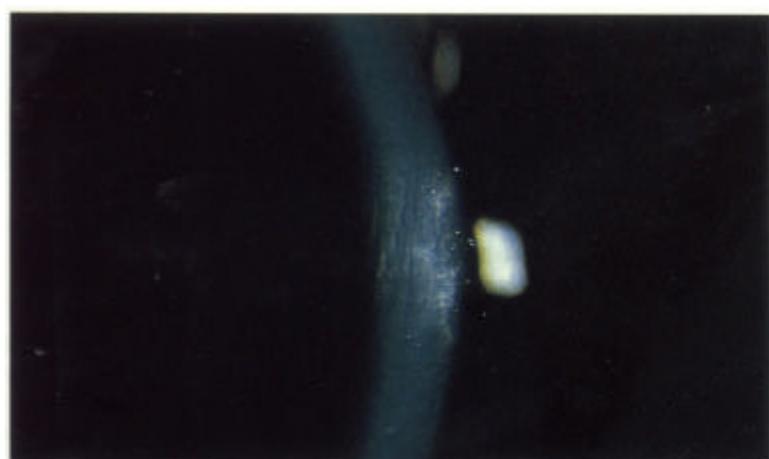


Fig. 6.49 Fine vertical folds occur near the apex of the cone (Vogt's lines) at the level of Descemet's membrane. By courtesy of Mr MG Falcon.

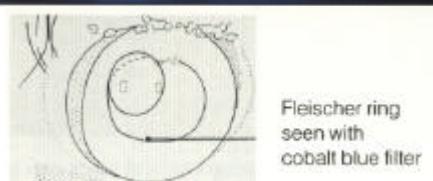
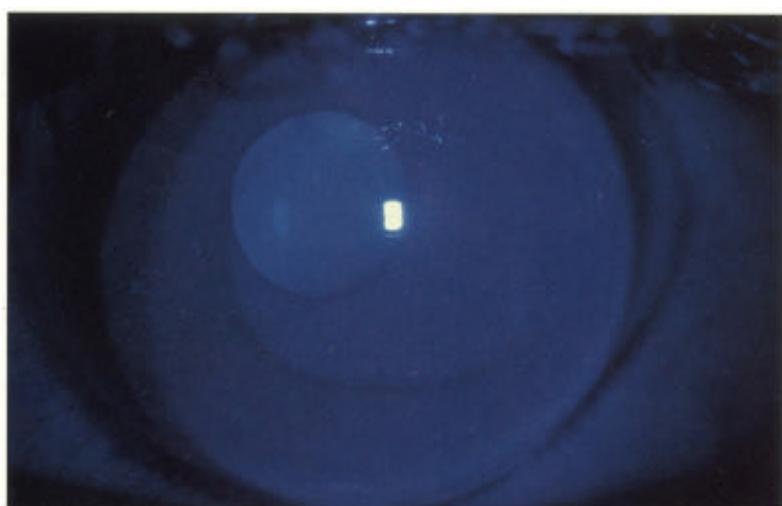
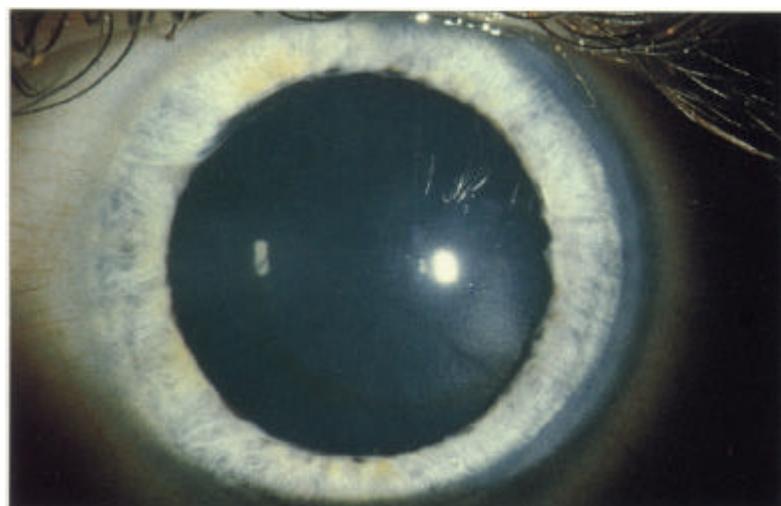


Fig. 6.50A deep epithelial iron deposit may occur around the base of the cone, best seen using the cobalt blue filter. This is known as a Fleischer ring. By courtesy of Mr MG Falcon.



Fig. 6.51 Keratoglobus is an extremely rare condition which differs from keratoconus in that the entire cornea is involved in the protrusion, however the principles of management are similar.

SALZMANN'S NODULAR DEGENERATION



Fig. 6.52 Salzmann's nodular degeneration is characterized by nodules of epithelial hyperplasia which become hyalinized and replace Bowman's membrane. It is associated with chronic ocular surface disorders such as trachoma or chronic blepharitis. The nodules can be removed by excimer laser superficial keratectomy in symptomatic patients.

CORNEAL THINNING AND MELTING DISORDERS

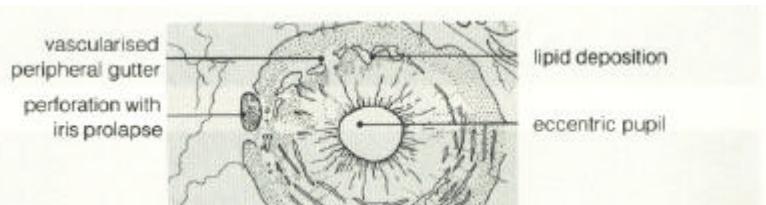
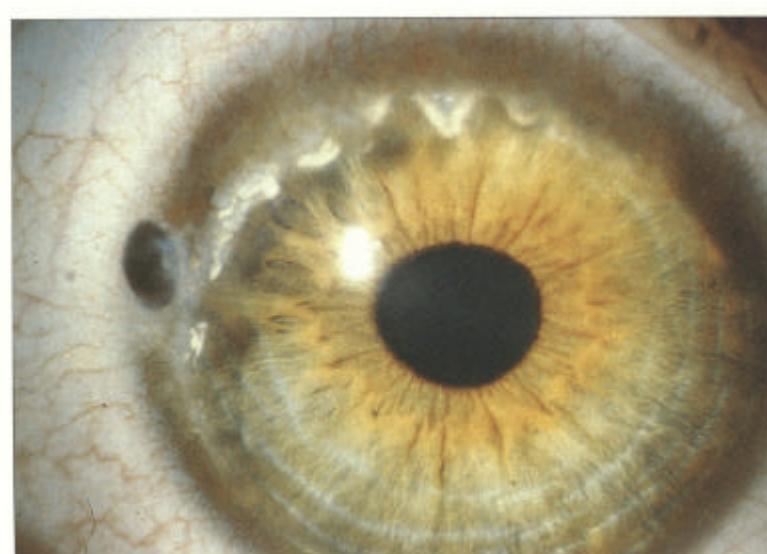


Fig. 6.53 Terrien's marginal degeneration is seen in either sex at any age and is usually bilateral although often asymmetrical. It usually begins in the upper cornea as a faint peripheral stromal opacity with minimal superficial vascularization and slowly progresses to stromal thinning in an arcuate fashion parallel to the limbus. The thinned area, which may become ectatic, has a steeper central edge marked by lipid accumulation. Pain is unusual, although inflammatory episodes may occur and some patients present with a pseudopterygium away from the horizontal meridian. Vision may be affected by induced astigmatism due to flattening in the meridian of the affected area. Spontaneous perforation can occur, as in this patient, or may be induced by minor trauma.

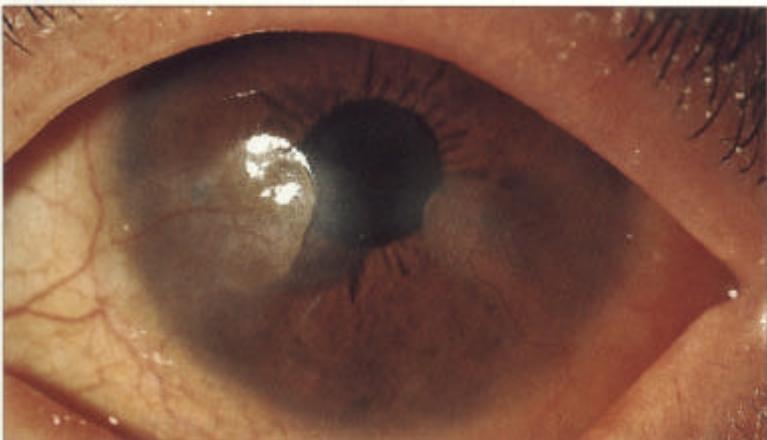


Fig. 6.54 Acne rosacea is a disorder of the pilosebaceous glandular complex of unknown cause. The cutaneous signs are facial hyperaemia with telangiectasis and sebaceous gland hypertrophy progressing in extreme cases to rhinophyma (see also Chapter 4). Blepharitis and meibomitis are almost always present and a range of corneal changes may ensue from staphylococcal hypersensitivity and keratoconjunctivitis, but the correlation between the severity of ocular and skin disease is poor. In advanced cases there is corneal neovascularization which is mainly superficial with thinning of the interpalpebral or inferior cornea, often with lipid deposition. These changes may extend to involve the visual axis but perforation is rare. Long term oral tetracycline is the mainstay of treatment.

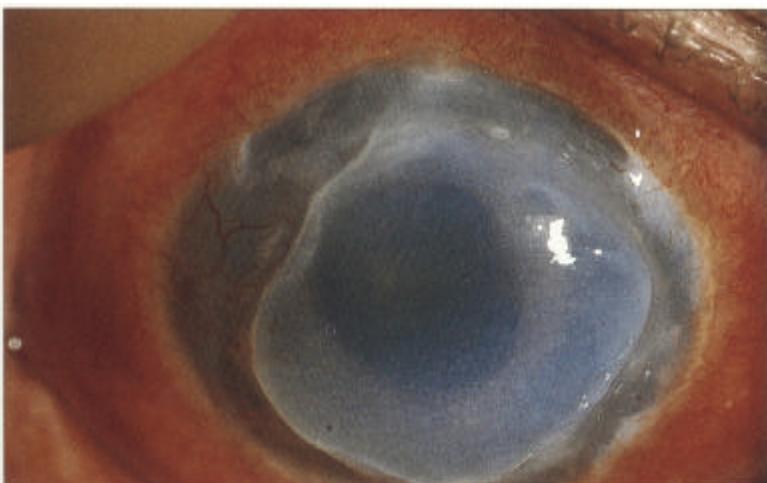


Fig. 6.55 Mooren's ulcer is a rare and painful idiopathic peripheral corneal ulceration which has been divided into a 'limited' unilateral disease occurring in older patients which responds to conservative measures and a more aggressive bilateral 'progressive' form occurring in younger adults. Onset is heralded by pain, photophobia and blurred vision due to induced astigmatism. A peripheral superficial stromal infiltrate (typically interpalpebral without a clear zone adjacent to the limbus), progresses to epithelial ulceration which deepens to involve the stroma creating an undermined central edge. Circumferential spread may involve the entire corneal periphery. Healing occurs to leave an opaque, vascularized and thinned cornea but perforation as well as cataract and glaucoma may occur. A variety of treatments have been used including topical and systemic immunosuppression or excision of the perilimbal conjunctiva. No systemic disease is associated with Mooren's ulceration although there may have been antecedent ocular infection or trauma including surgery.



Fig. 6.56 Circumferential marginal ulceration, particularly in association with adjacent scleritis, occurs in association with collagen vascular diseases such as systemic lupus erythematosus, polyarteritis nodosa, scleroderma, temporal arteritis, Wegener's granulomatosis, relapsing polychondritis, and seropositive rheumatoid arthritis. Peripheral corneal melting with minimal inflammatory signs occurs in the latter condition, usually in association with scleritis, as seen in this example, where thinning has progressed to produce a deep ulcer down to Descemet's membrane which went on to perforation. Surgery in these cases is difficult and this was treated with a soft bandage contact lens and tissue glue, eventually leaving the patient with a healed ulcer plugged by adherent iris.

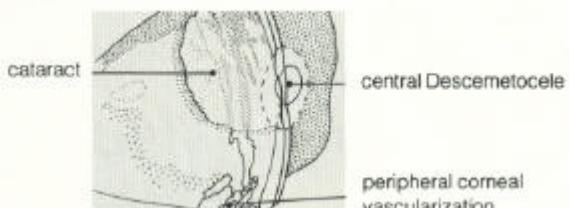
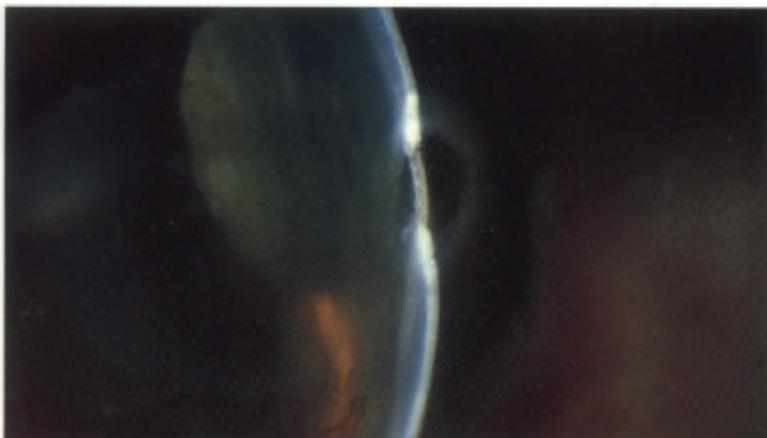


Fig. 6.57 Corneal involvement in rheumatoid arthritis is common and often occurs in association with keratoconjunctivitis sicca. This patient had a central corneal melt (keratolysis) and Descemetocle associated with scleritis. There is a strong possibility of perforation and such patients are often severely ill from their systemic disease. The corneal disease is best managed medically if possible by using a bandage contact lens with or without tissue glue. If surgery is required, a connunctival flap can be used to close the perforation.

CORNEAL ASSOCIATIONS OF SYSTEMIC DISEASE



Corneal changes are seen in a number of rare and interesting systemic diseases. Recognition of these may help to prompt further investigation for an underlying systemic disorder or help to confirm a putative systemic diagnosis.

Fig. 6.58 An arcus is due to deposition of cholesterol and related lipids in the peripheral cornea with sparing of the immediate perlimbal area. It is a common ageing phenomenon but its presence in patients under 40 years of age merits further investigation for an underlying hyperlipidaemia. It is a normal feature of megalocomea.

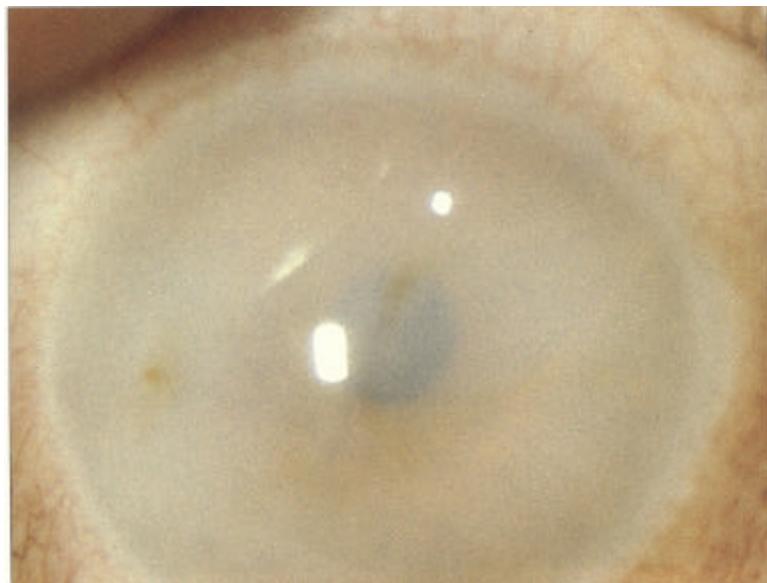


Fig. 6.59 The mucopolysaccharidoses are a group of recessively inherited lysosomal storage disorders (except Hunter's syndrome which is X-linked) associated with defects in the degradation of mucopolysaccharides leading to deposition of abnormal material in the body and excretion of the appropriate mucopolysaccharide in the urine. There are seven basic subtypes and corneal clouding is a feature of all except for Hunter's syndrome. A pigmentary retinopathy and optic atrophy are seen as a feature of some types. The example here is of Scheie's syndrome in which the enzyme alpha-L-iduronidase is deficient (absence causes the more severe Hurler's syndrome). The cornea is usually cloudy from birth with a slow progression which may require corneal grafting in adulthood. Other features are a claw hand with stiff joints and characteristic facies but the severe neurological and cardiological features of Hurler's syndrome are absent. No systemic treatment is available.

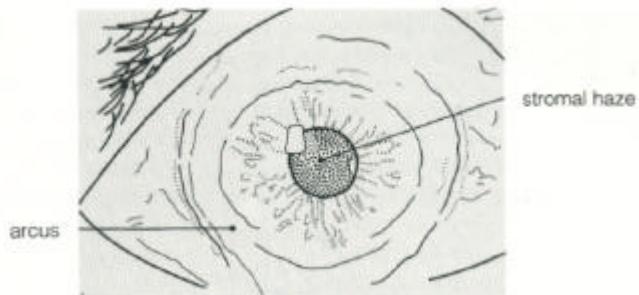
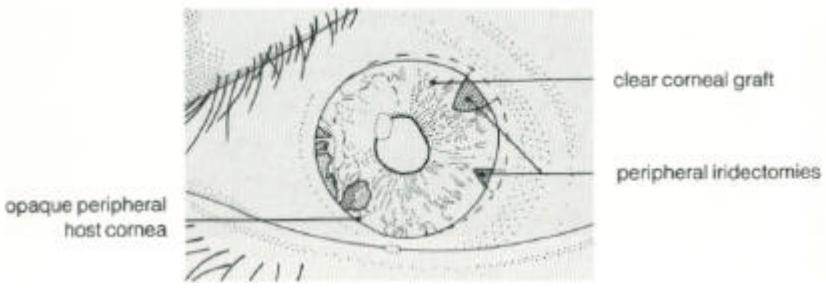
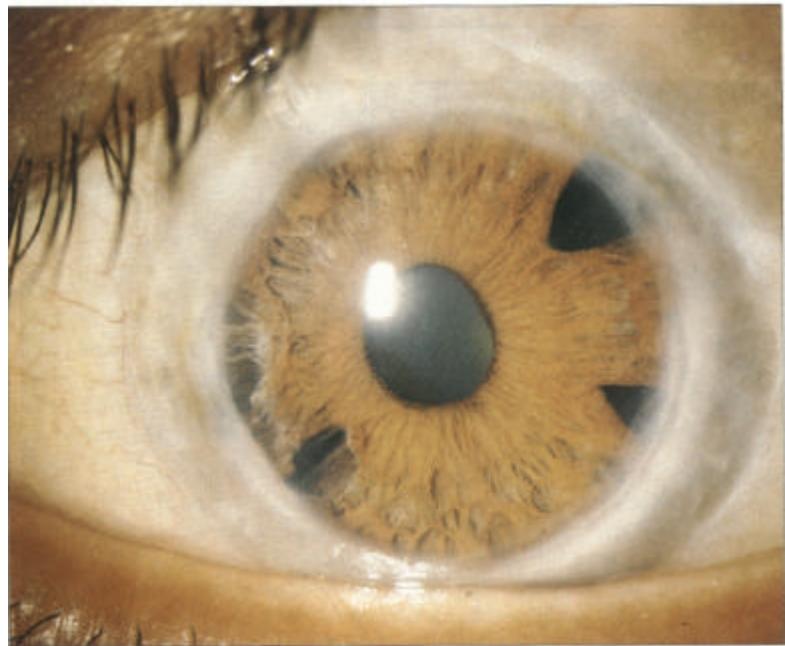
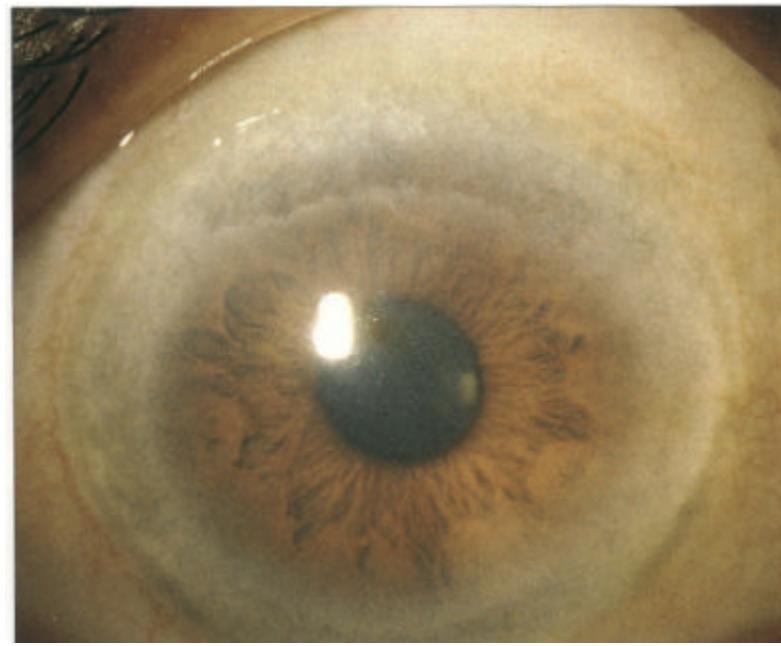


Fig. 6.60 Lecithin:cholesterol acyltransferase (LCAT) deficiency and Tangier disease are autosomal recessive disorders of lipid metabolism (dyslipoproteinaemias) with similar corneal changes of diffuse fine grey dots throughout the stroma but concentrated centrally which affect acuity less than might be expected from slit lamp appearances. This patient had acuity of 20/20 with the left eye. A corneal graft had previously been performed on the right eye which has remained clear for 10 years.



Fig. 6.61 Amyloidosis is a group of disorders in which there is deposition of extracellular protein in the body characterized by staining with Congo red and birefringence in crossed polarized light. Systemic forms occur either as a primary idiopathic disorder or secondary to other diseases such as multiple myeloma and chronic infection. Familial forms also exist. These patients may have amyloid deposition in a wide variety of ocular tissues but particularly the vitreous (see Chapter 12). A form of isolated ocular amyloidosis occurs with lattice corneal dystrophy. More rarely massive gelatinous subepithelial deposition may occur in the cornea, as in this patient. These patients usually have no evidence of systemic deposition.

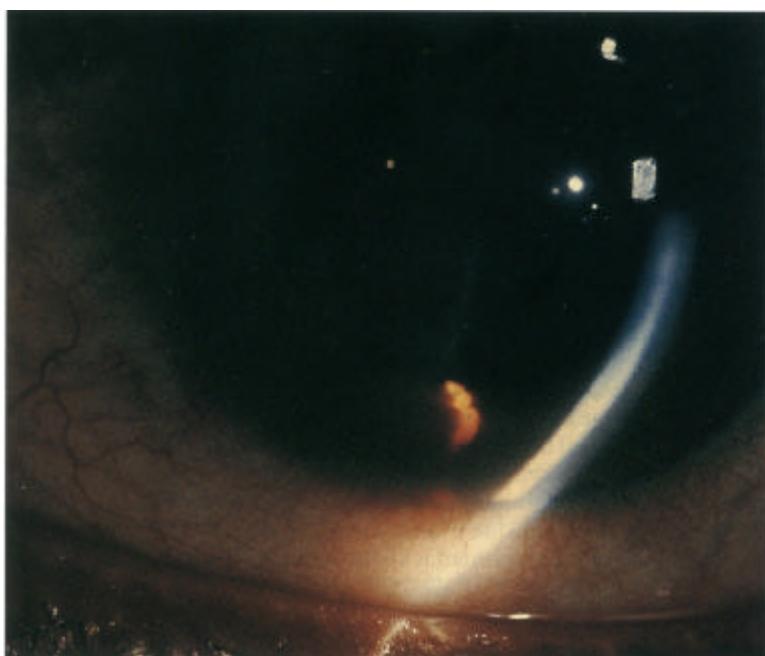
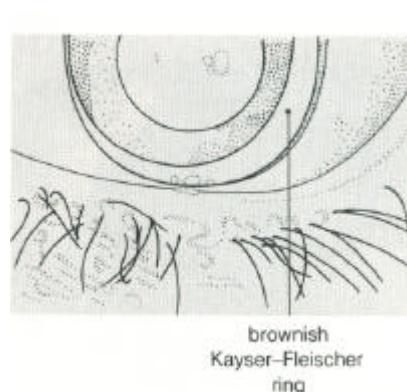
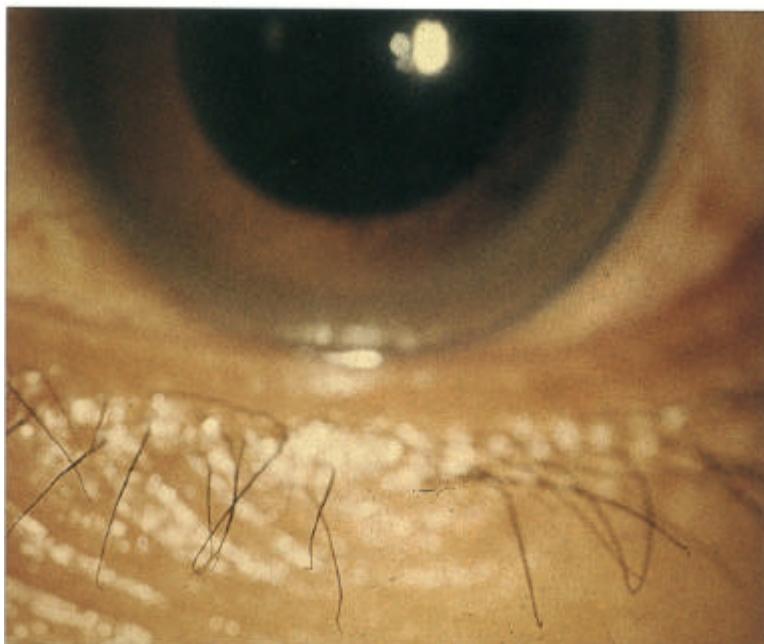


Fig. 6.62 Deposition of copper in Descemet's membrane (Kayser-Fleischer ring) occurs in Wilson's disease (hepatolenticular degeneration) from a deficiency of the transport protein caeruloplasmin in the blood with defective excretion of copper by the liver lysosomes. Patients present with liver failure and later neurological problems from deposition of copper in the basal ganglia. Kayser-Fleischer rings are seen as a peripheral orange, brown or green-brown discolouration, at the level of Descemet's membrane adjacent to the limbus and are often seen better with gonioscopy. They are present in virtually all patients with neurological manifestations of Wilson's disease but may be absent in early cases who usually present within the first two decades of life with jaundice and anaemia related to hepatic failure.

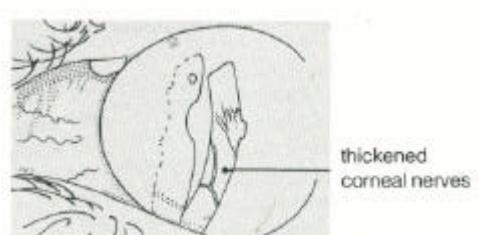
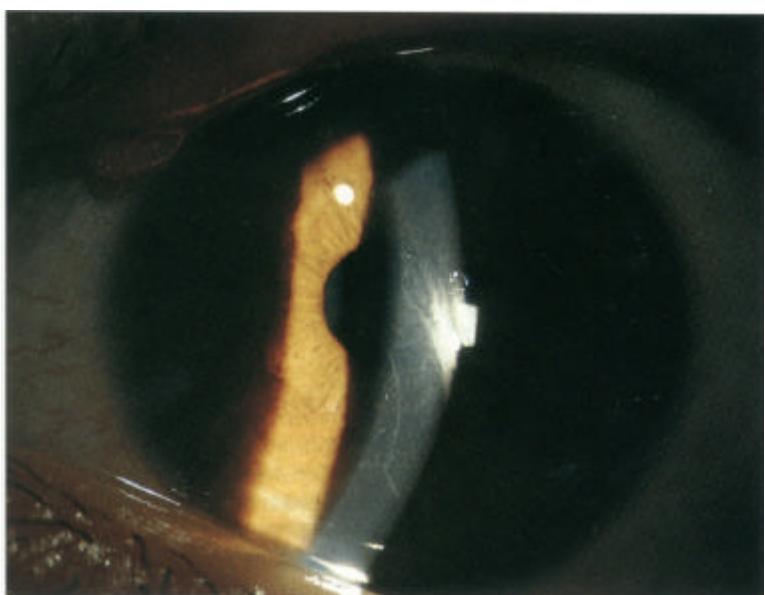


Fig. 6.63 Numerous thickened myelinated corneal nerves are a feature of the dominantly inherited multiple endocrine neoplasia (MEN) syndrome Type IIb. Patients have a marfanoid appearance and develop malignant tumours in organs of neural crest origin such as the thyroid, parathyroid and adrenal glands. This patient developed a medullary carcinoma of the thyroid gland at the age of 15. The lids and conjunctiva may also be thickened by abnormal nerves. By courtesy of Mr G Davies.

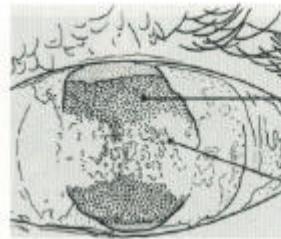
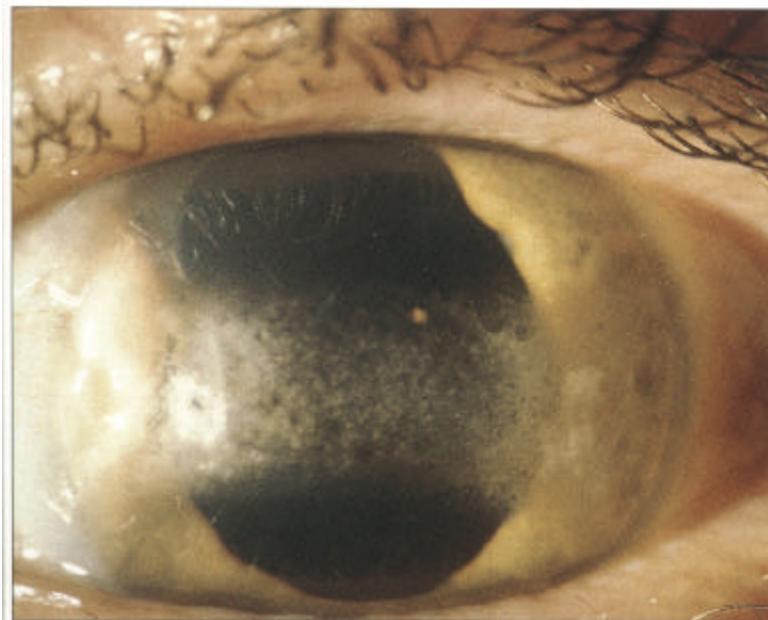


Fig. 6.64 Band keratopathy is associated with the low grade chronic iritis seen in children with juvenile chronic arthritis (see Chapter 10) and also in adult eyes with chronic inflammation or phthisis bulbi. A few cases are associated with hypercalcaemia but the majority are idiopathic. A characteristic interpalpebral 'band' of calcium deposition is seen at the level of Bowman's membrane with a clear area separating it from the limbus. Clear areas and small round holes can often be seen in the band, the latter representing the passage of nerves through the deposit. Large aggregated deposits may cause painful epithelial erosions. Treatment by surgical removal is indicated for those patients with painful band keratopathy or impaired acuity and this can be elegantly achieved by excimer laser superficial keratectomy.

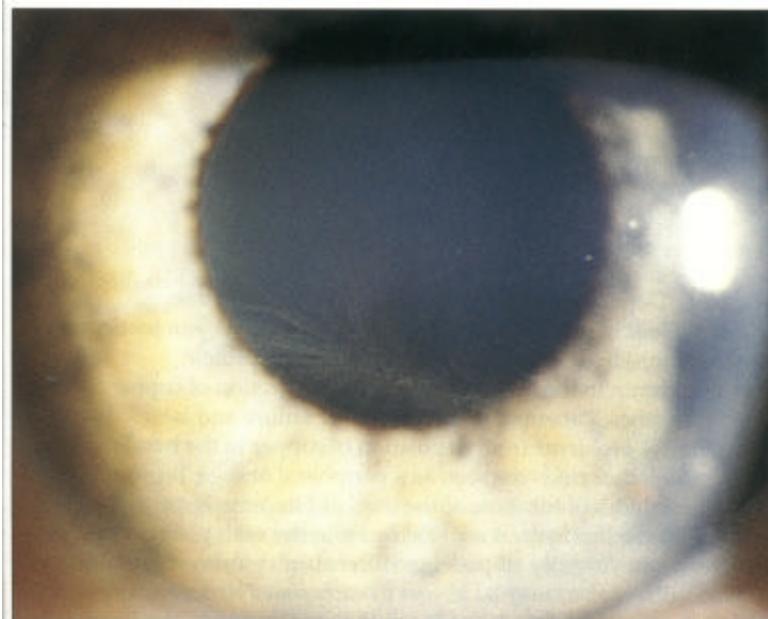


Fig. 6.65 Corneal verticillata are curvilinear deposits which appear to swirl out from a focal area just below the central cornea. They delineate epithelial migration patterns. Verticillata occur in patients on certain systemic drugs such as amiodarone (as in this example), or chloroquine. Identical changes also occur in Fabry's disease - an X-linked glycolipidosis due to a deficiency of the enzyme alpha-galactosidase associated with angiokeratomas in the skin from sphingolipid accumulation in vascular endothelium. By courtesy of Dr EM Graham.

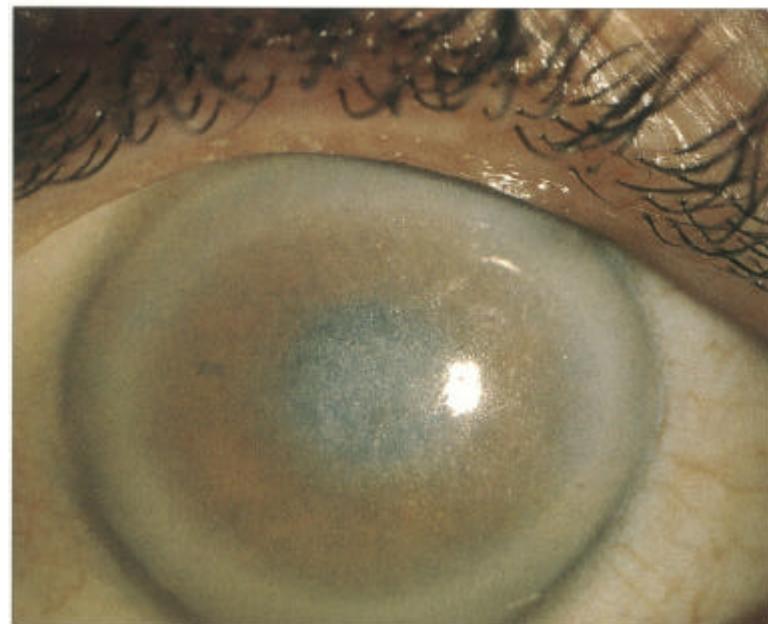


Fig. 6.66 Crystalline corneal deposits seen as grey or golden dots in the central cornea occur in cystinosis, oxalosis, gout, gold therapy, and Schnyder's crystalline dystrophy. This latter condition is dominantly inherited, bilateral, and is often associated with a prominent arcus, as in this example. Central corneal deposition of crystalline cholesterol esters occurs in the anterior corneal stroma and the condition appears to be a localized disorder of corneal lipid metabolism.

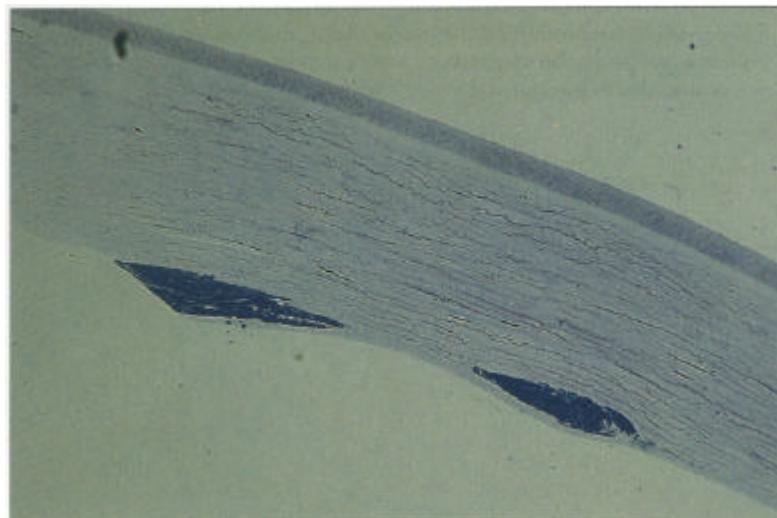
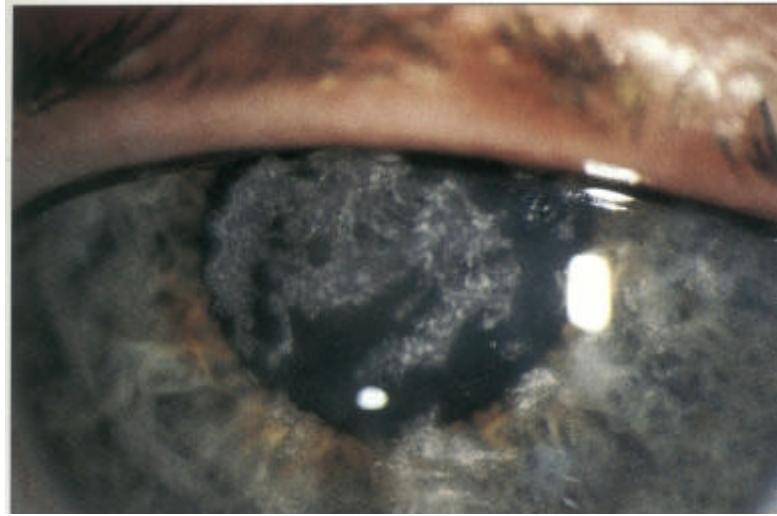
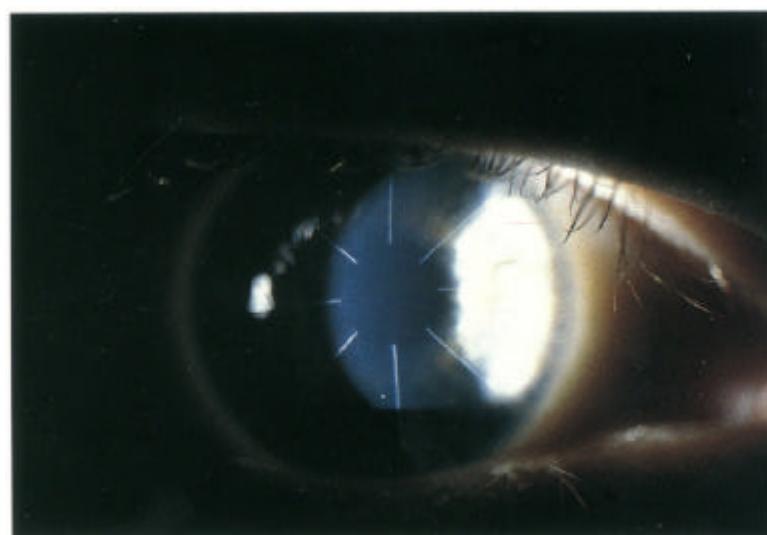


Fig. 6.67 Crystalline corneal deposits are also seen in rare cases of monoclonal gammopathy associated with multiple myeloma, lymphoproliferative disorders and benign monoclonal gammopathy. The crystals may be seen at any level of the corneal stroma or in the epithelium and may be intra- or extracellular. This patient had deep (pre-Descemet's) stromal crystalline deposition of IgG kappa light chains associated with lymphoma. By courtesy of Dr ACE McCartney (Toluidine Blue stain).

REFRACTIVE SURGERY



There is increasing interest in controlling refraction by surgically manipulating the shape of the anterior corneal surface. This can be successfully achieved for primary myopia and astigmatism or for induced astigmatism following, for example, cataract surgery, keratoplasty or corneal injury using relaxing incisions of varying configurations. Hypermetropia cannot, at present, be satisfactorily treated.

Fig. 6.68 Radial keratotomy relies on producing relaxing radial incisions to flatten an optical zone based around the visual axis. Overall short term results are good but there is a small risk of perforation or infective keratitis following the procedure. Long term complications include fluctuating myopia and haloes from encroachment of the incisions into the optical zone, a gradual hypermetropic shift over several years after the procedure and weakening of the cornea increasing the risks of future trauma. By courtesy of Mr W Jory.

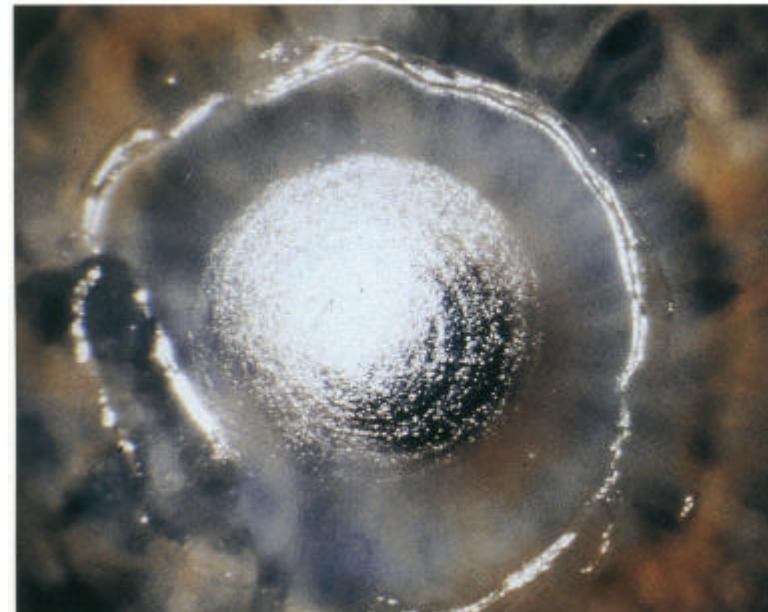


Fig. 6.69 Excimer lasers containing argon fluoride emit ultraviolet light at a wavelength of 193nm, with sufficient energy per photon to break the hydrocarbon bonds making up the surface structure of the corneal stroma. This allows an exceedingly precise removal of tissue with minimal adjacent tissue damage and no intraocular penetration of radiation. The excimer laser can be used to correct myopia by removing tissue using an expanding aperture so that more tissue is removed from the centre than the periphery of the treated optical zone (having first removed the epithelium), in effect producing a concave lens over the visual axis. Treatment of astigmatism is at present under experimental investigation.

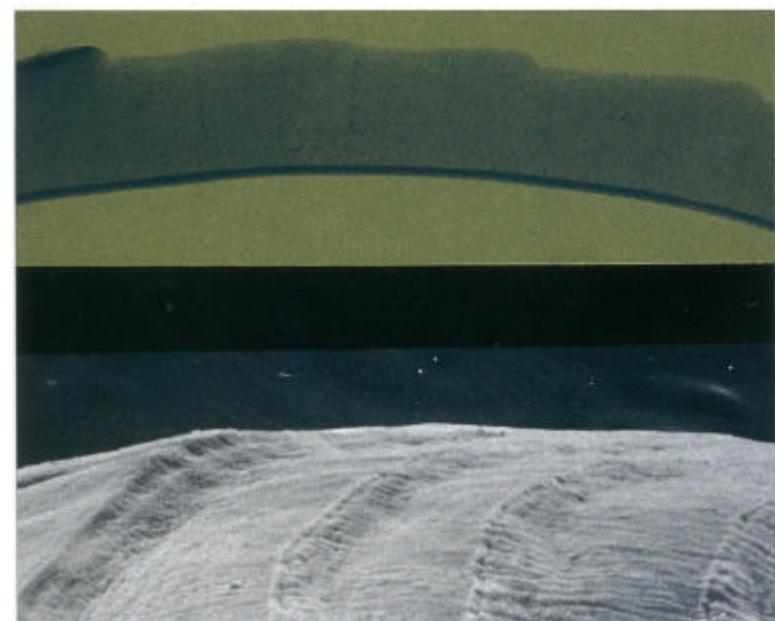


Fig. 6.70 Light microscopy and scanning electron shows the effect of excimer ablation on a corneal button. Each 'step' is produced as the laser aperture opens one stop during treatment creating a flattened ('less steep') corneal curvature. By courtesy of Prof J Marshall.

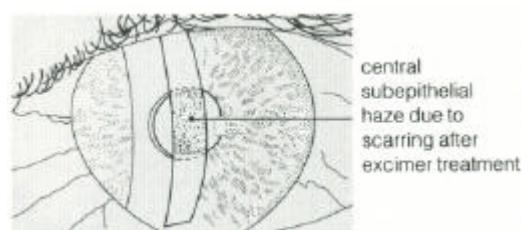
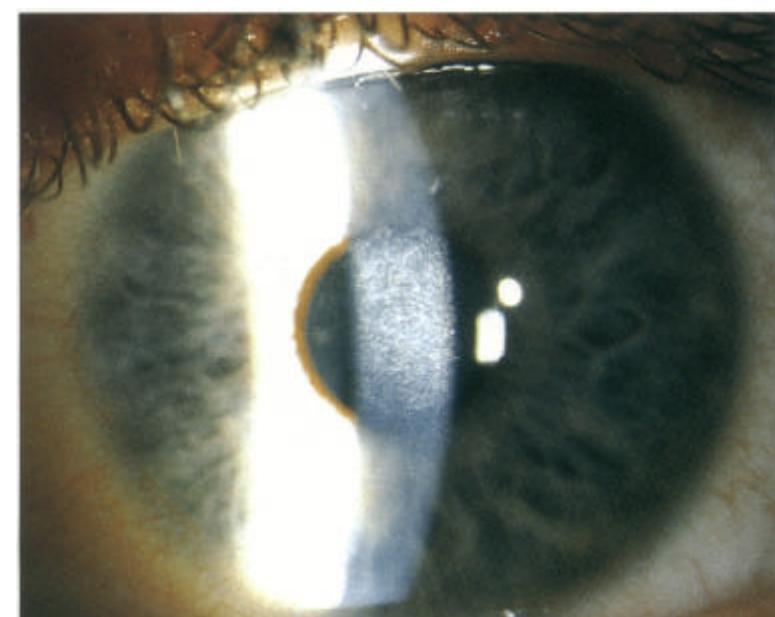


Fig. 6.71 Unwanted effects of excimer treatment include superficial stromal scarring which is seen as a central anterior stromal reticulated opacity on slit lamp examination or regression of the correction towards the initial level of myopia. The corneal haze usually resolves over several months after the procedure. With present techniques for corrections of more than 4 to 6 dioptres of myopia the induced refractive change is less predictable and the risk of corneal scarring greater.

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