Chapter 144

Management of Pterygium

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The term *pterygium* is derived from the Greek *pterygion* meaning "wing." Clinically, a pterygium appears as a fleshy, vascular mass that occurs in the interpalpebral fissure. The typical pterygium is triangular and is made up of a cap, head, and body. The cap, or gray zone, is an arcuate, gray-white, subepithelial, corneal opacity that is at the leading edge of the pterygium (Fig. 144.1). With chronicity, abnormal tear pooling in advance of the cap leads to the deposition of a corneal epithelial iron line (Stocker's line).[1] The head of the pterygium is an elevated white mass that forms a firm adhesion to the globe. The body of the pterygium is a fleshy fibrovascular mass that is demarcated from normal conjunctiva superiorly and inferiorly by sharp folds. Vital staining reveals selective rose bengal uptake on the surface of pterygia in approximately half the cases.[2] Although simultaneous nasal and temporal pterygia can occur, pterygia are more frequently located nasally rather than temporally.[3] Isolated temporal pterygia are considered an uncommon occurrence.[4] Bilateral ocular involvement occurs in approximately one-third of patients with pterygia.[3,4] Active pterygia are characterized by marked vascular engorgement and progressive growth. Some pterygia will become quiescent with resolution of the vascular injection and flattening of the pterygium mass. The ultimate reasons for variable growth characteristics of pterygia are largely unknown.

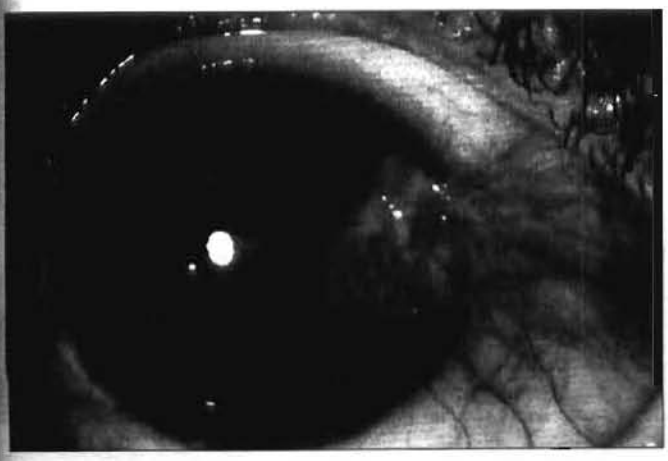

Fig. 144.1 Primary pterygium.

In advanced cases, the pterygium encroaches onto the cornea and may cause visual loss secondary to (1) loss of corneal transparency within the visual axis or (2) irregular corneal astigmatism (localized flattening). Regarding the latter phenomenon, a recent study disclosed that the induced irregular corneal astigmatism results largely from pooling of tears in advance of the pterygium apex.[5] In select cases, however, mechanical forces may predominate, leading to tractional corneal flattening.[6] Additional evidence suggests that both spatial contrast sensitivity and glare disability are worsened in patients with pterygia even when the Snellen visual acuity is minimally affected.[7]

Symptomatically, patients may experience foreign body sensation, burning, tearing, and blurred vision. Most of these symptoms are related to active inflammation of the pterygium. In some patients with advanced pterygia, ocular motility may be restricted, leading to diplopia in certain fields of gaze. Detrimental cosmetic effects caused by large pterygia are common.

Prevalence

Epidemiologic surveys indicate that the prevalence rates of pterygia vary, depending on the exact population under scrutiny. Overall, prevalence rates range from 0.7% to 31% in various populations around the world.[3,4,8–11] Prevalence rates for pterygia in the United States are reported to range from 2% in the northern states to 7% in the southern states.[8] As a general rule, prevalence rates for pterygia increase with age, although a decline in prevalence rates has been reported for patients over 60 to 70 years of age.[3,8] Reasons cited for this decline include a lack of self-reporting by the elderly and the regression of pterygia with senescence.[3] Furthermore, certain studies report an equal occurrence of pterygia in males and females,[3] while others report a male predominance.[8,9] It is possible that the reported differences in prevalence rates for men and women reflect different exposure rates to environmental risk factors. Additionally, prevalence rates for pterygia have been found to vary according to race. A population study in West Malaysia found that pterygia were more likely in those of Chinese descent as compared to those of Malaysian or Indian descent.[10] Other authors have similarly reported racial differences in prevalence rates.[4,12]

Pathogenesis

Early work by Cameron[13] indicated that pterygia occur more commonly where ultraviolet light intensity is highest. Specifically, a high prevalence of pterygia occurs in an equatorial belt bounded by latitudes 37° north and 37° south. Confirming Cameron's[13] observations, Mackenzie et al[14] found that those who live at latitudes less than 30° during the first 5 years of life have a 40-fold increased risk of pterygium development. Overall, it is generally accepted that ultraviolet light exposure is linked to the formation of pterygia.[15–19] Additional support for this theory is the observation that pterygia are more common in those who work outdoors, especially if the activity is on or near a highly reflective surface.[9,14]

Another suggested causative factor is the chronic ocular exposure to irritants such as dust. Detels and Dhir[4] reported that the age-adjusted prevalence of pterygia in factory sawmill workers (an indoor occupation) is approximately three times higher than that of a matched control group. Subsequently, Coroneo[15] has questioned the possible presence of reflected or scattered ultraviolet light in these particular work environments.

Interestingly, neither exposure to ultraviolet light nor exposure to irritants precisely explains the observation that pterygia are predominantly found on the nasal bulbar conjunctiva. Several theories have been put forth to explain this finding: (1) the temporal surface of the eye is normally shaded from light by the longer lashes and curvature of the temporal upper eyelid,[13] (2) the normal orbicularis contraction in bright light provides greater relative coverage of the temporal bulbar conjunctiva,[20] and (3) light incident from a posterolateral aspect to the eye is focused by the temporal peripheral cornea to the nasal limbus, causing focal limbal stem cell dysfunction.[15] Regarding the third theory, it is presumed that the normal anatomic relationships of the eyelids and nose would provide relative ocular shielding of incident light from the superior, inferior, and nasal directions.

In support of the notion that abnormal limbal stem cells are the primary abnormality in the pathogenesis of pterygia is the localization by immunohistochemical techniques of altered limbal epithelial stem cells at the leading edge of pterygia along the normal corneal epithelial basement membrane.[21] It is accepted that a healthy limbal stem cell population provides a stable junctional barrier that prevents conjunctivalization of the cornea.[22] Altered limbal basal epithelial cells produce elevated levels of matrix metalloproteinases (MMPs), which are collagenolytic enzymes probably responsible for the dissolution of Bowman's layer and extracellular matrix.[23] Based on these findings, pterygium formation may ultimately represent a focal limbal stem cell dysfunctional state. This tenet is in contradistinction to other pathogenetic theories that have focused on a primary degenerative response of the conjunctiva. Specifically, Hill and Maske[16] postulated that actinic damage to the corneal or conjunctival tissue causes abnormal antigenicity and leads to a chronic inflammatory cell infiltrate with a subsequent reparative fibrovascular response.

Historically, numerous other diverse theories have been put forward to explain pterygia formation to include local tear film abnormalities,[24] chronic ocular irritation,[4] chronic inflammation with production of a pterygium angiogenesis factor,[25] immunologic mechanisms related to type I hypersensitivity,[26] hereditary factors,[27] altered elastic tissue formation by actinically damaged fibroblasts,[28] and human papillomavirus.[29] Additionally, nearly one-half of pterygium samples show abnormal expression of *p53* tumor suppressor gene, a common marker for neoplasia known to control cell cycle, cell differentiation, and apoptosis.[30,31] The numerous different pathogenetic theories that have been proposed point to the fact that the ultimate pathogenesis of pterygia remains speculative.

Histopathology

The histopathologic features of pterygia were thoroughly outlined by Fuchs in the 1890s. These include an increased number of thickened elastic fibers, hyaline degeneration of the conjunctival tissue, concretions, and epithelial changes.[32] Austin et al[28] have similarly summarized the histopathologic findings as follows: (1) hyalinization of the subepithelial connective tissue of the substantia propria, (2) diffuse or lobular collections of eosinophilic granular material with an associated increase in the number of fibroblasts and other cells, (3) an increased number of thickened and tortuous fibers that stain strongly with elastic stains (elastotic material), and (4) concretions within the hyalinized and granular areas that may show either eosinophilia or basophilia.

In reference to the characteristic elastotic material within pterygia, the term "elastotic degeneration" was coined to describe the condition of tissue uptake by Weigert's and Verhoff's elastic tissue stains but the lack of tissue degradation by pancreatic elastase.[33] While this specific staining characteristic is not universal for pterygia,[33] it is generally accepted that the elastic fibers within pterygia are abnormal. Historically, Hogan and Alvarado[32] stated that the elastotic material within pterygia is formed from four sources: (1) degenerating collagen, (2) pre-existing elastic fibers, (3) abnormal fibroblastic activity, and (4) abnormal ground substance. Ultrastructural analysis by Austin et al[28] attributed the elastotic degeneration solely to abnormal fibroblastic activity with the production of abnormal maturational forms of elastic fibers. Moreover, collagen degeneration was demonstrated only in the subepithelial zone and accounted for the light microscopic finding of hyaline degeneration.[28]

Histopathologic analysis of the leading edge of pterygia by Cameron[34] disclosed the following: (1) fibroblastic tissue separating the basal corneal epithelial layer from Bowman's layer, (2) altered orientation of the basal corneal epithelial cells overlying the fibroblastic tissue, (3) destruction of Bowman's layer and the superficial corneal stroma underlying the fibroblastic tissue, and (4) normal corneal tissue proximal to the leading edge of the pterygium. As stated previously, immunohistochemical staining has demonstrated the presence of altered limbal basal stem cells

between the dissolved edge of Bowman's layer and the fibrovascular tissue of the pterygia.[21] Other histologic changes that have been identified in the epithelium of pterygia include squamous cell metaplasia, acanthosis, dyskeratosis,[35] increased goblet cell density,[36] and increased mast cells.[37]

A recurrent or secondary pterygium is defined as a pterygium recurrence after primary surgical excision. A secondary pterygium often has a more exuberant fibrovascular growth response than the original pterygium. The histologic findings of secondary pterygia differ from primary pterygia in that the typical degenerative connective tissue changes are absent. Cameron suggested that the surgical trauma after primary excision leads to an accelerated fibrovascular proliferative response.[13]

Management

In general, conservative therapy for pterygium is warranted unless one of the following circumstances arises: (1) loss of visual acuity either because of induced astigmatism or encroachment onto the visual axis, (2) marked cosmetic deformity, (3) marked discomfort and irritation unrelieved by medical management, (4) limitation of ocular motility secondary to restriction, or (5) documented progressive growth toward the visual axis so that it is reasonable to assume that visual loss will ultimately occur. In such circumstances, surgical intervention is required. Because recurrences after pterygium excision are frequent and aggressive, firm indications for surgical removal should exist before primary excision.

Preoperatively, a careful history and physical examination are mandatory to rule out the diagnosis of a pseudopterygium. A pseudopterygium is an inflammatory adherence of the conjunctiva to the cornea in response to chemical, thermal, or traumatic injury and can occur at any point around the limbus. Many corneal inflammatory disorders can also predispose to fibrovascular ingrowth that may resemble pterygia. Clues leading to the diagnosis of a pseudopterygium include: (1) any anatomic location other than the interpalpebral fissure, (2) diffuse corneal involvement in multiple locations, (3) historical information of a past significant ocular inflammatory event, (4) the lack of anatomic configuration ("body" and "head") typical of a pterygium, (5) a pterygium that bridges the limbus so that a probe can be passed underneath the body at the limbus, or (6) the presence of corneal thinning underlying the pterygium head. Depending on the ultimate etiology of the pseudopterygium, surgical excision may not be indicated. If the preoperative examination discloses corneal thinning underlying the pterygium head and surgery is to be performed, donor corneal tissue should be available intraoperatively in case a lamellar keratoplasty is required because of an inadvertent corneal perforation.

The differential diagnosis of pterygium should also include conjunctival intraepithelial neoplasia, squamous cell carcinoma, and a corneal macropannus. The characteristic features of these entities should distinguish these disorders from a pterygium. A limbal dermoid is also in the differential diagnosis but is less likely to be confused with a true pterygium.

Medical approaches

General recommendations for the prevention of pterygium formation should include the avoidance of exposure to ultraviolet radiation. A survey of patients in Australia disclosed that there was a doubling of risk for pterygium formation associated with never wearing a hat outdoors between the ages of 20 and 29 years.[14] Additionally, there was a ninefold increased risk of pterygium formation if glasses were never worn in the decade before the pterygium developed. Since the development of pterygium is strongly associated with ultraviolet exposure within the first 5 years of life,[14] parents should be advised to protect their children from ultraviolet exposure, especially if the latitude of residence is within 30° of the equator and a great deal of time is spent outdoors. Hence, in areas where exposure is high, the use of ultraviolet-absorbing protective spectacles, sunglasses, and hats is advisable. Lateral ocular exposure to incident light can be avoided with wraparound sunglass designs.

Mild irritative symptoms from pterygium may be managed with topical lubricants or a mild topical antihistamine/vasoconstrictor (e.g., naphazoline qid). A mild topical corticosteroid (e.g., fluorometholone 0.1% qid) or nonsteroidal may be useful for moderate to severe vascular injection and irritative symptomatology. Secondary dellen may be managed with preservative-free lubricating ointments and temporary patching for 24 hours.

Surgical approaches

The fact that numerous different techniques exist for the surgical treatment of pterygium underscores the point that no single approach is universally successful.[38] While this statement makes the actual treatment selected appear arbitrary, certain treatment techniques offer clear-cut advantages for success. The interested reader is referred to an article by Rosenthal for a review of the chronology of pterygium therapy.[39] What follows is a review of the surgical options currently available for the treatment of pterygia.

Pterygium excision or avulsion

All procedures, regardless of adjunctive measures employed, begin with the surgical removal of the pterygium from the globe. There are numerous techniques that have been published extensively in the literature.[40] Dissection may be carried out from the body to the head of the pterygium or, alternatively, from the head of the pterygium toward the body. As a general rule, when the pterygium head involves the cornea, care should be taken to perform only a superficial corneal dissection, just deep enough to remove the pterygium. Deep lamellar keratectomies offer no distinct advantages, since the resection may produce postoperative ocular surface abnormalities and alter corneal tensile strength. To avoid deep lamellar dissections, Rich et al[38] recommend avulsing thin, relatively transparent, primary pterygia by mechanically shearing off the pterygium head from the underlying cornea with the use of forceps. Advantages cited for this method include a resultant smooth

corneal surface, rapid epithelialization, and minimal scarring postoperatively. It should be noted that many pterygia cannot be avulsed from the cornea in a smooth continuous plane and must be excised. Another method described for removing the pterygium head that avoids inadvertent deep dissection dates back to the seventh century:[41] a suture is passed underneath the body of the pterygium and, with a sawing motion toward the cornea, the head is dissected from the underlying corneal tissue.

A reliable method of excision has been described by Kenyon et al[42] Retrobulbar anesthesia and a lid block are used, as the prolonged surgical time required for conjunctival autografting warrants this. However, if simple excision alone is to be carried out, adequate anesthesia may be obtained with topical tetracaine and a local subconjunctival injection of lidocaine. A rigid lid speculum aids in maximal ocular exposure. Limbal stay sutures are placed at the 12 o'clock and 6 o'clock positions to rotate the globe for maximal surgical exposure. Forced duction testing is performed to disclose restricted ocular motility. The head of the pterygium is dissected from the cornea by tenting up the pterygium apex with fine forceps and then performing a delineating keratotomy at the leading edge with a rounded sharp blade (e.g., No. 69 Beaver blade) to obtain a superficial plane of dissection. Alternatively, in certain cases a peripheral to central dissection is employed if the leading edge is indistinct. The remainder of the pterygium head is carefully dissected from the superficial cornea in a lamellar fashion up to the limbus with a Tooke knife. The conjunctival extent of the pterygium to be excised is then marked with a gentian violet marking pen. The pterygium body can be elevated with a subconjunctival injection of balanced salt solution to aid in the dissection and help protect the rectus muscle from inadvertent damage during the surgery. The gentian violet marks ensure that the extent of excision is accurate, since the subconjunctival injection alters the preoperative anatomic landmarks. Excision of the bulbar conjunctival extent of the pterygium is carried out up to the limbus using blunt dissection with Wescott scissors. The pterygium is then excised from the remaining limbal attachment with scissors. All involved conjunctiva, underlying Tenon's capsule, and scar tissue are ultimately removed down to bare sclera. During the dissection, care must be exercised to avoid damage to the underlying rectus muscle, which can become enmeshed in pterygium-associated fibrovascular tissue (especially in recurrent cases). The rectus muscle can be identified with a muscle hook and a traction suture if necessary. Wet field cautery is used to cauterize bleeding vessels as necessary. Remaining tissue attachments at the limbus are first scraped with a rounded sharp blade and then the cornea, limbus, and adjacent sclera are polished with a diamond burr.[43] Care is taken not to polish the tissue excessively with the diamond burr because a surface with multiple different levels and irregularities can be created with aggressive polishing. Forced duction testing is repeated as appropriate to ensure that normal ocular motility is restored. The exposed bulbar conjunctival margins are then tacked down to the sclera with several 10-0 nylon sutures (other authors advocate 8-0[41] or 9-0 Vicryl suture) with attention not to recess or advance the margins excessively. At this point, the surgeon can proceed with conjunctival autografting for either primary or recurrent pterygium.

After pterygium excision, numerous authors in the past advocated a "bare sclera" technique in which the resultant scleral and corneal defects would be left to epithelialize postoperatively. It was theorized that a pterygium recurrence would be prevented if the corneal epithelium could heal before the conjunctival epithelium reached the limbus.[44] Many authors claimed impressive success rates with this bare sclera technique.[44–46] Unfortunately, controlled studies were not performed to validate these reports. Indeed, using a similar bare sclera technique, Youngson[44] reported a pterygium recurrence rate of 37% and concluded that "the procedure is unsound" and "pterygia should not be treated surgically." Krag and Ehlers reported a 91% recurrence rate (20 of 22 patients) using a bare sclera pterygium resection technique in combination with excimer laser corneal ablation to smooth the corneal surface.[47] Variations in follow-up times, dropout rates, and definitions of recurrence make direct comparisons between the studies difficult.

Transplantation of the head of the pterygium

Various techniques originated in the nineteenth century to redirect the head of the pterygium away from the cornea to prevent recurrences. The surgical procedure consisted of burying the pterygium head underneath the normal conjunctival edge inferiorly after surgical dissection of the head from the cornea. Unfortunately, recurrence rates of 30% to 75% were reported with these techniques.[40,41] Such transplantation procedures have been largely abandoned secondary to high recurrence rates and poor postoperative cosmetic results.

Conjunctival flaps and conjunctival autografts

Various surgical strategies for the treatment of pterygium have developed using the premise that close approximation of healthy conjunctival tissue at the denuded limbus after pterygium excision prevents recurrences. The three basic variations on this theme include excision with primary conjunctival closure, excision with conjunctival flap formation, and conjunctival autografts.

Primary conjunctival closure after pterygium excision is achieved by undermining adjacent normal superior and inferior bulbar conjunctiva and pulling the cut conjunctival edges together. Such a strategy was employed as early as 1911 by Terson.[40] While controlled studies are not available, recurrence rates have varied from 2.1% to 88% using this technique.[48,49] Patient age less than 40 years and aggressive pterygium activity have been cited as risk factors for recurrences.[48]

Rotational conjunctival flaps to cover the pterygium excisional site have been employed since the 1940s.[40] Aratoon[50] in 1967 reported a recurrence rate of less than 1% in a series of 150 consecutive procedures by using a conjunctival pedicle flap after pterygium resection. Unfortunately, Aratoon's study did not include a control group. A report by Wilson and Bourne[51] discussed a redirectional

conjunctival flap technique originally described by Stocker.[52] Known as a conjunctival z-plasty, the procedure involves rotating a flap of normal conjunctiva into a limbal position while simultaneously rotating the remaining pterygium body laterally onto the bulbar conjunctiva after resecting the pterygium head from the cornea. While no recurrence figures are quoted, the authors cite two advantages of the procedure: the preservation of normal conjunctiva for possible future autografting and the formation of a barrier of normal conjunctival tissue adjacent to the limbus to prevent recurrent pterygium growth onto the cornea. McCoombes et al[53] reported a recurrence rate of 3.2% by using a sliding conjunctival flap after primary pterygium excision in 258 eyes with an 86% follow-up rate for a minimum of 1 year. With the same method of surgery, Lei[54] reported a recurrence rate of 1.6% in 913 patients with primary pterygium after an average follow-up of 5.7 years. The low recurrence rate and the avoidance of potentially dangerous adjunctive measures are encouraging.

Conjunctival autograft transplantation was described as a treatment for pterygium by Kenyon et al[42] in 1985. In this technique, a free conjunctival graft from the superotemporal bulbar conjunctiva is used to resurface the exposed scleral surface after pterygium resection. A 5.3% recurrence rate was reported after 57 procedures (41 recurrent pterygia and 16 primary pterygia) with a mean follow-up of 24 months.[42] The authors recommended this treatment modality for advanced primary and recurrent secondary pterygium, especially when concurrent fornix reconstruction is required or when conjunctival scarring involves the extraocular muscles. Lewallen[55] reported a randomized trial of conjunctival autografting versus a bare sclera technique for pterygium in the Caribbean. While not statistically significant, there was a lower recurrence rate for conjunctival autografting (3 of 19 cases) as compared to a bare sclera control group (6 of 16 cases). Another retrospective review of 93 pterygia treated by conjunctival autografting by Allan et al[56] in Australia reported a 6.5% recurrence rate with a minimum of 6 months' follow-up. A retrospective survey of 71 patients with primary pterygium by Figueiredo et al[57] showed a 1-year recurrence rate of 16% in those treated with conjunctival autograft and 40% when treated with simple excision. Overall, recurrence rates after conjunctival autografting are low. Pooling data from eight studies using conjunctival autografting in the treatment of pterygium gives an overall recurrence rate of 21 in 265 cases (7.9%).[56] Of course, it must be recognized that such pooled data have limitations, since variations exist among the specific surgical techniques used, the proportion of secondary recurrent pterygia treated, the postoperative medical regimens prescribed, the age and location of the populations studied, the length of the follow-up periods, and the specific definition of a recurrence used by a given author.[56] A prospective randomized study in patients with primary pterygium comparing conjunctival autograft versus conjunctival rotation autograft showed equal recurrence rates (approximately 6%) after a mean follow-up of 11 months.[58] The inclusion of limbal tissue in the conjunctival autograft may be beneficial as a barrier. Al Fayez[59] compared conjunctival autograft to conjunctival–limbal autograft for advanced primary and recurrent pterygium, and found zero recurrences (28 primary, 15 recurrent) in the limbal group compared to 8.3% (primary 2/24 patients) to 33.3% (recurrent 4/12 patients) in the autograft alone group with a minimum follow-up of 3 years.

Complications from conjunctival autografting are infrequent and not generally sight threatening. Before performing an autograft, the interested reader is referred to an excellent review of postoperative problem prevention and management for conjunctival autografts that was published by Starck et al[60] in 1991. Minor problems such as conjunctival graft edema, corneoscleral dellen, and epithelial inclusion cysts are encountered infrequently. Less common problems include corneal astigmatism, hematomas, Tenon's granuloma, retraction and/or necrosis of the graft, and extraocular muscular disinsertion. For optimal surgical results, Starck et al[60] emphasize careful dissection of Tenon's tissue from the conjunctival graft and recipient bed, minimal manipulation of tissues, and accurate orientation of the graft. Allan et al[56] concur with the low complication rate of conjunctival autografting while reporting one Tenon's granuloma, one conjunctival inclusion cyst, and three wound dehiscences after 93 procedures performed. All complications in Allan's series[56] were corrected with minor surgical revision without recurrences. Vrabec et al[61] reported two cases of subconjunctival fibrosis at the harvest site causing extraocular muscle restriction with concomitant diplopia in one patient. Suggestions for management of this fibrosis included early frequent topical corticosteroids and/or possible primary closure of the harvest site conjunctiva at the time of the original surgery.

The specific procedure for conjunctival autografting has been previously published by Kenyon et al.[42] With only a few variations from Kenyon's original report,[42] what follows will be a description of the general procedural technique for conjunctival autografting (Fig. 144.2). After the excision of the pterygium as described previously in this chapter, the size of the scleral defect created is measured with Castroviejo calipers. The globe is then rotated downward using the stay sutures to expose the superior bulbar conjunctiva. The dimensions of the intended conjunctival graft (adjacent to the limbus) are marked with a gentian violet marking pen based on the previous measurements of the recipient bed. The gentian violet marks not only aid in the excision of an appropriately sized donor graft but are invaluable in preventing inadvertent upside-down orientation of the graft in the recipient bed. Adamis et al[41] note that free grafts as large as 15 × 15 mm can be prepared and used without difficulty. Balanced salt solution is then injected subconjunctivally outside of the gentian violet marks to elevate the conjunctiva to aid in the conjunctival dissection. Blunt Wescott scissors are used to incise the conjunctiva outside the gentian violet marks along the posterior border of the graft. The conjunctiva is then undermined using blunt dissection with care taken to not include underlying Tenon's capsule in the final graft. The lateral edges of the donor graft are incised outside of the gentian violet marks as the dissection is carried forward. It is

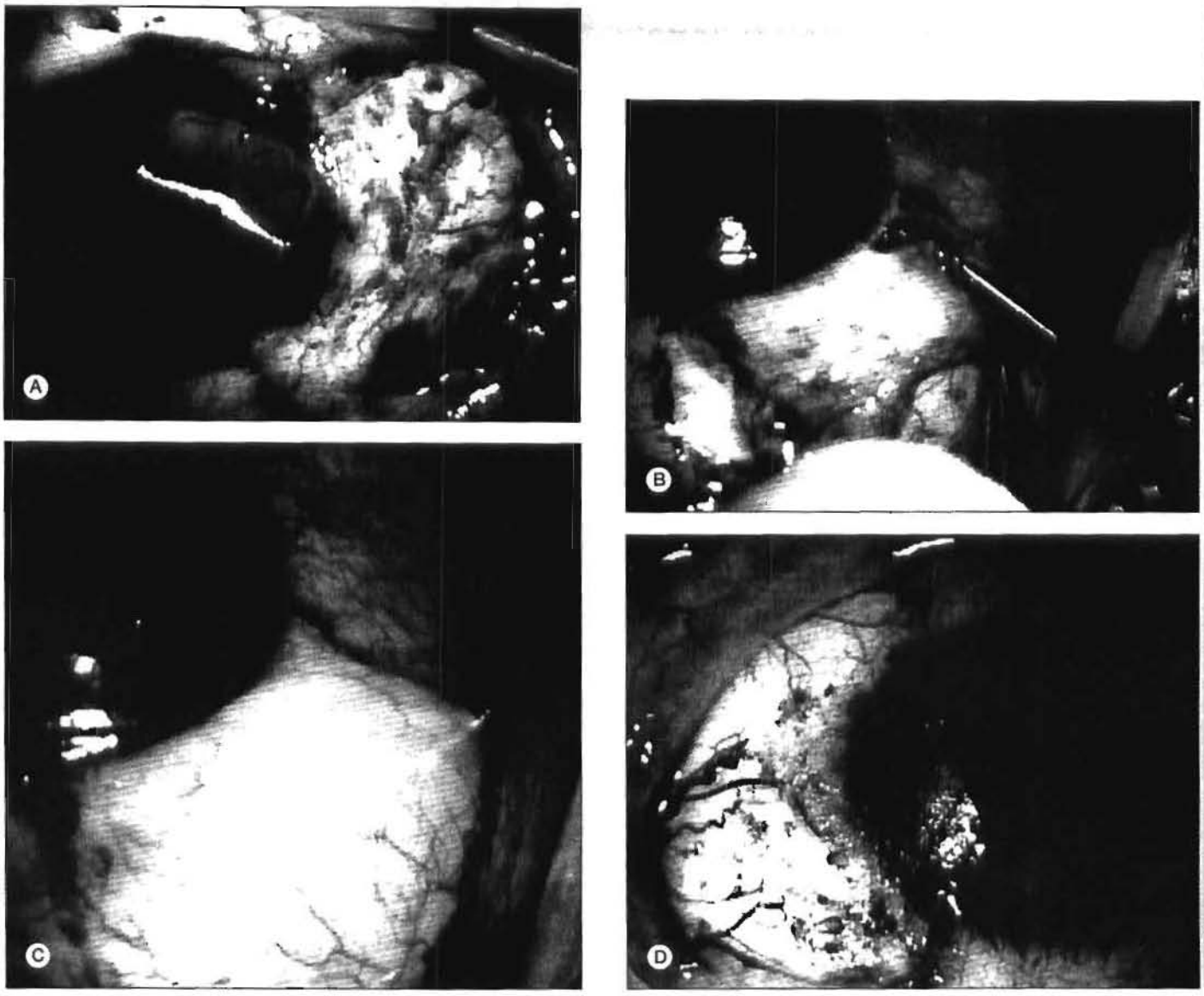

Fig. 144.2 Conjunctival autograft. **A**, Conjunctival defect present immediately after excision of pterygium. The central corneal polygonal material protects the fundus from light toxicity. **B**, Harvesting of conjunctival autograft tissue from the superotemporal quadrant. Gentian violet demarcates the margins of the autograft. Balanced salt solution is injected subconjunctivally. **C**, Excision of the conjunctival autograft starts with the posterior border of the graft, followed by each lateral border. The limbal border is removed last. Note that the incision is made outside of the gentian violet mark to retain the marks on the graft. These marks assist the surgeon in orientating the graft. **D**, Conjunctival autograft is secured over bare sclera with interrupted 10-0 nylon sutures.

important to note that the graft is purposely excised outside of the gentian violet marks so that these marks can be used for later orientation. (In the final graft, the limbus is the edge without any marks.) The donor conjunctival graft should be as thin as possible so that postoperative healing will occur with less shrinkage. It is also important that the limbal conjunctiva is incised last after the entire graft has been dissected forward to the limbus. This assures that the graft will not retract and become difficult to handle. The tissues are not allowed to dry during the procedure and are moistened with frequent applications of balanced salt solution. Handling of the donor conjunctival tissue only occurs with nontoothed forceps (e.g., a McGregor conjunctival forceps) so as to avoid a buttonhole in the conjunctiva. At this point the graft is repositioned into the recipient bed, with adjustment of the traction sutures as necessary. The graft is oriented with the unmarked limbal donor edge adjacent to the limbus in the recipient bed and the gentian violet marks on the exposed surface of the conjunctiva. Adamis et al[41] advocate securing the graft with approximately eight 8-0 Vicryl sutures; we routinely secure the graft to the recipient conjunctival edge and underlying episclera with numerous 10-0 nylon sutures (buried knots) along with Vicryl sutures to avoid a postoperative graft dehiscence. The majority of these sutures usually extrude or dissolve on their own by 1 month postoperatively, while the rest usually epithelialize and remain buried. Because of the use of permanent sutures, patient

discomfort is usually not a problem. The occasional exposed stitch can be removed after adequate conjunctival healing in the early postoperative period. The donor harvest site is left to epithelialize on its own, which usually occurs in the first several days postoperatively. Kenyon et al[42] advocate postoperative steroid and antibiotic ointments. We typically use a steroid–antibiotic drop six times a day during the first 1 or 2 weeks and switch to a steroid drop alone after that time. Drops are titrated according to the degree of inflammation and may be continued for 4 to 8 weeks, depending on the clinical circumstance (Fig. 144.3).

The primary disadvantage of the conjunctival autograft technique is the prolonged operative time required when compared to other bare sclera or primary closure techniques. Additionally, an operating microscope is required for optimum results, which can be a problem for ophthalmologists in developing countries.[62] However, these disadvantages are outweighed by the lack of sight-threatening complications and the relatively low recurrence rates after conjunctival autografts.

Amniotic membrane transplantation (AMT)

Human amniotic membrane is a thin, semitransparent, avascular tissue forming the innermost layer of the fetal membrane. The membrane has a thick and continuous basement membrane with a full complement of collagen types IV and VII, fibronectin, and laminin-1 and -5.[63] It has been recognized that basement membrane facilitates migration of epithelial cells, reinforces adhesion of basal epithelial cells,[64] promotes epithelial differentiation, and prevents epithelial apoptosis (programmed cell death).[65] The stroma is composed of loose connective tissue that contains growth factors that may modulate stromal fibroblasts to decrease subconjunctival fibrosis, and protease inhibitors important for promoting epithelial healing and reducing stromal inflammation and ulceration.[66–68] Amniotic membrane is typically placed on the ocular surface with basement membrane up and stroma (Weck-Cel sponge will stick to stroma side only) down. It can be anchored to adjacent episclera and conjunctiva with 8-0 or 9-0 Vicryl sutures, and 10-0 nylon when used on the cornea.

There are a number of studies that show efficacy for AMT in primary pterygium excision. Prabhasawat et al[69] noted that the recurrence rate for primary pterygium following excision with AMT in a prospective study (mean follow-up 11.0 months) was 10.9%, which was higher than the 2.6% rate obtained with conjunctival autografting in a retrospective study (mean follow-up 23.2 months). Tekin et al[70] treated 28 patients with AMT with a recurrence rate of 10.7% with a mean follow-up of 14.9 months. Lower recurrence rates (3.0%) have been reported when more extensive removal of fibrovascular tissue is combined with intraoperative and postoperative subconjunctival injection of long-acting corticosteroids.[71] Ma et al[72] retrospectively compared AMT to conjunctival autograft and postoperative 0.2 mg/ml mitomycin drops and found equal recurrence rates: 3.8%, 5.4%, and 3.7%, respectively.

Results are less promising for recurrent pterygium, a more aggressive disorder. Prabhasawat et al[69] looked at recurrent pterygium treated with AMT and found a recurrence rate of 37.5% (mean follow-up 11.0 months) compared to 9.1% (mean follow-up 23.2 months) using conjunctival autograft. An eye with recurrent pterygium that has undergone multiple surgeries usually lacks a great deal of normal nonscarred surrounding tissue and may have fornix shortening, symblepharon, and motility restriction. The

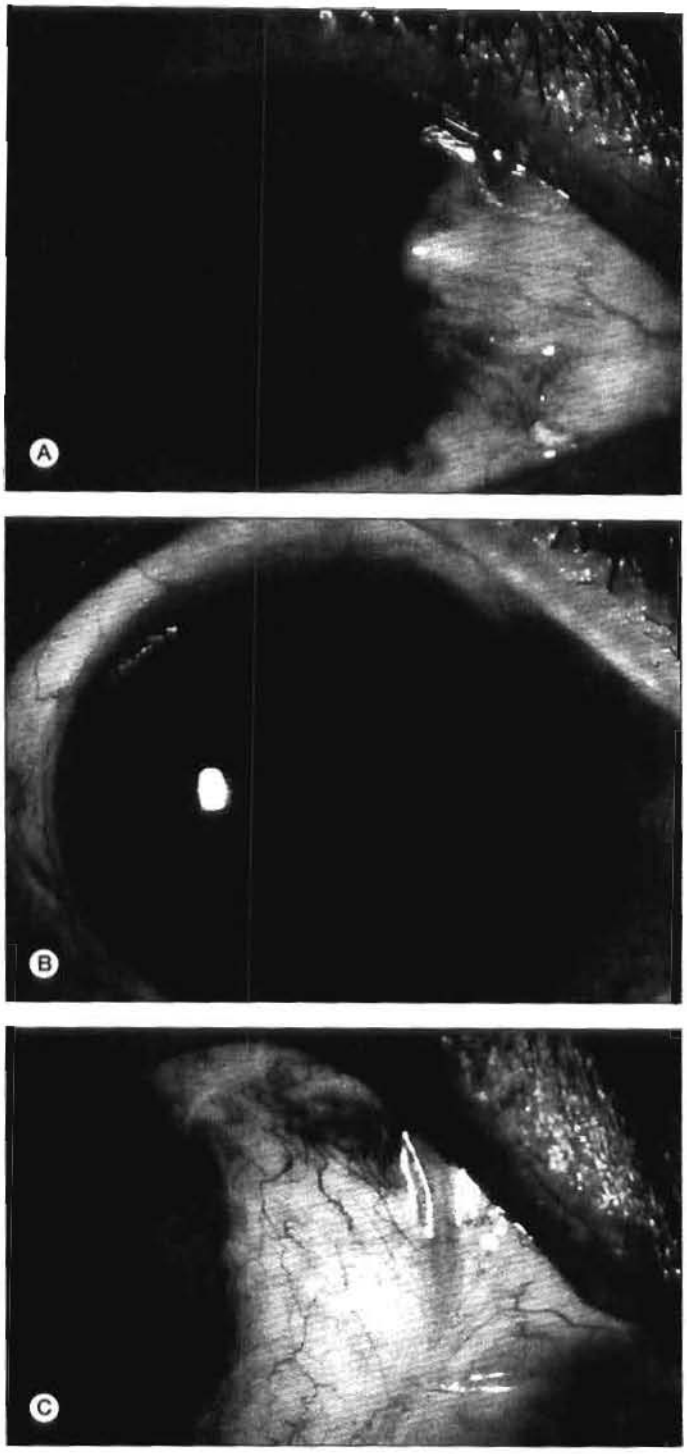

Fig. 144.3 Conjunctival autograft. **A**, Preoperative appearance of pterygium. **B**, Slit lamp appearance 2 months after pterygium excision and conjunctival autograft. **C**, Note a well-healed conjunctival autograft.

use of AMT combined with conjunctival autograft may be considered, especially when there is a shortage of healthy tissue to completely cover the defect. Both Kim et al[73] and Shimazaki et al[74] combined AMT with conjunctival–limbal autograft in a total of 13 patients and found no recurrences with mean follow-up of 24.3 and 13.8 months, respectively. Amniotic membrane may suppress inflammation and the formation of fibrovascular tissue, while the conjunctival–limbal autograft replenishes limbal stem cells. Amniotic membrane can be especially useful under certain circumstances: when there is a double-headed pterygium and not enough conjunctiva to cover the defect; a patient with recurrent pterygium who has already undergone conjunctival autografting; and patients with glaucoma with a need to preserve the superior conjunctiva for possible filtering surgery.

Lamellar keratoplasty and penetrating keratoplasty

If significant corneal thinning is present as a consequence of previous pterygium surgery, a lamellar keratoplasty may be indicated to restore the normal ocular surface integrity. Additionally, various authors have recommended a lamellar keratoplasty as a barrier to pterygium regrowth.[75] While the reported series are small, recurrence rates after lamellar keratoplasties have been reported between 0%[76] and 60%.[44] The successful use of lyophilized donor tissue has been described in the treatment of recurrent pterygia with only one recurrence in 13 eyes.[77] In severe cases where the visual axis is affected by thinning and scarring, a penetrating keratoplasty may be indicated to visually rehabilitate the eye.[40]

Mucous membrane grafts and skin grafts

In cases in which sufficient conjunctiva is not available for a pedicle graft, Trivedi et al[78] recommend the use of a mucous membrane graft from the lower lip after a pterygium excision. Trivedi et al reported no pterygium recurrences in 140 patients after mucous membrane grafting for a follow-up period of 6 to 12 months.[78] While these results are impressive, the clinical circumstance of generalized conjunctival disease preventing rotational flaps or autografting is uncommon.

Wong[79] reported that a split-thickness skin graft decreases the incidence of recurrence in cases of secondary recurrent pterygia and presents an acceptable "white" eye postoperatively. Unfortunately, the study was not controlled. While the postoperative photographs included in the report indeed show a "white" patch in the area of the previously excised pterygium, the cosmetic appearance of skin grafting does not approach the excellent results achieved by conjunctival rotational flaps or autografting. Based on the paucity of reports using skin grafts, the technique has not gained widespread acceptance in the treatment of pterygia.

Adjunctive therapy

In an effort to lower the recurrence rates after primary pterygium excision alone, investigators have combined excisional techniques with various adjunctive treatment modalities. In the circumstance of secondary recurrent pterygium, the known aggressive clinical course certainly warrants some additional treatment strategy other than a repeat bare sclera excision. Other than conjunctival flaps or autografts, certain investigators recommend the use of adjunctive chemotherapy or radiotherapy to decrease recurrence rates. The following adjunctive therapies have been variably recommended for both advanced primary and secondary recurrent pterygium.

Chemotherapy

Thiotepa

The nitrogen mustard analog thiotepa, or triethylenethiophosphoramide, has been advocated as an adjunctive measure to reduce the postoperative recurrence of pterygium since 1962.[80] Thiotepa is an alkylating agent that interferes with normal mitosis and cell division in all rapidly proliferating tissues. It was postulated that thiotepa reduced the recurrence of pterygium by inhibiting vascular endothelial proliferation at the operative site.[40]

While certain studies advocate different concentrations of thiotepa for patient use,[80] a common recommendation in the literature is to mix 15 mg of thiotepa in 30 ml of Ringer's solution for a final dilution of 1:2000 strength.[81] The patient uses the medication topically every 3 hours during the day starting 2 days postoperatively for a total of 6 to 8 weeks.[81] Gerde reported good results with a final thiotepa concentration as low as 1:5000.[82] Concerning the stability of this medication, Liddy and Morgan reported no loss of potency when the solution was stored at room temperature or at 3°C over a 15-day period, while Cooper reported that the thiotepa solution at 2 weeks lost 35% of its potency at room temperature versus only losing 5% of its potency when refrigerated.[80] Ehrlich recommended replacing the thiotepa solution at biweekly intervals for the 6-week treatment duration because of the lack of stability data for the solution at 6 weeks.[81]

A review of the literature by Olander et al[80] in 1978 quoted pterygium recurrence rates between 0% and 16% after pterygium excision and adjunctive treatment with thiotepa. It was noted that the recurrence rate rises precipitously if thiotepa is used for only 2 to 4 weeks postoperatively.[81] One study by Kleis and Pico[83] with a minimum of 1 year follow-up used the fellow eye as a control in 48 patients and demonstrated a 31.3% recurrence rate in the control eyes treated with excision alone versus a 8.3% recurrence rate when excision was followed by 6 weeks of thiotepa therapy.

While no systemic toxicity of topical thiotepa therapy has been reported, complications reported include early- and late-onset poliosis and periorbital skin depigmentation that can be permanent (especially in darkly pigmented patients), prolonged conjunctival injection, irritation, conjunctival deposition of black pigment, allergic reactions, and scleral perforation.[84] Sun exposure during therapy was suggested as a contributing factor in skin and lash depigmentation. The periorbital skin depigmentation has been cited as the major reason why thiotepa has not gained

widespread acceptance in the postoperative treatment of pterygia.[41]

Mitomycin

Mitomycin-C is an antibiotic that was first isolated from *Streptomyces caespitosus* by Hata in 1956.[85] Clinical trials with mitomycin-C in the United States began in the late 1960s for a variety of solid tumors to include breast, prostate, gastric, and bladder cancers.[86] Systemic therapy with mitomycin-C carries risks of myelotoxicity, hemolytic-uremic syndrome, pneumonitis, hepatic veno-occlusive disease, and rare cardiotoxicity. The topical use of mitomycin-C to prevent pterygium recurrence was first described by Kunitomo and Mori in the early 1960s in Japan.[87] Since that time, numerous investigators have reported that topical mitomycin-C is efficacious in decreasing recurrence rates after pterygium excision.

Following reductive activation, mitomycin-C interacts with DNA to form monofunctional adducts as well as covalent cross-links between the two complementary strands of DNA. Monofunctional adduct formation occurs 10 to 20 times more frequently than cross-linking. The preferred molecular target in DNA for covalent attachment by mitomycin-C is the N^2 position of guanine.[86] These modifications of DNA are responsible for the antibiotic and antineoplastic activity of mitomycin-C because molecular synthesis cannot progress normally with such permanent structural alterations. Additionally, the production of toxic oxygen free radicals from mitomycin-C in vivo has been postulated that could cause significant damage to any membrane with unsaturated lipids. Overall, mitomycin-C has the greatest antiproliferative effect on those cells showing the highest rate of mitosis.

The use of topical mitomycin-C after pterygium surgery was popularized in the United States by Singh et al.[88] In a double-masked prospective fashion after pterygium excision, patients were treated with either 1.0 mg/ml mitomycin-C eye drops, 0.4 mg/ml mitomycin-C eye drops, or placebo four times a day for 2 weeks. With an average of 5 months' follow-up, recurrences were found to be 89% in the placebo group versus 2.3% in the mitomycin groups combined.[88] Patients receiving the 1.0 mg/ml mitomycin dosage experienced worse conjunctival irritation, superficial keratitis, and excessive lacrimation when compared to the patients receiving the 0.4 mg/ml mitomycin dosage. No systemic toxicity was reported for either dosage. A subsequent publication by the same authors confirmed only one recurrence in 58 mitomycin-treated patients followed for 1 to 2 years.[89] Subsequent investigations by other authors have confirmed the low recurrence rates after treatment with 0.4 mg/ml topical mitomycin.[90] Other authors report good success with shorter courses of 0.2 mg/ml mitomycin drops with recurrence rates between 5% to 9%.[91–95] Chen et al[96] compared conjunctival autograft to postoperative 0.2 mg/ml mitomycin drops bid for 5 days after bare sclera excision for primary pterygium in a predominantly young Hispanic population, and found recurrence rates of 39% and 38%, respectively, after approximately 1 year. These rates are significantly higher than those of other studies for both types of surgeries, but may be explained by the patient population. Mahar,[97] in a study with the same dose of mitomycin and length of follow-up, found a recurrence rate of 9.4% in the mitomycin group versus 25.9% in the conjunctival autograft group, although the difference was not statistically significant. Overall, these studies indicate that adjunctive topical mitomycin-C is effective in reducing recurrences after pterygium excision. Other comparisons and concurrent series suggest that the effectiveness of mitomycin in reducing pterygium recurrences is better than radiation therapy and at least as good as conjunctival autografting.[98]

Although Singh et al[88,89] report no significant complications from mitomycin therapy and contend that the use of mitomycin is safe, insufficient long-term surveillance exists to make this statement with certainty. Indeed, reports have been published to the contrary. Yamanouchi et al[99] reported on 15 patients with severe scleral complications following topical mitomycin instillation after pterygium excision. Hayasaka et al[100] reported four cases of scleral ulceration 18 to 25 years after the use of 0.4 mg/ml mitomycin drops four times a day for 2 to 3 weeks after simple pterygium excision. Postoperative mitomycin as an adjunct to conjunctival autografting for recurrent pterygium has been studied in a small number of patients, with 2 of 12 having early wound dehiscence and 2 of 12 experiencing recurrence within 9 months.[101] Additionally, Rubinfeld et al[102] described the findings in ten patients who experienced serious, vision-threatening complications associated with the use of mitomycin after pterygium surgery. These complications included severe secondary glaucoma (four patients), corneal edema (three patients), corneal perforation (one patient), correctopia (two patients), iritis (eight patients), sudden-onset mature cataract (two patients), scleral calcification (one patient), and incapacitating photophobia and pain (eight patients). Six patients required 20 operative procedures as a consequence of their complications. Five eyes had a final visual acuity of 20/200 or worse. Since three of the six patients with the most severe complications had concomitant chronic external diseases, Rubinfeld[103] stated that mitomycin-C after pterygium excision is contraindicated in patients with keratitis sicca, Sjögren's syndrome, neurotrophic keratitis, or severe meibomian gland dysfunction blepharitis. A review of the Japanese literature by Rubinfeld et al.[102] revealed reports of scleral ulceration, necrotizing scleritis, perforation, iridocyclitis, cataract, infection, glaucoma, scleral calcification, and loss of an eye after pterygium excision with adjunctive mitomycin therapy. While the exact incidence of these complications is unknown, the contention that mitomycin-C therapy is safe remains to be determined with future long-term trials.

Intraoperative application of mitomycin to the scleral bed has been advocated by many authors since its use has become routine in glaucoma filtration surgery. Frucht-Pery et al[104] compared bare sclera excision with and without intraoperative 0.2 mg/ml mitomycin for 5 minutes in both primary and recurrent pterygia, and found recurrence rates

of 4% versus 46.7%, respectively, with a mean follow-up of approximately 22 months. Cano-Parra et al[105] showed similar results in a study of primary pterygia with intraoperative 0.1 mg/ml mitomycin for 5 minutes after a mean of 14.1 months' follow-up. Mastropasqua et al[106] studied recurrent pterygia removed with bare sclera technique with and without intraoperative 0.2 mg/ml mitomycin for 3 minutes, and found recurrence rates of 12.5% and 35.6%, respectively, after a mean of 35 months' follow-up. All three of these studies reported no serious complications. Recurrence rates are similar in studies that compare intraoperative mitomycin to postoperative drops.[107–109] Scleral thinning is more likely to occur after bare sclera excision with the use of postoperative mitomycin drops[109,110] or higher doses (0.4 mg/ml for 5 minutes) of intraoperative mitomycin.[111] Rubinfeld and Stein[110] studied 289 patients with both primary (155) and recurrent (134) pterygia treated with intraoperative 0.2 mg/ml mitomycin for 3 minutes followed by conjunctival closure, and found a recurrence rate of 2.7% with a mean of 26 months' follow-up with no serious complications. Intraoperative 0.2 mg/ml mitomycin for 3 minutes with conjunctival closure has also compared favorably with conjunctival-limbal autograft in recurrent pterygia.[112] Corneoscleral melt has been reported in a patient who underwent intraoperative 0.2 mg/ml mitomycin for 3 minutes with a sliding conjunctival flap.[113] Again, long-term data are scarce, but caution should be taken whenever using mitomycin intraoperatively or postoperatively in drop form. If mitomycin is used, we recommend intraoperative application with complete covering of the exposed sclera.

Unfortunately, the optimum dosage and treatment length of topical mitomycin to maximize both effectiveness and safety are not precisely known. Clues to the optimum dosage of mitomycin-C may be inferred from a study on the inhibitory effects of mitomycin-C on human Tenon's capsule fibroblasts in cell culture: cell colony formation was inhibited at mitomycin concentrations of 0.1 mg/ml, cell death ensued at mitomycin-C concentrations of 0.3 mg/ml, and the LD_{50} for these fibroblasts was 0.2 mg/ml.[85] Other investigators are currently evaluating the effects of various mitomycin-C concentrations and application times on vascular endothelium and limbal stem cells in rabbits to ascertain a dose–response curve.[103] Regarding stability of the topical solution, reconstituted mitomycin has a pH of 6 to 8 and is stable for 2 weeks when refrigerated at 2–8°C.[90]

Daunorubicin

Daunorubicin is an anthracycline antibiotic that is primarily used for the treatment of leukemias. It inhibits DNA and RNA synthesis by inhibiting topoisomerase-II enzyme, and has recently been used intraoperatively during primary pterygium excision. Dadeya and Kamlesh[114] showed intraoperative application of 0.02% daunorubicin for 3 minutes to be more effective than bare sclera excision alone, with recurrence rates of 6.7% and 33%, respectively, after a mean follow-up of 15 months. In a subsequent study, the patients treated with daunorubicin also had equal recurrence rates when compared retrospectively to a group of patients treated with conjunctival autograft, 7.1% and 8.3%, respectively, with a mean follow-up of 27 months.[115] There were no serious complications; however, long-term studies are needed for safety and additional studies for determination of efficacy in recurrent pterygia.

Radiation therapy

Until the 1950s, radon bulbs, radium plaques, Grenz rays, and X-rays were employed in the treatment of pterygia with variable success.[40,116] In 1952, strontium-90 was introduced for the treatment of neoplastic disease and has been used extensively for the treatment of pterygia since that time. Strontium-90 is produced in the fission of uranium-235 and has a half-life of 28 years. Strontium-90 decays to yttrium-90, with a half-life of 64 hours, which, in turn, decays to zirconium-90, which is stable.[117] Beta rays from strontium-90 have an average energy of 0.21 MeV per disintegration while beta rays from yttrium-90 have an average energy of 0.89 MeV per disintegration.[117] Beta rays expend their energy maximally within the superficial 2 mm of tissue as the dose drops to 41% at 1 mm, 19% at 2 mm, 9% at 3 mm, and 1% at 5 mm.[40] This low penetration profile for strontium-90 is important, since cataracts may develop should the dose to the crystalline lens approach 1500 to 2500 rep (1 rep = 1.08 rad).[40]

Recurrence rates after pterygium excision with beta irradiation have varied widely, with a low of 0%[118] to a high of 80%[119] reported in the literature. Of the larger series reported, recurrence rates vary between 1.7% (825 cases),[120] 6% (975 cases),[121] and 12% (764 cases).[122] Direct comparison of the various studies is difficult because of the variations in the populations studied, follow-up intervals, dosage regimens, and definition of a recurrence. The mechanism of action of beta irradiation in reducing recurrences is thought to be through the inhibition of mitosis in rapidly dividing cells such as vascular endothelial cells.[41]

Various investigators report different opinions on the total dosage required, the need for fractionation, or the optimal time for delivery of beta irradiation after pterygium excision. A literature review by Paryani et al[120] disclosed that the total dose of beta irradiation has varied from 1800 to 6000 rad given in one to six fractions in different reports. Apparently there is some degree of flexibility in the total dose and the fractionation of beta irradiation delivered after pterygium excision, with different investigators reporting efficacy with widely varying protocols. Most investigators, however, hold that the optimal dose is between 1000 and 3000 rad given at the time of surgery or within a few days of surgery.[41] Aswad and Baum[123] reported that a single 2000 rad dose given in the immediate postoperative period had a lower recurrence rate than a similar dose given 4 days postoperatively in patients with secondary recurrent pterygia. No statistically significant difference in the timing of the beta irradiation was found in patients with primary pterygia. Furthermore, applying the beta irradiation at the time of surgery may also allow better control and localization of the treatment and may save the patient additional time and expense.[40,123]

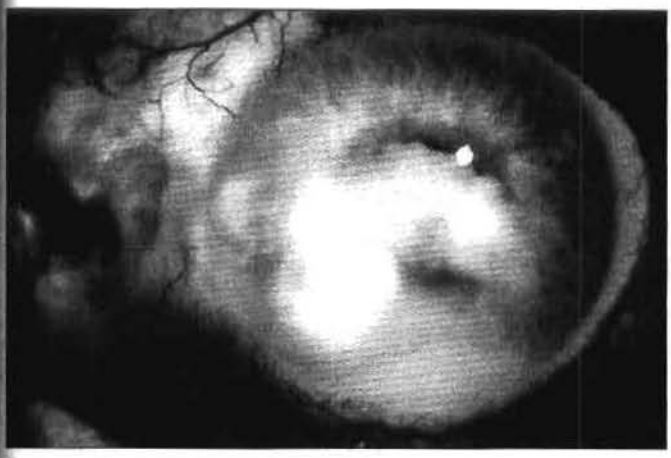

Fig. 144.4 Necrotizing scleritis and secondary *Pseudomonas* sclerokeratitis occurring 17 years after beta irradiation for pterygium.

While beta irradiation lowers the recurrence rate of pterygia, significant long-term complications have been reported, including cataract formation and scleral necrosis (Fig. 144.4). The risk of scleral complications following beta irradiation may be lessened by decreasing the treated surface area, as the sclera's relative avascularity is particularly vulnerable to radiation-induced ischemia.[124] MacKenzie et al[122] reported a 13% rate of scleromalacia with a 4.5% rate of severe scleral thinning in a large population-based study with 10 years' follow-up. Additionally, endophthalmitis as a consequence of the scleral necrosis was seen in two patients. Tarr and Constable[125] reported on 63 eyes with complications after pterygium excision with beta irradiation evaluated from 3 to 20 years postoperatively. Scleral ulceration was reported in 51 eyes, and nonvisually disabling sectoral lens opacities were identified in 19 eyes. Reduced vision secondary to a radiation-induced cataract occurred in three eyes. *Pseudomonas* endophthalmitis occurred in four patients with scleral necrosis. Other less frequently encountered complications included corneal ulcers, symblepharon, iris atrophy, ptosis, and thinned conjunctival tissue. Dusenbery et al[126] reported that 13 of 36 eyes treated with beta irradiation developed complications that included epithelial defects or corneal thinning, symblepharon, cataract, and corneal ulceration with an associated *Pseudomonas* keratitis.

Four of the five eyes that were previously irradiated had an 80% complication rate. Moriarty et al[127] reported 11 cases of secondary fungal or bacterial infections as a consequence of beta irradiation-induced scleral necrosis. The average latency between the beta irradiation and the onset of the complications was 14.5 years. Seven patients required a penetrating keratoplasty to remove the associated infection or treat a full-thickness or incipient perforation. Scleral thinning or perforation can be treated surgically with patch grafting using banked sclera. Scleral necrosis due to both mitomycin[128] and beta irradiation[129] has also been successfully treated with hyperbaric oxygen in selected cases that failed conjunctival grafting.

Because conjunctival autografting offers a low rate of pterygium recurrence and is free from long-term sight-threatening complications, it appears that autografting offers patients a safer alternative when compared to beta irradiation.[127] Because scleral necrosis and possible late infectious complications occur years after the original surgery, it is not surprising that numerous short- and intermediate-term studies deemed beta irradiation safe. While it is debatable whether the reported complications from beta irradiation or mitomycin therapy are at an acceptably low rate, the serious nature of these untoward late effects make conjunctival autografting a viable alternative in the treatment of both primary and secondary pterygia.

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