KERATOCONUS & RELATED DISORDERS

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INTRODUCTION

The cornea is affected by several distinct disorders that produce marked thinning without significant ocular inflammation. They are keratoconus, pellucid marginal degeneration, posterior keratoconus, and keratoglobus. Keratoconus and posterior keratoconus cause centralized thinning. Pellucid degeneration produces a marginal ectasia usually inferiorly. Keratoglobus is associated with generalized thinning of the entire cornea. All of these conditions are poorly understood.

KERATOCONUS

Keratoconus is the most frequently encountered of this interesting and perplexing group of disorders. It is characterized by a variably progressive central thinning of the cornea which commonly results in conically shaped protrusion. Keratoconus has remained a scientific enigma. Despite more than one-hundred years of exhaustive study little progress has been made in understanding its cause. Clinically, it is a frustrating disease for both the patient and doctor. When severe, it can result in crushing disability for the patient and strong psychological effects. The unknown course and uncertain prognosis also make management of these challenging. Fortunately, our limited understanding has only complicated but not prevented our treating patients with keratoconus.

CLINICAL PRESENTATION AND DIAGNOSIS

Keratoconus is characterized by progressive stromal thinning within the central cornea. As the cornea thins, the structurally weakened tissue bulges forward to produce the cone like shape that the disorder was named for. The condition is almost always progressive although the rate of progression and ultimate severity are quite variable. From the patient's perspective, keratoconus is primarily a visual disorder. The majority of patients will present early in the course of the disease complaining of decreased or distorted vision. In cases where keratoconus is suspected and Snellen acuity remains relatively normal, significant decreases in contrast sensitivity based measurements of visual function may be evident.[1] When a history is available, a progressive or sometimes precipitous increase in myopia and corneal astigmatism may have occurred. In unilateral or highly asymmetric cases, good vision from the better eye may delay presentation until the affected eye has developed advanced disease.

Although keratoconus can present in any age group it most commonly affects patients in their late teens or early twenties. Occasionally, young children may be affected although this is rare. Most early studies have shown a female predominance.[2,3] However, more recent reports show either no significant sex differences or male predominance.[4] My own experience suggests that the majority of affected patients are

young males. Keratoconus occurs throughout the world and affects all races without significant difference. Estimates of the incidence of keratoconus in the general population vary widely.[5,6,7,8,9] The majority of reports range from 50 to 230 per 100,000 population. This variance is primarily due to differences in the definition and means used to diagnose keratoconus. It is likely that the sensitive computer-assisted topography instruments now in use will reveal an even higher incidence than previously suspected.

The diagnosis of mild or early keratoconus can be challenging. In such cases, it may be difficult to distinguish early keratoconus from regular myopic astigmatism. However, recent advances in computerized corneal topography have made it much easier to establish a diagnosis in questionable cases.[10] The early identification of keratoconus has recently become of greater importance to the clinician. Studies using computerized corneal topography suggest that many more patients have this disorder than was previously thought.[11] Using this new technology the clinician can now establish the diagnosis earlier and more reliably than was possible using conventional instruments such as corneascope. Being able to closely follow the progression of the disease may provide greater insight into the prognosis for a specific patient. The growing interest in refractive surgery is another reason for the early diagnosis of keratoconus. There is a

good deal of evidence to suggest that patients with keratoconus are poor candidates for these procedures.[12,13,14,15]

Despite the greater sensitivity of computer-assisted instruments, conventional instruments are still valuable in establishing a diagnosis. The retinoscope can be used as a sensitive indicator or early keratoconus. As the beam is swept across the pupil a scissors or oil droplet reflex will often be evident. These aberrant reflexes are caused by the characteristic refractive changes that occur in keratoconus. The scissors reflex is seen earlier in the course of the disease and represents increased irregular astigmatism. As the cone progresses the scissors motion is replaced by a central or paracentral darkened oil droplet like reflex which is caused by internal reflection within the more pronounced cone. The ophthalmoscope when focused and held at an appropriate working distance may be used in a similar fashion.[16] This reflex can be helpful in establishing a diagnosis even in early keratoconus when viewed through a fully dilated pupil.[17] Although conventional keratometry measures a small central area of the cornea, more advanced keratoconus will typically manifest with marked astigmatism containing a significant irregular component. The irregularity precludes precise alignment of the keratoscopic mires. Topographic abnormalities of early keratoconus may be not be easily detected using a conventional keratometer.[10] Modifications to the keratometer have been devised that permit topographic

measurement. However, the amount of astigmatism will often exceed the measurement range of the normal keratometer. Techniques to extend the range have been described.[18,19]

As keratoconus progresses physical findings become more apparent and the diagnosis more clear-cut. There are several classically described slit lamp findings. Fleischer's ring is a rust colored deposit that may fully or partially encircle the base of the cone. The ring is comprised of hemosiderin that is deposited in the deeper layers of the epithelium. Like the other such deposits it is likely produced by disruption in normal tear film dynamics — in this case from the sudden topographic variation caused by the cone. Fleischer's ring may not be clinically identifiable in all patients but it is probably present in the overwhelming majority of keratoconic patients. It may be quite variable in presentation, ranging from faint and barely perceptible to quite prominent. The color of the ring may also vary from yellowish to dark brown. The physical characteristics of the ring often correlate with the progression the cone. As the condition progresses, Fleischer's ring increases in density, becomes thinner and more defined, and tends to completely encircle the cone. Although it is usually visible using white light upon direct slit lamp examination, a cobalt[20] or red free filter will sometimes aid in visualizing the ring.

Vogt described fine striae in the deep stroma just anterior to Descemet's membrane that temporarily disappear when light pressure is applied to the globe.[21] The striae are usually oriented vertically and parallel to the steep axis of the cornea. They are seen in moderately advanced to severe keratoconus beneath areas of pronounced thinning. On slit lamp examination they are most easily observed using a narrow oblique beam and white light. In practice the striae are extremely fine and densely packed white lines reminiscent of the parallel line bundles that are seen in fingerprints. Although the etiology of these characteristic findings remains uncertain, vertical striae are most likely stress lines caused by deformation of Descemet's membrane. Their transient disappearance as light digital pressure is applied to the globe is produced by increased intraocular pressure which counteracts the localized stress. The application of a rigid contact lens may induce striae before they would otherwise be clinically detectable.[22] This may be of prognostic value in detecting early keratoconus.

Less frequently observed slit lamp findings include increased visibility of corneal nerve fibers which may be associated with the presence of fine white dots. This may be caused by thinning and outward bowing of the ectatic cornea.[21] Fine white subepithelial fibrillary lines may be observed, They run in concentric bundles with a wreath like appearance just inside Fleischer's ring.[23] In some patients they appear to connect with deep stromal nerves. On slit lamp examination they are best visualized

using broad oblique illumination. Regardless, fibrillary lines are at best a subtle finding. They are reported to occur in approximately one-third of patients with keratoconus but in practice they are far less commonly observed. The corneal endothelial reflex may show increased intensity. Breaks in Bowman's layer may be visible on slit lamp examination as superficial clear spaces. They have been reported to occur in 38% of consecutive eyes (38%) with keratoconus.[24] These clear spaces are believed to be ruptures in Bowman's layer that are discovered prior to scarring of the affected area. Superficial apical scarring is a common finding in keratoconus. Scarring that occurs naturally must be distinguished from secondary scarring caused by excessive bearing from rigid contact lens wear. Many patients who never wore rigid contact lenses will present with scarring over the thinned corneal apex. Such idiopathic scarring may partially resolve over time with some residual scars usually persisting. Keratoconic patients wearing lenses with excessive apical bearing will frequently develop scarring from localized surface damage. I have found that these superficial scars will usually resolve — in many cases completely — once the fitting relationship is corrected to allow more even distribution of lens bearing forces. Deeper scarring may occur after breaks in Descemet's membrane. These breaks may compromise the endothelial barrier and produce acute stromal edema. This is referred to as acute corneal hydrops or acute keratoconus. Although the edema generally subsides within 4 to 6 months residual scarring may remain.

As keratoconus progresses there is an increase in stromal thinning. This is frequently visible on slit lamp examination as thinning of the central cornea which is greatest at the apex of the cone. Thinning and protrusion of the cone is responsible for several additional findings associated with keratoconus. Corneal sensitivity is diminished in keratoconus. This hypoesthesia coincides with the area of greatest corneal protrusion.[25] Munson's sign is seen in advanced keratoconus where the lower lid is bowed outward by the protruding cone on down gaze. Several aberrant light reflexes have been reported with keratoconus. A central dark shadow or 'oil droplet' reflex is visible with a retinoscope or direct ophthalmoscope and is produced by total internal reflection within the cone. Rizzutti's described a simple diagnostic test using a penlight.[26] With the penlight shinning on the temporal side of a normal cornea anterior to the plane of the iris, the focused light evenly illuminates the nasal limbal area. In keratoconus, the light is tightly focused inside of the nasal limbus. This focusing effect is more pronounced and more extreme in advanced disease. A positive result is termed Rizzuti's sign.

THE TOPOGRAPHY OF KERATOCONUS

The topography of keratoconus is dynamic. It changes as the disease progresses and varies from patient to patient. Measurement of abnormalities in corneal shape has

traditionally been accomplished using the Placido's disk. The disk consists of multiple concentric rings that are either projected or reflected off of the corneal surface. Until recently improvements in the Placido disk have involved enhanced lighting techniques or photodocumentation and measurement using instruments such as the Corneascope. Today computer assisted topographic analysis of Placido images has dramatically expanded our understanding of the subtleties of corneal topography. A new, non-Placido disk based technique for calculating corneal topography and curvature has been developed. Vertical planes of light are projected onto the cornea. Curvature values are calculated and a contour map generated from the projected images.[27] Other technologies will likely be developed as computer-assisted topography becomes a more commonly instrument in ophthalmic offices.

Despite a lack of precision and a need for creative interpretation, significant topographic information was obtained using conventional instrumentation. Amsler extensively investigated and documented the spectrum of topographic changes associated with keratoconus using a conventional Placido disk.[2] Later authors used the corneascope to analyze the progression of the disorder.[28] In 1980 Perry et al described two distinct types of cones in advanced keratoconus.[29] A nipple shaped or round cone is more commonly observed and has an apex that is typically inferonasal. A larger oval,

sagging cone shows an inferotemporal apex and is more commonly associated with complications such as hydrops, pronounced scarring, and contact lens failure.

Computer-assisted corneal topographic analysis has permitted earlier and more detailed analysis of morphologic changes in keratoconus. Recent studies using these new instruments have yielded much new information about keratoconus and its progression. The first topographic change evident in keratoconus is inferior corneal steepening.[10] The cone steepens as the condition progresses.[11] Computerized analysis has also revealed new information about the topographic alterations seen in keratoconus. One group discovered two distinct types of cones — peripheral and central.[30] In this study, the majority of patients (72%) had peripheral cones, with steepening commonly restricted to one or two quadrants but extending to the limbus. Some of these patients had changes that involved nearly the entire corneal surface. The remaining patients had steepening that primarily involved the central cornea. Other studies have confirmed the classic picture of a well defined zone of inferior to inferotemporal steepening.[31] However, the more detailed analysis provided by computer-assisted devices has revealed other changes including: nasal, superior, and central steepening, as well as extension of the inferior steepening superiorly. Significant flattening was found in some portions of the cornea away from the cone, particularly in the

superonasal quadrant. Automatic screening programs to detect keratoconus topography patterns have been devised.[32]

In general, symmetry appears to be common finding in keratoconus.[30,31] However, in most patients a large disparity remains between the two eyes in the power at the apex of the cone and the total cylinder. Studies using computer-aided topographic analysis have also shown unilateral keratoconus to be extremely rare.[30] One study compared conventional slit lamp and corneascope examination to computer-assisted analysis. The authors found that examination using conventional techniques often miss subtle changes in the fellow eye that are discernable using computer-aided instruments.[33] Another benefit of computer-assisted analysis is greater sensitivity to the subtle changes characteristic of sub-clinical or form fruste expressions of keratoconus.[10,11]

HISTOPATHOLOGY & BIOCHEMISTRY

Keratoconus is a progressive disorder involving every layer of the cornea. Early corneal thinning suggests that there is a functional loss of structural elements. A reduction in corneal tensile strength is expressed by signs of rupture and scarring in Bowman's layer, scarring in the stroma, and breaks in Descemet's membrane. The pathogenesis of keratoconus remains obscure. However, the earliest changes appear to occur in the anterior cornea. There is early degeneration of the basal epithelial cells and disruption

of the basement membrane.[34] Particulate material has been observed in a thickened subepithelial basement membrane layer,[35] between basal epithelial cells and on the surface of Bowman's layer.[36] The significance of these particles is uncertain. As the disease progresses the epithelium becomes increasingly thinned and disorganized in the area of the cone. In many patients the cone is surrounded by a partial or complete yellow-brown ring composed of ferritin deposits in the basal epithelium.[37,38]

Bowman's layer also undergoes significant change in early keratoconus. Initially fibrillation and irregularity is seen. Breaks in Bowman's layer are common and are likely responsible for the anterior clear spaces that occur in some patients.[24] These breaks may fill with stromal collagen, keratocytes and epithelial cells.[36,39] Scarring occurs as the breaks are repaired with connective tissue produced by the stromal keratocytes.[40] Z shaped interruptions of Bowman's layer formed by epithelium growing posteriorly and stromal collagen growing anteriorly are a classically described finding in keratoconus.[36,41] Deposits of a fine granular periodic acid-Schiff (PAS)-positive material are also found within these interruptions.[42] These deposits may be produced by abnormal keratocytes in the areas of thinning as well as the stroma.[34,36,39,41]

Stromal thinning is a primary finding in keratoconus. However, its mechanism is poorly understood. Over 70% of the cornea's dry weight is composed of collagen, a protein

containing glycine, proline, and hydroxyproline in a finely structured arrangement. Seven distinct types of collagen have been identified. All but type II are normally found in the human cornea. Corneal transparency and structure depends upon the regular alignment of stromal collagen fibers. Stromal collagen fibrils are normal in size and lamellae normal in thickness but they decreased in number in the areas of thinning.[41] Some researchers have found an abnormally high concentration of type IV collagen in the keratoconic epithelium and basement membrane.[43,44] While others no differences in collagen distribution between normal and keratoconic corneas.[45] This suggests that the structural changes in keratoconus are not directly related to alterations in collagen composition and distribution. Defects in the structure or cross linking of collagen have been postulated as the cause of reduced mechanical stability in keratoconus. However analysis, shows no difference in the cross-linking pattern or the composition of amino acids of collagen from keratoconus corneas compared to normal corneas.[46] However, weakened interlamellar adhesion allowing lamellae to separate from one another has been hypothesized.[47] The extracelluar matrix of the stroma is mostly composed glycosaminoglycan proteoglycans which are acid mucopolysaccharides bound to a small protein core. The normal cornea is predominantly composed of the glycosaminoglycans keratin sulfate and, to a lesser extent, chondroitin-4-sulfate. Keratoconus corneas appear to contain an increased amount of glycosaminoglycans and other polyanions.[48] Recently, a disruption in Proteoglycan bridges along and

between corneal collagen fibrils and an apparent loss of keratan sulphate has been demonstrated by electron-histochemical and x-ray diffraction techniques.[49,50] Small focal scars are sometimes seen within the stroma.

The deeper layers of the cornea are affected in the later stages of the disease. Endothelial cell polymorphism and polymegathism are common findings but may be related to contact lens wear in the keratoconic patient population.[51] In general endothelial damage correlates with the severity and duration of the disease with 9 years being the dividing line between mild and severe endothelial cell damage. Acute hydrops is marked by stromal edema following a rupture in Descemet's membrane. Breaks are covered by corneal endothelium which lays down new Descemet's membrane to seal the defect.[52] Although rare, corneal perforation may occur in acute hydrops.[53,54]

Keratoconus appears to be a heterogeneous disorder that may caused by a variety of unrelated abnormalities in metabolism or biochemistry.[55,56,57] Lysosomal enzymes are naturally present in the epithelium, stroma, and endothelium of corneas both normal and keratoconus corneas. However, corneas with keratoconus had significantly higher than normal levels of acid hydrolases, acid phosphatase, acid esterase, and acid lipase in the epithelium, especially the basal epithelium.[58] This is consistent with hypothesis

that the corneal epithelium is the primary site in the pathogenesis of keratoconus and that abnormal tissue degradation processes may play a role in the disease. Biochemical studies have shown an increase in collagenolysis and of reduceable collagen cross-links.[50,59] Stromal keratocytes isolated and cultured from keratoconus corneas show increased gelatinolytic activity.[60] The majority of proteolytic activity appeared due to gelatinase (type IV collagenase). Interestingly, both normal and keratoconus corneas show no significant differences in amounts or types of extractable gelatinases, nor in the amounts or types that they synthesize in culture.[61] Since gelatinases primarily exist in the inactive form in both the normal and keratoconus corneas it seems likely that proteinase inhibitor levels are an important factor in the pathogenesis of keratoconus. Gelatinolytic activity appears related to the interaction between matrix metalloproteinase (MMP-2) and tissue inhibitors of metalloproteinases (TIMP).[62] Decreases in TIMP levels may explain why gelatinolytic activity in keratoconus corneas appears to be significantly higher than in normal corneas.[63] Increased gelatinolytic activity in the affected eye of a patient with unilateral keratoconus supports the relationship between gelatinolytic activity and the clinical signs of keratoconus.[64]

ETIOLOGY AND ASSOCIATED CONDITIONS

Keratoconus appears to be a heterogeneous disorder whose expression may be caused or stimulated by a variety of environmental stimuli or innate characteristics.[55] It is also

associated with so many conditions that it is sometimes uncertain if keratoconus is the 'chicken or the egg'. Several factors seem to be of significance. Keratoconus appears to be inherited in a percentage of cases. Refinements in detecting subclinical keratoconus will likely increase the both our information and the number of patients who appear to have genetically linked disease. The association of keratoconus with atopy and more specifically with eye rubbing appears to be clinically important both from a prognostic and preventative perspective. Like with other aspects of this unusual disorder, contact lens wear appears to be both a boon and a bane; in some cases possibly contributing to the genesis of the disease, while in other cases being a sight saving last resort.

HEREDITY

A genetic basis for keratoconus has long been suspected. However, making an absolute case for genetic transmission has proved illusive. Keratoconus is a complex disorder with a large variety of associated factors and conditions. Several cases of familial transmission have been reported,[65,66,67,68] including some cases occurring in identical twins.[65,67,69,70] However, separating and distinguishing heredity from a myriad of other potential causative factors is a daunting task. Many authors believe that keratoconus shows autosomal dominant transmission[65,67,68] with incomplete penetrance and variable expressivity,[71] although both sex linked and autosomal recessive

transmission have been considered. Variation in diagnostic criteria makes comparison of different studies difficult. Amsler recognized a mild forme fruste variant of keratoconus using a Placido's disk.[2] More recent studies, utilizing computer-assisted topographic analysis, have confirmed a significant percentage of variably affected relatives of patients with clinical keratoconus.[72,73,74] These studies support earlier conclusions of dominant inheritance with variable expressivity and incomplete penetrance. In practice somewhere between six to eight percent of all cases of keratoconus appear genetically transmitted. However, the certainty of genetic transmission is muddled by incomplete penetrance, variable expressivity, and the role of numerous partially understood factors that likely play a role in facilitating the expression of this disorder. .

EYE RUBBING & ATOPY

Upon questioning, an overwhelming number of keratoconus patients will admit to vigorous eye rubbing. The close relationship between eye rubbing and keratoconus has been noted by several authors.[75,76,77,78] The prevalence of eye rubbing among keratoconus patients is reported to range from 66% to 73%.[76] This extraordinarily high figure is strongly suggestive of a causal relationship. The mechanism by which eye rubbing produces corneal change appears to be direct trauma. A breakdown in

corneal tissue already weakened from prior inflammation or disease has been hypothesized as the cause.[78] However, this has not been proven.

Eye rubbing may also explain the link between keratoconus and a variety of systemic and local ocular disorders and conditions. Any stimulus that produces itching or irritaion can also cause eye rubbing and hence keratoconus. Although atopy is frequently cited as a concomitant of keratoconus, the eye rubbing associated with it may be a more proximate cause. In a review of sixty-seven patients with keratoconus, patients with and without atopy did not differ significantly with regard to sex, age of onset, or rate of keratoplasty. However, patients with very high IgE levels were more prone to graft rejection.[79] Atopy was less common in patients with unilateral keratoconus, and keratoconus occurred more frequently on the side of the dominant hand.

CONTACT LENS WEAR

In a perverse twist, contact lenses appear to be both the treatment of choice as well as a possible cause of keratoconus. Although the etiology of keratoconus is not fully understood, significant evidence points to corneal trauma as capable of precipitating the disease in susceptible patients. Despite being of vastly different magnitudes, it seems possible that the gross trauma caused by vigorous eye rubbing and the

concentrated micro-trauma of rigid contact lens wear may both produce similar consequences. Several studies suggest that prior contact lens wear is a factor in the development of keratoconus.[80,81,82,83] However, the reader should be cautioned that cause and effect are not clear in this contact lens causes keratoconus equation. Keratoconus is a heterogeneous disorder[55] with complex links between causative factors and difficult to isolate individual factors. For example, increased eye rubbing associated with contact lens wear may be a more proximate cause than lens wear itself.[78] Patients with early or subclinical keratoconus may also be more likely to choose rigid contact lenses over eyeglass correction because of the improvement in vision that contact lenses afford. This tendency is also reflected in the high incidence of contact lens wear and keratoconus among prospective refractive surgery candidates.[84]

The diagnosis of keratoconus may be muddled by prior contact lens wear. It is important to differentiate corneal warpage caused by contact lens wear from true keratoconus. Corneal warpage occurs in both rigid and soft contact lens wearers and can be either transient or permanent.[85,86,87,88,89,90,91] Nearly all reports of warpage have been in patients wearing rigid lenses, especially those made from older and less permeable materials. This may be due to molding effects associated with contact lens induced corneal edema.[92] However, corneal distortion does occur in soft lens wearers and in some cases may so closely mimic keratoconus that even the expert examiner

may be fooled. Rigid lens patients are more likely to suffer from corneal warpage and less likely to be symptomatic because of the masking effects of rigid lenses.[90] In most patients, cessation of lens wear will resolve lens induced warpage. However, in rigid lens wearers, it may take up to 6 months to achieve stable topography.[93] Resolution in soft lens wearers usually takes several weeks. Corneal warpage may be permanent in some patients. When apparently permanent corneal distortion is encountered in a soft lens wearer, keratoconus must be suspected as the cause. However, this is not necessarilly true in rigid lens wearers. I have found that restoration of normal topography may be accomplished by refitting affected patients with thinner rigid lenses and more permeable materials — making parameter changes as needed. Prior contact lens fitting relationships and position may have a marked effect on the topography of corneal warpage with relative flattening of the cornea underlying the habitual resting position of the contact lens.[90] High riding lenses produce superior flattening and inferior steepening characteristic of keratoconus or in some cases pellucid degeneration.[93]

Differentiating early keratoconus from lens induced warpage may be difficult. One important clue is that lens related warpage will often have distinct borders that approximate the habitual position of the contact lens.

The question of whether contact lens wear can lead to keratoconus is an important one, especially for patients who are interested in wearing contact lenses. Unfortunately, this is a difficult question to answer. Several cases of unilateral keratoconus have occurred in patients who had worn a rigid lens only in the affected eye prior to developing the disease. The pathologic examination of a corneal button from a contact lens wearer who developed keratoconus was also consistent with keratoconus.[94] While this evidence is suggestive, it is not conclusive. Currently, all published studies lack adequate controls and a large enough populations to draw firm conclusions from. Two large retrospective studies examined the prior contact lens history of patients diagnosed with keratoconus.[95,96] These studies showed 17.5%[95] and 26.5%[96] of patients had worn contact lenses prior to the diagnosis of keratoconus. Again, this data is highly suggestive but not indicative of a cause and effect relationship. The most comprehensive review of keratoconus patients to date examined 398 eyes of 199 patients with keratoconus and found 106 eyes of 53 patients with an association between contact lens wear and the development of keratoconus.[97] Keratoconus was diagnosed after a mean of 12.2 years of contact lens wear. A comparison of this group to patients with sporadic keratoconus unrelated to prior contact lens wear showed that they were older at the time of diagnosis, had central vs. decentered cones, and had a tendency toward flatter corneal curvatures. The

differences between these two groups were highly suggestive of a causal link between contact lens wear and keratoconus which the authors concluded was likely.

An overview of the evidence seems to suggest that prior contact lens wear may be a risk factor for the subsequent development of keratoconus. However, this may be true only in patients who are otherwise susceptible or have additional risk factors for the disease. Contact lens related corneal warpage may precede the development of full-blown keratoconus or it may be an associated but unrelated phenomenon. If the former is true and there is a "point of no return" where disease irreversibly begins, it may be possible to intercede before keratoconus develops. Contact lens practitioners should be aware of this possible link between rigid lens wear and keratoconus and monitor patients proactively. New computer assisted topography devices will be helpful in discovering early signs of corneal warpage.

ABNORMALITIES IN OCULAR RIGIDITY & STRUCTURE

Several authors have suggested that biomechanical abnormalities or defects in the tensile strength of ocular tissues may be a factor in eyes with keratoconus. It is uncertain if such abnormality is a causal factor in the development of keratoconus or a manifestation of a generalized ocular defect of which keratoconus is one part. Abnormally low scleral rigidity has been suggested as a possible etiology of

keratoconus.[98] However this hypothesis has been questioned.[99] Measurements of Young's Modulus (Y), which represents the elastic properties of tissues, and ocular rigidity (E) are abnormally low in eyes with keratoconus.[100] Ocular rigidity also appears to correlate well with corneal thinning,[101] suggesting that a common etiology is at play.

This can cause Goldmann applanation pressures to be falsely low especially in eyes with lower ocular rigidity and significant corneal thinning. However, pressures taken by Mackay-Marg tonometry appear to be normal in keratoconus eyes. Several studies have demonstrated reduced stress at the corneal apex in keratoconus.[101,102] The limited loss of structural tissue and lower rigidity in the cone results in reduced apical stress and decreased likelihood of rupture.

SYSTEMIC DISEASE

Keratoconus has been associated with systemic and ocular diseases. The role of atopy has already been discussed. Down's syndrome or trisomy 21 is a systemic disorder caused by a chromosomal anomaly: usually an extra chromosome at position 21. A high prevalence of keratoconus in these patients has long been recognized.[103] The reported incidence of keratoconus in Down's syndrome patients varies from about 5% to 15%.[104,105,106,107,108] Comparison of patients with Down's syndrome to other mentally retarded patients in the same institution show a much higher incidence of keratoconus the Down's syndrome patients.[106,108] However, behavior may play a role in

the pathogenesis of keratoconus in these patients. Down's syndrome patients have been observed to be frequent and vigorous eye rubbers.[104] This also may explain the increased incidence of acute hydrops that occurs in patients with Down's syndrome and keratoconus.

Keratoconus has been associated with systemic connective tissue disorders and dysplasias. Although the reason for this relationship is uncertain a shared defect in collagen biochemistry (synthesis, turnover, or metabolism) that effects both the cornea and collagen in other body tissues would seem likely. Several studies have linked joint hypermobility and mitral valve prolapse with keratoconus. Excessive joint hypermobility, especially of the metacarpo-phalyngeal and wrist joints is statistically linked to keratoconus.[109] Mitral valve prolapse appears to have a similar link.[110] Fifty-eight percent of patients with advanced keratoconus were found to have mitral valve prolapse by two dimensional echocardiography.[111] This compares to only 7% of patients in a group of age and sex-matched controls. The clinical, histopathological and biochemical similarities between the two conditions and keratoconus support the hypothesis that they may all be different manifestations of similar defects in collagen metabolism. Despite the logic of this, other investigators have failed to find an association between mitral valve prolapse, joint hypermobility and keratoconus.[112]

Keratoconus has been associated with the systemic collagen disorders: osteogenesis imperfecta, Marfan's syndrome, and Ehlers-Danlos syndrome. However, it is most commonly seen with the latter disorder. Ehlers-Danlos syndrome is actually a heterogeneous group of disorders with abnormally cross-linkage of collagen. Affected patients have tissue fragility, hypermobile joints, hyperextensible skin and bleeding diathesis. Type VI Ehlers-Danlos syndrome is associated with significant ocular findings including keratoconus.[113] Blue sclera, a common finding associated with osteogenesis imperfecta, has also been linked to keratoconus.[114] There have also been several reports of keratoconus with bone and connective tissue dysplasias such as Marfan's syndrome[115,] and Crouzon's syndrome.[116]

Several other systemic disorders have been reported to occur with keratoconus. The relevance and importance of these sporadic reports must be questioned. I have observed a case of bilateral keratoconus in a patient with Steven's Johnson syndrome. However, in this case vigorous eye rubbing was a more likely cause than the disease itself. It is important to evaluate these possible associations in the context of the disorder. Keratoconus is also relatively common. There mere coincident presentation of another disorder with keratoconus is not proof that the two conditions are linked.

OCULAR DISEASE

In addition to the ocular manifestations of systemic disorders such as atopy, keratoconus has been associated with a variety of disorders limited to the eye and surrounding structures. Ocular disorders that occur with keratoconus may share a common etiology, or be causal or coincidental. The majority of ocular conditions are most likely coincidental.

Several authors have reported an association between tapetoretinal degeneration such as retinitis pigmentosa and keratoconus.[117,118] Leber's congenital amaurosis, an infantile form of tapetoretinal degeneration has been frequently associated with keratoconus and cataract.[119] Although some authors have postulated that keratoconus in these patients is due to eye rubbing associated with poor vision (the oculo-digital sign), a recent study conducted in schools for the blind found that Leber's amaurosis rather than poor acuity was specifically associated with keratoconus.[120] Acquired retinal diseases have also been associated with keratoconus. A patient with a bilateral pigmented retinopathy following measles and keratoconus was recently reported.[121]

Disorders of the iris have been associated with keratoconus. Although keratoconus has been reported to occur with aniridia this has not been substantiated. Iridoschisis in a patient with keratoconus was recently reported.[122] The authors believed that the common embryological derivation of the posterior layers of the cornea and the iris

stroma suggest an inter-related pathogenesis. Progressive essential iris atrophy and keratoconus has been described.[123] Several discrete corneal findings appear in patients with keratoconus. Posterior polymorphous dystrophy and familial keratoconus have been reported.[124,125] Keratoconus has been associated with endothelial dystrophy,[126] Fuch's dystrophy,[127] Avellino dystrophy,[128] corneal amyloidosis,[129] and Terrien's marginal degeneration.[130] However, even where there is considerable evidence of an association, as is the case with posterior polymorphous dystrophy, the relationship between keratoconus and other corneal disorders remains uncertain.

The eyelids appear to play an important role in keratoconus. Although the relationship has not been investigated, meibomitis and blepharitis are both frequenly observed in keratoconus patients. Vernal kerato-conjunctivitis, produces an intense papillary reaction primarily beneath the upper lids. Numerous reports link vernal catarrh and keratoconus.[131,132,133] There is high rate of acute hydrops in patients with keratoconus and vernal keratoconjunctivitis. Both keratoconus and subsequent acute hydrops may be related to the excessive eye rubbing that is a frequent concomitant of atopy. Unfortunately, keratoconus patients with vernal keratoconjunctivits are less successful with contact lens wear or penetrating keratoplasty than are patients with keratoconus alone. Floppy eyelid syndrome is a recently described entity, which usually involves overweight individuals. A causative role in the genesis of keratoconus has been

suggested.[134] The characteristic findings are an upper lid that readily everts, tarsal laxity, and a frequently associated diffuse papillary conjunctival of the upper lid. Floppy eyelid syndrome appears to be a mechanical disorder caused by the habitual eversion of the lids while sleeping. It is typically more pronounced on one side. A strong association between keratoconus and floppy eyelid syndrome has been observed. Interestingly, these patients will usually sleep on the more affected side. The relationship appears to be mechanical in origin. Many patients report inadvertently traumatizing their eyes with knuckles or the edge of a pillow while sleeping. Keratoconus is often worse in the eye with the more severe case of floppy eyelid syndrome. Surgical intervention for lid laxity problems may be necessary in severely affected patients before treatment of keratoconus begins.

PSYCHOLOGICAL ASPECTS OF KERATOCONUS

Keratoconus is a disorder that typically affects patients over a period of many years. As it runs its course, it may be complicated by a variety of conditions. The condition usually progresses slowly but unpredictably. Patients never know what to expect and this uncertainty appears to be extremely disturbing and destabilizing to many of them. Anyone who has worked extensively with patients who have keratoconus come to recognize what is often termed "the keratoconus personality."

Although it is difficult to adequately describe exactly what constitutes the "keratoconus personality" its presence is usually clearly apparent to the examiner. Often the behavior appears compulsive with depression a frequent concomitant. Some patients have a strong need to retain control and may present management difficulties. Other patients are nervous, overly preoccupied with the minute aspects of their condition, and while usually willing, they are sometimes unable to comply with instructions. Many patients come to the office with long "laundry lists" of questions. Some questions are repeated several times and are merely reworded variations of those previously asked. Interestingly, patients are often hesitant to surrender their lists to the examiner.

Psychological evaluation of keratoconus patients has been inconclusive. One study using the Minnesota Multiphasic Personality Inventory (MMPI) found scores indicative of psychological abnormality in 15 of 28 (54%) keratoconus patients compared to .4 of 16 (25%) control patients with herpes simplex keratitis.[135] Keratoconus patients who had undergone penetrating keratoplasty had a lower rate of abnormal scores. Another study of 109 subjects, using a standardized personality inventory (the Millon Clinical Multiaxial Inventory) that measures 20 normal and pathologic personality indicated that chronic eye disease rather than keratoconus had an impact on personality functioning. However, no specific complex of personality characteristics attributable to keratoconus could be identified.[136]

TREATMENT

The treatment of keratoconus can be divided into two categories: surgical and non-surgical. There is currently no medical treatment available. The primary goal of all treatment is to provide adequate vision. The first surgical attempts to managing keratoconus consisted of paracentesis followed by pressure patching.[137] This was followed by a variety of less than effective techniques ranging from partial surgical removal of the cone to repositioning of the pupil to avoid the cone. The first penetrating keratoplasty for keratoconus was performed by Castroviejo in 1939. In recent years, other surgical strategies have emerged. Inlay lamellar keratoplasty, onlay lamellar keratoplasty (epikeratophakia) and thermokeratoplasty have all been advocated by various authorities. The non-surgical management of keratoconus is essentially refractive. When spectacles no longer provide adequate vision contact lenses are the preferred form of treatment for keratoconus. A variety of contact lenses have been used including scleral and corneal lenses, rigid, soft and hybrid lenses, and piggyback designs.

CONTACT LENS MANAGEMENT

Contact lenses are an effective therapeutic option for a majority of patients with keratoconus. Interestingly, the very development of contact lenses appears owed, at

least in part, to their utility in treating keratoconus. In the first published description of scleral contact lenses, Adolf Fick describes their ability to correct irregular astigmatism caused by keratoconus.[138,139] He proceeded to fit scleral lenses on several patients including one with keratoconus. A contemporary, Dr. Eugene Kalt, also fitted several keratoconus patients with glass shell scleral lenses during the same period.[140] Although newer materials have once again made scleral contact lenses a viable option in severe keratoconus,[141,142,143] the majority of patients are fitted with corneal rigid gas permeable designs. Fitting keratoconus patients can be extremely challenging, however, with care and experience, approximately 90% of keratoconus patients will be able to successfully wear contact lenses. In one series of 190 keratoconic eyes 165 eyes (87%) were successfully fitted or refitted.[144] Another large, 20 year retrospective study of contact lens use in keratoconus showed a success rate of 95%.[145] In the hands of an expert, even previous contact lens failures can often be refitted. This is proven in several recent studies reporting a majority of previously contact lens intolerant keratoconus patients being successfully refit and achieving excellent visual acuity and prolonged wearing times.[146,147,148] Contact lens options should be fully exhausted by an experienced specialist prior to surgical intervention in these patients.

The primary indication for fitting contact lenses in keratoconus patients is vision that is no longer adequately corrected by spectacles. Visual function is highly subjective. Not

all patients with poor vision, especially when one eye still functions well, are sufficiently motivated for contact lens wear. Fortunately, myopia often precedes the frank presentation of keratoconus and a surprisingly large number of patients have prior contact lens experience. For the inexperienced patient who might benefit from contact lens fitting, a demonstration of the visual improvement with topical anesthetic can provide strong motivation. Once a patient begins contact lens wear, they tend to become dependent upon their lenses and unhappy when they are unable to wear them.

RIGID CONTACT LENSES

Corneal lenses made from rigid gas permeable materials are commonly used in the correction of keratoconus. Over the past decade, rigid gas permeable materials have largely replaced older PMMA. These new materials have been helpful in extended wearing times and reducing complications of rigid lens wear. A number of special and unique lens designs have been developed specifically for keratoconus fitting. However, the skilled application of conventional lens designs are often extremely effective.

Proper fitting with conventional RGP lenses requires careful manipulation of the lens' sagittal depth. The sagittal depth is controlled by a combination of lens radius and diameter. Three basic and distinct fitting relationships are achievable. Each relationship has advantages and disadvantages. An "apical bearing fit" applies the bulk

of lens generated forces over a relatively small area corresponding to the corneal apex. It produces a large contact patch and flattening over the corneal apex. Advantages of this design include relative ease of fit and the possible use of larger lens diameters with a lid attachment fit for increased stability. Small improvements in visual acuity have been noted.[149] The "apical clearance fit" 'vaults the central cornea with the bulk of lens support and bearing applied to the paracentral and, to a lesser extent, the peripheral cornea. This design is rarely used in practice since the paracentral bearing area often creates an effective seal that interferes with the tear flow beneath the lens. The "three-point touch" fit evenly distributes lens support and bearing over the corneal apex and paracentral cornea. This fitting approach usually offers the best results but is most demanding for the fitter. Only a small number of lens base curve and diameter combinations will result in an even distribution of bearing forces.

Clinically, the apical touch fit is ideal for patients with small and steep nipple cones who experience glare and flare when a smaller lens fit is attempted. Such visual disturbance is especially common in younger patients with larger pupillary diameters. A three-point-touch design in these patients often requires an extremely small lens diameter. However, caution must be used with an apical touch fit. Excessive lens bearing combined with even moderate lens movement can lead to apical scarring and rapid visual loss. The smaller the lens' contact patch the greater the likelihood of scarring. I

have found that controlled movement and reasonable distribution of lens bearing forces requires a contact patch of not less than 4 mm. Once the appropriate lens radius is determined and the size of the contact patch idealized, the diameter of the lens can be varied to control edge lift and bearing. Patients fit with this technique require frequent follow-up visits to insure that excessive apical staining and scarring does not result. In cases where scarring occurs alternative designs should be considered.

For most patients with keratoconus, a three point touch contact lens design is ideal. This technique produces a lens that floats gently over the irregular corneal surface effortlessly and with minimal bearing. It is achieved by controlling the sagittal depth of the lens to match the topographic profile of the cone. Since the diameter and steepness of the cone can vary significantly, it is difficult to create a simple formula to generate a successful three-point-touch lens fit. In general, the steeper the corneal apex the smaller the lens radius that will be required. The explanation for this requirement of lens design is that this type of fit requires that the contact lens mimics the average topography that it overlays. As the corneal surface steepens, the variation in topography increases more rapidly over smaller and smaller corneal surface areas. The smaller the diameter of the contact lens the less the lower the amount of topographic change that needs to be accommodated.

Several specially designed contact lenses have been developed. Perhaps the best known of these is the Soper Lens.[150] In some ways the fitting philosophy is opposite to that of the of the three-point-touch design. The sagittal vault is increased by decreasing base curve radius but with Soper design lens the diameter is increased. This requires a bicurve design with a steep central curve to accommodate the cone and a flatter peripheral curve to align with the relatively normal peripheral cornea. Soper lenses are fitted by varying the sagittal depth until just before apical touch is achieved. Maguire also produced a similar fitting set. Although this type of design may be helpful in more challenging cases where other approaches fail it is difficult and time consuming to fit properly. Several proprietary keratoconus designs have been introduced. The most popular, the Rose K, was designed by New Zealand optometrist, Paul Rose.

Aspheric lens designs optimized for keratoconic corneas are a viable option for some patients.[151] These include the Elipsicon by Conforma Labs. Similar lens designs are available from other specialty rigid lens laboratories. I have found that these lenses are more easily fitted than keratoconus specific Soper or Maguire lens designs. Computer assisted fitting techniques may be also useful with these new lenses.[152] They are especially helpful in complex cases where the corneal topography is overly demanding.

ALTERNATIVE CONTACT LENS DESIGNS

When conventional rigid lenses cannot be fitted several alternatives are available. Hybrid lens designs such as the SoftPerm by Ciba Vision are may be used especially in patient with mild or early disease.[153,154] This lens consists of a rigid center and a soft skirt. From the patient's perspective, the effect is a lens with the comfort of a hydrophilic lens and visual characteristics approaching that of a rigid lens. Until recently such designs were only useable in early keratoconus. The available parameters were generally too flat to adequately fit most keratoconic corneas. However, a special limited set of keratoconus lenses have been introduced with steeper central and peripheral curves. Fitting this lens requires a special, high molecular weight fluorescein (Fluoresoft™) that is not absorbed by the soft carrier portion of the lens. The fluorescein is instilled into the bowl of the inverted lens before it is placed in the eye. Conventional SoftPerm lenses almost always will produce a large central bearing area. However, support by the soft periphery helps to mitigate some of the bearing forces and reduces possible damage to the corneal apex. In some cases a lens that appears overly flat will produce a comfortable and functional result. The primary problem with this lens is that the relationship between the central and peripheral elements of the lens cannot be varied. Because the central cornea is much steeper than the periphery, there is a tendency to fit the lens too steeply to accommodate the cone. This can cause an overly tight and immobile lens and an acute red eye. This is

especially problematic with the recently introduced keratoconic set where the peripheral relationship is especially tight.

Another possible approach in fitting patients with more advanced keratoconus is the piggyback fit. This entails first fitting a soft lens as a base followed by a rigid lens to optimize the vision. The soft lens in the piggyback system assists in stabilization of the rigid lens by essentially flattening and elevating the cone.[155] It can also dramatically increase patient comfort.[156] a moderate plus carrier lens provides a more stable base. However, too much plus power should be avoided. Improved centration of an unstable rigid lens can also be achieved by using a specially designed carrier lens with a central depressed groove. The lens nests within the depression which reduces movement and lid contact. Currently, Flexlens, Inc. (?) makes a custom designed lens for this purpose. Both lenses need to be fitted with care. Both the soft carrier and rigid component should center well and have adequate movement. Generally, fitting a rigid lens in this manner is much easier than fitting the same keratoconic cornea directly.

Contact lens discomfort is serious problem for some keratoconus patients. Although soft lenses might be ideal solution, corneal distortion and irregular astigmatism may preclude a successful fit. In many mild or early cases soft lenses can be effective.[157] In more advanced cases specially designed soft toric lenses will be necessary. When

spherical lenses are necessary, vision can be sometimes be maximized with spectacle overcorrection.

PROBLEM SOLVING KERATOCONUS CONTACT LENSES

The problems that are associated with contact lens fitting and keratoconus can be divided into two distinct groups: contact lens complications and fitting problems. The contact lens complications associated with keratoconus are, for the most part, similar to those encountered by normal contact lens wearers. There is a higher incidence of atopy in this population which can affect lens comfort and, in severe cases, the very ability to tolerate contact lenses wear. Rigid lenses can compress the cornea to produce an anterior mosaic, a pattern highlighted by sodium fluorescein that is normally produced by pressure on the cornea through the closed eyelids.[158] Transient rigid lens-induced striae in the deep cornea in early keratoconus has been reported.[22] Both of these findings are transient and do not appear to be harmful. Corneal abrasion as demonstrated by fluorescein staining is common with rigid lenses. Patterns unique to keratoconus are pooling within central epithelial folds from compression of the thinned cone and hurricane keratopathy, a swirl pattern overlying the corneal apex caused by excessive lens bearing and movement over the cone.

Poor vision despite an adequate contact lens fit may have several distinct etiologies. Reduced vision may be due to coexisting pathology unrelated to the keratoconus. It may be caused by corneal scarring or opacification. Apical scarring occurs in patients who have never worn contact lenses, However, a poorly fitted lens having excessive apical bearing can cause superficial — and in some patients — dense apical scars.[159] High irregular astigmatism and corneal distortion that is not sufficiently masked by the contact lens can profoundly reduce vision. Solutions include flatter fitting relationships (this is subject to debate and current investigation), thicker lens designs, and aspheric base curve contact lenses. Perhaps the most common but frequently overlooked reason for reduced vision in these patients is residual astigmatism. This is often due to a lenticular component or in some cases by extremely high corneal cylinder. Spectacles provide the simplest and most direct mode of overcorrection in the keratoconic contact lens wearer. Attempts at fitting anterior toric or bitoric lens designs are almost always doomed to failure because of the extreme surface irregularity encountered in these patients. It is important to perform a careful sphero-cylindrical over-refraction in any keratoconic contact lens patient with unexpectedly poor acuity.

There has been some debate as to the stabilizing influence that contact lenses may have upon the cornea with keratoconus. The relationship between contact lenses and the genesis of keratoconus has already been discussed (see page 17). However, there

is some question in the literature over their "therapeutic" effect on the disease. Despite much debate regarding the supposed ability of rigid lenses to retard the progression of keratoconus there is no definitive evidence that rigid contact lenses have any long term on the progress of the disease.

PENETRATING KERATOPLASTY

Penetrating keratoplasty (PK) is the generally preferred and most commonly performed surgical procedure for the correction of keratoconus. It is also among the safest and most successful surgeries performed on the eye. Two large series of penetrating keratoplasties, each with more than 300 patients, showed a percentage of clear grafts in excess of 90%.[160,161] Keratoconus currently accounts for approximately 10% to 22% of all PK's performed.[162] The primary indications for penetrating keratoplasty in patients with keratoconus are contact lens intolerance, progression of the cone toward the corneal limbus, and, in severe cases, threatened corneal perforation. Uncomplicated corneal hydrops, although frightening to the patient in appearance is not an indication for surgery. A majority of contact lens intolerant keratoconus patients can be successfully refitted with some effort.[163,164] Because of the high success rate in refitting these patients, reevaluation of the contact lens intolerant patient prior to surgery is prudent.

Penetrating keratoplasty is highly successful in keratoconus patients. A study of 201 penetrating keratoplasties in 198 eyes of 158 patients covering a 20 year period showed a five year graft survival of 97%.[165] Despite high postoperative astigmatism and myopia the majority of patients experience a significant improvement in vision. Another study found a mean postoperative (sutures-out) astigmatism of 5.4 diopters, 45.5% of patients saw 20/20, 90.7% 20/30 or better, and 97.7% 20/40 or better one month after suture removal with spectacle correction.[166] A rapid recovery of post-surgical visual acuity is common. By 12 months, 91% of patients attain best-corrected vision of at least 20/40.[167] The rapid recovery in acuity has been confirmed by computerized topographic analysis.[168] The improvement occurs in both Snellen acuity and contrast sensitivity.[169]

Surgical techniques vary. The procedure is usually performed under local anesthesia — either peribulbar or retrobulbar. Intravenous sedation is commonly used. In cases where patient cooperation is poor or with younger patients, general anesthesia may be necessary. To reduce the likelihood of expulsive choroidal hemorrhage or protrusion of the intraocular contents, preoperative reduction of intraocular pressure is accomplished either by digital massage combined with devices such as the Super Pinky or Honan Balloon. Occasionally, hyperosmotic agents such as intravenous mannitol are used. Penetrating keratoplasty is precise and exacting. It requires an extremely stable field.

The patients head is carefully positioned so that a vertical line passing straight through the corneal apex is perpendicular to the horizontal. A sponge headrest placed beneath the head is frequently used to help maintain stability and patient comfort.

The globe may be stabilized by one of two methods. In phakic patients, traction sutures are placed though the superior and inferior recti and then fixed to the surgical drape. In the aphakic or pseudophakic patient a Flieringa ring (scleral ring) is sutured to the sclera approximately 3-4 millimeters from the limbus. Sutures extend from the ring to the surgical drape for additional fixation. Some surgeons prefer to use a scleral ring at all times. Donor tissue is obtained from a certified eye bank. The enucleated globe is obtained as rapidly as possible after death of the donor and kept refrigerated without freezing. While whole eyes may be used up to 48 hours after death of the donor, the cornea with a surrounding rim of sclera may be maintained in a storage medium such as K-Sol (chondroitin sulfate) for up to 7 days after donor death. The criteria used to select donor material are both extensive and comprehensive. It is designed to insure viability of the tissue and to prevent transmission of disease.

A trephine, a device resembling a cookie cutter, is used to remove the corneal button in both the donor and the recipient. The depth of the trephine blade is adjustable and the actual cut is made by circular rotation of the device. Freehand trephines are most

commonly used although suction assisted and motorized trephines are available. Trephines come in several sizes depending upon the desired graft size. In general, larger grafts are used in keratoconus or with eccentric corneal thinning or scarring. Smaller grafts are preferred when existing corneal disease has an inflammatory component that might lead to vascularization and rejection and when transplants are performed on pediatric patients. The donor button is obtained by trephination from the endothelial side. Many surgeons select graft sizes of 8.0 to 8.5 mm for keratoconus patients. Tissue from younger patients is preferred to increase long-term survivability of the graft. The relative size of the donor button may be a more important consideration than is absolute size. The button is typically made 0.25-0.50 mm. oversize, since a cut from the endothelial side is smaller in diameter than one made from the epithelial side. However, recent reports suggest that oversize donor buttons cause increased corneal curvature and a significant increase in myopia.[170] Large donor buttons also have a greater propensity for later graft rejection.[171] The use of grafts 0.25 mm smaller than the trephine opening in the host (i.e., 8.00 mm button with an 8.25 mm opening) for penetrating keratoplasty in keratoconus appears to reduce postoperative astigmatism and myopia.[172]

The recipient bed is created by using the trephine to produce a partial thickness incision in the cornea. Prior to the cut, the trephine is carefully centered over the pupil and a

light impression made in the superficial epithelium. When alignment is confirmed, the cornea is dissected to between 50 and 90% of the corneal thickness. Care is used to not penetrate the anterior chamber with the trephine. The anterior chamber is entered with a sharp pointed knife and allowed to gently decompress. The incision may be completed with the blade run around the trephined ring or curved scissors may be used to complete the incision. Ideally, the wound edges are made square, however, some surgeons prefer a slight posterior bevel so as to form a gasket like seal around the host-donor interface. Excessive posterior bevel can create irregular astigmatism.

A viscoelastic material is used to deepen the anterior chamber and the donor button is brought to the recipient bed. The button is carefully fixed in position by a suture placed at 12 o'clock. 10-0, 11-0 monofilament nylon or a combination of both are most frequently used. Most surgeons place additional interrupted sutures at the 3, 6, and 9 o'clock meridians. Final suturing technique varies with surgeon preference. Either interrupted, running, or a combination of both types are used. An advantage of the concurrent use of running and interrupted sutures is that selective interrupted suture removal may be helpful in mitigating postoperative astigmatism.[173] Keratometry and, to a even greater extent, computerized corneal topography, is helpful in planning selective suture removal strategies. In all cases the sutures penetrate approximately 70-80% of the corneal thickness. They are placed 0.75 mm. into the donor tissue and

extend close to the limbus. Tension is equalized between individual sutures or bites of a running suture and any exposed knots are buried. After the traction sutures or the Fileringa ring is removed, most surgeons inject antibiotic and steroid medication subconjunctivally. The eye is patched using a rigid shield and the patient is scheduled for examination the next day. Postoperatively, patients are followed closely and treated with topical steroid drops at least until anterior segment inflammation is minimal. Patients must be carefully monitored for complications of topical corticosteroids such as posterior subcapsular cataract and increased intraocular pressure.[174] Suture removal depends on several factors. Selective suture removal may begin as early as several months postoperatively. In cases where acuity is excellent with the sutures in place, the surgeon may opt to leave them in place for a longer period. Since healing typically progresses more rapidly in younger patients, sutures are often removed earlier in the young.

Although penetrating keratoplasty is often successful, post surgical complications range from visually disruptive to serious and sight threatening. An excellent surgical result may not always translate to a good visual outcome. Patients find it especially disconcerting to hear that their surgery was successful when they cannot see any better than before the surgery. Postoperative myopia and astigmatism are may reduce vision directly or from aniseikonia. Myopia is common in keratoconus patients and may not

be related to the surgery or surgical technique.[175] Residual postoperative astigmatism has been especially problematic and has resisted various techniques to eliminate or reduce it. Recently, several new approaches to reducing refractive complications have been described. The use of smaller size donor material may help to reduce postoperative myopia and astigmatism.[172,176] Surgical technique may also play an important role in reducing postoperative astigmatism. Selective positioning of the donor button using a Troutman Keratometer [177] and the using the Krumeich guided trephine system may significantly reduce final postoperative astigmatism compared to more conventional surgical approaches.[178] However, improvements using these advanced techniques have not been consistent.[179] Increased interest in refractive surgery has also produced new techniques to manage astigmatism in post-penetrating keratoplasty patients. Relaxing incisions, compressive resuturing, and augmented relaxing incisions can reduce postoperative cylinder significantly.[180]

Relaxing incisions reduce post-surgical residual astigmatism and surface irregularity. Arcuate incisions are made 180° apart at both ends of the steep meridian. The effect of the incisions is dependent upon length, depth, and proximity to the visual axis. The effect increases dramatically the more central the incision. Incisions are usually made at the slit lamp or operating microscope under topical anesthesia. A careful refraction and keratometry are performed. Computerized corneal topography is invaluable in planning

the incision sites and characteristics. A relaxing incision can eliminate between five and ten diopters of astigmatism. If additional reduction is required augmentation sutures are placed 90° from the steep meridian. Typically six sutures are used, three to a side. The middle suture is made the tightest for increased steepening along the flat meridian. The sutures are removed as the incisions heal and stabilize.

A corneal wedge resection is performed when higher amounts of corneal cylinder are involved. In this procedure, a wedge of corneal tissue is removed along the flatter corneal meridian at the graft margin. The edges are sutured tightly together and the wound allowed to heal over several months. The wedge resection can create significant irregularity that may complicate rigid lens fitting. Relaxing incisions are preferred when contact lenses are to be worn.

Corneal surface irregularity, high amounts of astigmatism, or significant anisometropia, may require contact lenses to restore adequate vision in the post-penetrating keratoplasty patient. In most cases, rigid gas permeable lenses will be needed. Fitting these patients can be a challenge. Post-keratoplasty contact lens fitting is often more difficult than fitting keratoconus patients prior to their surgery. Adjunctive keratorefractive surgery maybe helpful in reducing corneal cylinder prior to contact lens

fitting. More recently LASIK surgery has been performed post-keratoplasty with variable success.

Graft rejection is the most serious yet common postoperative complication. The incidence of graft rejection in keratoconus patients is reported to vary from 10 to 20%.[165,181] Graft failure is rare. However, the reported rates vary. Some authors have reported a 37% incidence of allograft rejection and 9% rejection-related graft failure rate.[182] This is significantly higher than normally encountered in clinical practice. Factors associated with higher incidence of rejection include loose sutures, traumatic wound dehiscence, grafts larger than 8.5 mm, and bilateral grafts.[165,171] Factors that cause corneal irritation and inflammation, including contact lens wear may precipitate graft rejection. A dramatic increase in the incidence of rejection in patients with bilateral grafts has been reported.[183] There appears to be an increased risk of rejection in the first graft after the second eye is grafted. Because of this, some surgeons use topical steroid drops bilaterally after the second eye is operated on. Other investigators have not found an increased risk of rejection in these patients.[184,185]

Rejection episodes may occur at any time after surgery, from a few months to many years. Graft rejection is usually easily to recognize. It may involve only the epithelium or the entire cornea. Epithelial rejection initially presents as a slightly elevated line that

moves rapidly across the cornea. It will often progress to endothelial rejection if left untreated. Subepithelial infiltrates, similar to those seen in adenovirus infection, may also be seen. Epithelial rejection alone is a relatively benign condition that rapidly responds to topical steroids. A full blown endothelial rejection is far more ominous. Interference with normal endothelial function produces corneal edema and stromal thickening. The edema may be primarily central with a relatively sudden onset, keratic precipitates on the endothelium and a marked anterior chamber reaction. Alternately, it may occur at the host-graft interface with engorgement of marginal blood vessels, fine keratic precipitates, and anterior chamber cell and flare. The keratic precipitates may form a Khodadoust (rejection) line on the endothelial surface.

Signs of corneal rejection include pain, injection, tearing, ocular discomfort, and reduced vision. These symptoms also occur as a complication of contact lens wear, creating possible confusion for patients. Patients with corneal transplants should be advised to report such symptoms immediately. The prognosis is generally good if the rejection is recognized quickly. Rapid treatment is critical. Initial treatment with a topical steroid like prednisolone acetate 1% every waking hour followed by steroid ointment (Dexamethasone 0.1%) at night. Cycloplegia may be helpful in reducing discomfort. Concurrent management of elevated IOP may also be necessary. Patients who do not respond may require more aggressive systemic or subconjunctival steroid

treatment. Prolonged or uncontrolled rejection episodes may lead to graft failure. As inflammation subsides, antiinflammatory treatment is tapered slowly. The overwhelming majority of rejection episodes can be controlled medically.[181] However, even when successfully managed, graft rejection can have a deleterious effect on corneal endothelial cell density.[186]

Although grafts in keratoconus are generally successful, graft failure and subsequent regrafting can be problematic. Graft survival after multiple regrafts is typically poor.[187] Risk factors for graft survival in transplant patients include the primary diagnosis, number of previous corneal transplants, previous transplant failures from rejection episodes, transplant size, recipient corneal vascularization, donor age, recipient age and sex, past blood transfusions, and even the number of pregnancies.[188] Immunologic mechanisms, particularly cellular immunity, appear to be responsible for the majority of cases of graft failure.[189] Cellular immunity appears to be under the genetic control of a region on chromosome 6 known as the major histocompability complex (MHC). The expression of cellular immunity in humans is controlled by the human leukocyte antigen (HLA) system. Greater understanding of the distribution of HLA system major histocompatibility antigens in the cornea has suggested that tissue typing and matching class I and class II HLA antigens result in a higher success rate for corneal transplantation. Several studies have confirmed that HLA-A, B and DR compatibility

between donor and recipient appears to have a positive effect on transplant survival.[190] HLA tissue matching is advised in high-risk patients. In keratoconus patients this includes individuals that have had prior transplants or graft failure. Keratoconus has been reported to recur in grafts.[191,192,193]

An unusual complication of penetrating keratoplasty in keratoconus patients is the Urrets-Zavalia syndrome: a fixed dilated pupil, iris atrophy, and secondary glaucoma.[194] Several reports of this syndrome appear in the literature.[195,196] A keratoconus patient presenting with a fixed dilated pupil prior to penetrating keratoplasty has also been described.[197] The authors attributed this case to local ischemia of the iris' sphincter muscle. The prevalence of Urrets-Zavalia syndrome is variable. Many surgeons have not encountered a single case while others report an incidence of nearly 18%.[195] No etiology has been conclusively identified although prior iris abnormalities and strangulation of the iris sphincter have been suggested.[196] Atropine and other strong mydriatics instilled postoperatively do not appear to play a role.[198]

LAMELLAR KERATOPLASTY

Although not presently favored by most surgeons, lamellar keratoplasty was advocated as a surgical treatment for keratoconus in the past,[199] This procedure has several advantages over penetrating keratoplasty. It is less invasive. The corneal endothelium

is not penetrated or involved in the surgery, precluding any possibility of endothelial rejection. The primary indication for lamellar keratoplasty is to replace damaged or missing tissue in the central cornea.

The procedure itself is technically difficult and requires experience and skill. The recipient bed is first outlined with a trephine and then prepared by lamellar removal of the diseased tissue. In keratoconus and other diseases where the corneal lamellae have been weakened or damaged, it is often possible to simply peel off the diseased tissue. In advanced cases of keratoconus, little tissue need actually be removed. When surgical dissection is required, a variety of techniques have been described. Regardless of technique, care must be used to avoid penetration of the anterior chamber and to achieve an evenly surfaced recipient bed. If the anterior chamber is penetrated conversion to a penetrating keratoplasty is usually necessary.
The donor material is usually prepared from a whole donor eye to facilitate dissection of the lamellar graft. If only a small amount of host tissue remains a full thickness donor button can be used after the endothelium is removed. The graft is usually cut larger than necessary and trimmed either with a trephine or free hand using scissors. It is typically made slightly thicker and larger than required. Suturing using 10-0 interrupted nylon is usual although some surgeons prefer to use interrupted sutures only to

position the button. They are then removed after a continuous running suture is placed. Removal of the sutures can begin as soon as 6 weeks after surgery.

Although endothelial graft rejection is impossible, the procedure has several potential problems that limit its utility. Foremost is possible penetration of the anterior chamber during surgery. The surgeon must be prepared to convert to a penetrating keratoplasty in this eventuality. Foreign material may also become trapped beneath the donor button during surgery. Visual results may be poor. Irregularity caused by poor technique in preparing the recipient bed or the donor button can cause optical and structural irregularity. Surgical technique and experience plays an important role in visual outcome. A recent study showed impressive visual results and progressive improvement of visual acuity in lamellar keratoplasty patients over time.[200] At six months, 11 of 23 patients (48%) had visual acuity of 20/30 or better. At one year, 17 of 23 (74%) had 20/30 or better, and at two years, 21 of 23 (91%) had 20/30 or better. Age is also an important factor. All patients less than 32 years old obtained visual acuity of 20/30 or better after two years and reached this level much sooner than patients over 32 years of age. Because of variability in outcome and technical difficulty lamellar keratoplasty has been replaced by epikeratophakia as the surgical treatment of choice for keratoconus when penetrating keratoplasty is not indicated.

EPIKERATOPHAKIA

Epikeratophakia is a form of lamellar keratoplasty. In this procedure a preshaped button of donor stromal tissue called a lenticule is placed on the deepithelialized anterior surface of the recipient cornea. Where conventional lamellar keratoplasty is primarily directed at structural reinforcement of diseased or absent tissue, epikeratophakia is specifically aimed at restoration of vision. Epikeratoplasty lenticules can be prepared from donor tissue or are commercially available in freeze-dried or unfrozen form.

The primary indication for therapeutic epikeratophakia in adults is unilateral aphakia and keratoconus. Plus lenticules are used when unilateral aphakic patients are unable to tollerate contact lenses. In keratoconus, plano lenses are used as an onlay lamellar graft to reinforce and flatten the keratoconic cornea.[201] Since the lenticule is placed over intact corneal tissue, the underlying cornea must be devoid of scarring within a 1 mm. zone surrounding the visual axis.

Epikeratophakia is less demanding than conventional lamellar keratoplasty. The host cornea is prepared by first removing the epithelium. Since epithelial cells trapped beneath the lenticule can cause later problems the surface is carefully cleaned and rinsed. A trephine is then used to create a groove like keratectomy approximately 0.3 mm deep and 0.5 mm smaller than the lenticule. This can be accomplished with a

conventional trephine followed by removal of a 0.5 mm strip of cornea tissue from the inner wall of the incision. However, use of a specially designed Barron twin blade suction trephine is preferred. It creates a 0.5 mm beveled groove with the deeper edge at the periphery. Some surgeons will perform a lamellar dissection of the stroma at the keratectomy extending about 1.0 mm toward the limbus to permit tucking of the peripheral flange of the lenticule into the shelf created by the dissection. The lenticule is carefully rinsed and placed over the host cornea. Typically 16 interrupted sutures of 10-0 nylon are placed. During suturing, external pressure may be required to flatten the central cornea. This ensures close apposition of the edge of the lenticule to the peripheral edge of the keretectomy. The ectatic central cornea of the keratoconus patient will often wrinkle and fold as it is compressed by the lenticule. These folds will usually disappear within 6 to 8 weeks after surgery. Regardless of technique, insertion of the donor tissue unto the recipient bed is much like a tongue and groove fit used in fine cabinet making. Extreme care must be used to make sure that the graft is evenly placed and tension in the sutures is evenly distributed. Failure to do so results in unwanted astigmatism and surface irregularity. At the conclusion of surgery a subconjunctival injection of antibiotic and steroids administered. Some surgeons also instill topical cycloplegic drops although their is some concern about permanent pupillary dilation. The eye is either patched or a bandage contact lens placed over the graft.

Postoperatively, the patient is examined the following morning. A bandage lens is continued or when the patient is intolerant of the lens the eye can be pressure patched until reepithelialization is complete. Patients should be reexamined every 48 hours when wearing bandage contact lenses or every twenty-four hours is they have been pressure patched. Topical antibiotic and cycloplegic drops are also used adjunctively throughout the postoperative period. The sutures are removed in about 8 to 12 weeks or sooner in younger patients or when sutures loosen or stimulate vascularization. The more common complications of epikeratophakia include failure of the graft to reepithelialized and persistent epithelial defects. Corneal scarring is a generally reported to be a rare complication. However, persistent folds in Descemet's membrane and interface scarring can reduce acuity dramatically. Histopathologic examination in these patients shows epithelial irregularity, subepithelial fibrosis and folds in Descemet's membrane and focal posterior stromal fibrosis in the host cornea.[202] Visual acuity may be also be reduced by movement of a preexisting scar into the visual axis as the cornea is compressed by the graft. However, persistent epithelial defects and irregular astigmatism are the principal factors in delay in visual recovery for most patients.[203]

Epikeratophakia is a relatively successful surgical procedure for the treatment of keratoconus. Functional success of 91% was reported in a series of 11 keratoconic

patients.[204] The improvement in acuity and structural integrity can be substantial. In another study, five of six keratoconic eyes had 20/40 or better spectacle-corrected and 20/25 contact lens-corrected acuity postoperatively; average corneal flattening was 6 D.[203] A nationwide study of epikeratophakia for the treatment of keratoconus involving 69 surgeons in the United States examined the results of the procedure on 177 eyes and was generally positive.[205] In all but two patients uncorrected visual acuity improved. In 78% of patients postoperative acuity of 20/40 or better was achieved. Eight patients required no postoperative overrefraction. The mean flattening reflected by keratometry readings was 9.36 diopters, and the mean decrease in myopia was a spherical equivalent of 5.26 D.

In comparing epikeratophakia to penetrating keratoplasty some authors believe that the visual outcome in penetrating keratoplasty is superior.[206,207] Compared with penetrating keratoplasty, epikeratoplasty offers the advantages of maintaining an intact globe surgically and postoperatively in a population that is typically young and active. It avoids potential immune rejection and is largely reversible. These benefits make epikeratophakia valuable in the treatment of mentally retarded patients.[208] The primary disadvantages are a prolonged healing period compared to penetrating keratoplasty (3 months vs. 12 months) and difficulty in define the limits of the cone to preoperatively select suitable candidates.[209] In cases where severe scarring or poor visual outcome

necessitates subsequent penetrating keratoplasty after epikeratophakia the prior surgery has not been found to adversely affect the outcome of subsequent penetrating keratoplasty.[210,211] Patients who require or desire contact lenses after epikeratophakia can be refitted successfully.[212] Epikeratophakia may also helpful as an adjunctive procedure in fitting patients who were formerly unable to wear contact lenses because of extreme corneal topography.[213]

OTHER SURGICAL PROCEDURES

Thermokeratoplasty flattens the cone by the carefully controlled heat shrinkage of stromal collagen. Although it was a once popular procedure[214,215] it has been associated with significant problems and it is rarely used today. Complications include a inadequate visual improvement, corneal topographic instability, corneal basement membrane damage and persistent epithelial defects.[216,217]

Recently, excimer laser photorefractive keratectomy has been successfully used to reduce the steepness of the cone. This resurfacing reduced astigmatism and increased visual acuity.[218] There were no problems with wound healing or any signs that treatment with the excimer laser adversely affected the cornea or further activated the keratoconus disease process. Although problems with radial keratotomy in keratoconic

patients[13,14,15] cast doubt on the safety and efficacy of photorefractive keratectomy, it may yet prove to be among the most useful therapeutic options.

PROGNOSIS AND PATIENT MANAGEMENT

Keratoconus is a chronic disorder with an unpredictable course. Patients are naturally concerned with the effects that a disease will have on their lives and functioning. Unfortunately, there is no accurate way to predict the actual course of keratoconus. Typically keratoconus begins around puberty and progresses at a variable rate for the next ten to twenty years. There is tremendous variability in both the rate of progression and the severity of the disorder. This is further complicated by individual differences in a patient's ability to accept and adapt to the vagaries of the disease. While some patients are perfectly content with 20/40 vision, others may be frustrated by anything less than perfect 20/20 acuity. Acuity may also be a poor indicator of visual function in these patients. The distortion caused by the cone can have profound effects on the quality of vision while Snellen acuity remains relatively normal. Glare may be inordinately disruptive. Night vision complaints are also common and the disturbance to night vision may be so severe that driving may be impossible. Although it may be difficult to differentiate real from exaggerated complaints, indicators of visual function obtained in the office may not correlate well with the patient's actual experience in the real world. Therapeutic intervention should be geared to resolving

the patient's functional complaints rather than merely addressing the in-office measures of visual function.

Therapy should be staged depending upon the patients current physical state and functional and psychological needs. Minor intervention may have profound effects. Since eye rubbing appears to play a causal role in the development and progression of the disease I counsel patients to avoid this behavior. The use of cold compresses and topical vasoconstrictors and antihistamine drops may also be helpful. Patients can and should be encouraged to take an active role in the management of their disease. This gives them a sense of "controlling their own destiny". Tinted lenses such as the excellent Corning CPF™ series can also provide tremendous functional benefits at minimal cost. The least invasive approaches should be tried first. Whenever possible spectacle correction should be attempted before contact lenses are prescribed. Contact lenses should be fitted before surgery is contemplated. There are significant differences in the ability some patients to accept the various corrective modalities. While some patients are contact lens intolerant while others are irrationally fearful of surgery. However, almost universally, almost all patients will want to know if they will ultimately require surgery. Several factors have been identified as having significant prognosic value in determining the likelihood of a patient requiring penetrating keratoplasty. Relevant factors included: the maximum and minimum keratometry, a

corneal cylinder of more than 1.9 mm, Snellen acuity, the racial group and the age at presentation.[219] The base curvature of the initial contact lens fitted may also be of prognostic value.[220] Although generally successful, the outcome of keratoconus surgery is still unpredictable. Patients may become convinced that surgery is the ultimate and absolute "cure" for their condition. It is important to insure that the patient does not misunderstand the limits of current surgery. The outcome of surgery is never certain.

Keratoconus is a lifelong disorder. Although dealing with keratoconic patients can sometimes be trying it can also be extremely rewarding. As is true with all disorders, ignorance does the greatest harm. Although the clinician may be unable to provide the patient with an absolute prognosis, both the best and worse case scenarios should be described. An explanation of the various treatment options should be provided to every patient regardless of the state of the condition. Knowledge is the most effective cure for the fear and uncertainty that often pervades this disorder.

PELLUCID MARGINAL DEGENERATION

Pellucid marginal degeneration is a localized corneal ectasia typically involving the inferior peripheral cornea.[221] One case of superior corneal thinning has been reported.[222] The condition is usually bilateral but often asymmetric in presentation. It is most commonly seen in patients between 20 and 40 years of age and may slowly

progress over time. On slit lamp examination, there is a thin band of marked thinning in the inferior cornea, usually in the region extending from 4 to 8 o'clock. The thinned area is between 1 to 2 mm. in width and is usually separated from the limbus by an unaffected area of normal cornea. There is no evidence of inflammation or vascularization. Crescent-shaped, deep corneal scars above the ectatic area have been observed in some patients.[223] Although previously not described, there is often a flat and thin band like scar immediately below the area of greatest thinning. It originates at the level of Bowman's layer anteriorly and radiates obliquely downward to intersect with Descemet's membrane posteriorly to form a "V" with Descemet's membrane. The cornea above the ectatic area often bulges forward causing marked against-the-rule and irregular astigmatism. Topographic analysis shows marked flattening of the central cornea along a vertical axis and marked steepening of the inferior corneal periphery.[224] In advanced cases hydrops and corneal scarring may occur.[225,226] Rupture of the ectatic area is a rare complication. Although there have been no reports of an iron line corresponding to the Fleischer's ring seen in keratoconus, I have observed cases where an iron line immediately above the ectatic area was present. This line resembles a Hudson-Stähli line but does not appear related to lid position. Vertical stress lines similar to Vogt's striae may occur.

Pellucid marginal degeneration appears to be a unique entity distinct from keratoconus. However, significant evidence links the two conditions. In Japan, a number of cases of simultaneous keratoconus and pellucid marginal degeneration in the same eye have been reported.[227] Histopathologically, there are also similarities, including stromal thinning and loss of Bowman's layer. [228] The Ultrastructural changes after acute hydrops are similar to those observed in acute keratoconus.[229] Treating pellucid degeneration may be difficult. The induced corneal astigmatism can exceed 20 diopters. That combined with distortion make spectacle correction impractical. Contact lenses may be valuable when adequate lens centration is achievable. Large custom toric lens designs or hybrid (rigid center, soft skirt) SoftPerm® lenses have been used with success. Piggy back fitting techniques may also be a viable alternative. In advanced cases surgical intervention may be necessary. Several options are available for the corneal surgeon including wedge resection,[230] crescentic resection,[231,232] penetrating keratoplasty with a large eccentric graft,[233] and epikeratoplasty.[234] However, crescentic peripheral lamellar keratoplasty appears to offer the highest rate of success and the best prognosis.[235]

POSTERIOR KERATOCONUS

Posterior keratoconus is a rare disorder of the cornea that is generally classified as a developmental anomaly. Most cases are congenital although some appear to have be

acquired secondary to trauma.[236,237] The condition is typically unilateral although bilateral cases have been reported.[238] Clinically it is characterized by circumscribed (keratoconus posticus circumscriptus)[239] or generalized (keratoconus posticus generalis)[240] corneal thinning and posterior concavity of the cornea. The entire posterior corneal surface is involved in keratoconus posticus generalis. In keratoconus posticus circumscriptus only a small paracentral area is abnormal. In both variants, the affected area is thinned with a resultant increase in posterior corneal curvature. Stromal scarring overlying the affected area may be seen. Bowman's layer is absent over the thinned area. Developmental anomalies involving Descemet's membrane and the corneal endothelium are often present. A thickened ring of Descemet's membrane may surround the thinned zone.[238] Guttae, Descemet's excrescences, and posterior synechiae adherent to the affected area may be present.[241,242,243] Posterior keratoconus has been associated with several ocular and, less frequently with a variety of systemic abnormalities. The ocular findings include choroidal and retinal sclerosis and abnormalities of the crystalline lens.[241,244,245] Although the inheritance of this condition appears sporadic several familial cases have been reported.[246]

Although patients with posterior keratoconus may have visual complaints that are related to their corneal abnormality, the visual effects are somewhat tempered by the small difference in refractive index between the aqueous and the cornea. Keratometry

and photokeratoscopy provide an incomplete picture of the surface changes associated with posterior keratoconus. Although the corneal surface has traditionally been thought to be topographically normal, a recent study utilizing computer assisted corneal topography found a central steepened "cone" overlying the area of circumscribed posterior keratoconus and paracentral flattening.[247] This may account for much of the visual impairment that sometimes occurs in this condition. Treatment is usually not required. However in cases with severe scarring penetrating keratoplasty may be indicated. The visual prognosis is guarded in congenital cases since amblyopia is often a factor.

KERATOGLOBUS

Keratoglobus is an unusual and rare bilateral thinning disorder of the entire cornea. The cornea is clear but has a globoid appearance caused by steepness and protrusion. The thinning may be dramatic, and may approach 20% of normal corneal thickness, especially in the periphery. Patients have high myopia and astigmatism. Nystagmus is also a frequent concomitant. Keratoglobus has been observed to occur in families affected by keratoconus.[248] Autosomal recessive transmission has been suggested, however, no inheritance pattern has been definitively established.[249] Although one case of acquired keratoglobus has been reported, the disorder is generally present at birth and is non-progressive or minimally progressive.[250] Because of this it may be mistaken

for infantile glaucoma or megalocornea. Megalocornea presents with a large corneal diameter but can be differentiated by the lack of thinning and normal curvature. In juvenile glaucoma, intraocular pressure is elevated. The cornea is often clouded and the entire eye may be enlarged by the increased pressure. Keratoglobus has been frequently associated with Leber's congenital amaurosis, blue sclera and a variety of connective tissue abnormalities that share many of the clinical characteristics of Ehlers-Danlos syndrome type VI.[249,251,252,253] Other associated ocular conditions include orbital pseudotumor, vernal keratoconjunctivitis, and chronic marginal blepharitis with chronic eye rubbing.[254] Corneal hydrops is frequent. In one series, hydrops occurred in 19 of 21 eyes with keratoglobus.[254]

Unlike keratoconus where perforation is rare, the cornea is extremely fragile in keratoglobus. There are numerous reports of perforation secondary to minor trauma, or in some cases, spontaneously.[252,255] Because of this propensity for corneal rupture, extreme care must be used in fitting these patients with contact lenses. Protective spectacles should be worn to shield the eyes from accidental trauma. Treatment options are similar to those of keratoconus. Spectacle correction is the first choice although contact lenses may be used with caution in selected cases. Surgical procedures to treat keratoglobus included large-diameter lamellar and penetrating keratoplasty, and limbus-to-limbus epikeratoplasty. Penetrating keratoplasty requires large grafts and is technically difficult because of the need to suture into the thinned peripheral cornea. There is also an increased risk of graft rejection because of the large size of the graft and the proximity to the limbal vasculature. Glaucoma has also been reported as a complication of penetrating keratoplasy in these patients.[254] Epikeratoplasty using a large (12.5-mm) lenticules is successful in a majority of patients.[256] When central scarring interferes with vision, epikeratoplasty can also provide tectonic support prior to penetrating keratoplasty.

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