INVESTIGATION OF CORNEAL DISEASE

particularly bacteria, while the patient waits. Polymerase chain reaction (PCR) may provide rapid identification of herpes viruses, acanthamoeba, and scrapings, although it may have to be empirical based upon the clinical features. Specimens have been obtained. It is important that therapy is not withheld if an organism cannot be identified on microscopic examination of corneal scrapings, stained with Gram’s and Giemsa’s stains, may allow identification of the organism, which may be achieved as soon as possible. Examination of corneal scrapings, stained with Gram’s and Giemsa’s stains, may allow identification of the organism, which may be achieved as soon as possible. Photophobia in corneal disease is the result of painful contraction of an inflamed iris. Dilation of iris vessels is a reflex phenomenon caused by irritation of the corneal nerve endings. Photophobia, severe in most corneal disease, is minimal in herpetic keratitis because of the hypesthesia associated with the disease, which is also a valuable diagnostic sign.

Although tearing and photophobia commonly accompany corneal disease, there is usually no discharge except in purulent bacterial ulcers.

INVESTIGATION OF CORNEAL DISEASE

Symptoms & Signs
The physician examines the cornea by inspecting it under adequate illumination. Examination is often facilitated by instillation of a local anesthetic. Fluorescein staining can outline a superficial epithelial lesion that might otherwise be impossible to see. The slitlamp is essential in proper examination of the cornea; in its absence, a loupe and bright illumination can be used. One should follow the course of the light reflection while moving the light carefully over the entire cornea. Rough areas indicative of epithelial defects are demonstrated in this way.

The patient’s history is important in corneal disease. A history of trauma can often be elicited—in fact, foreign bodies and abrasions are the two most common corneal lesions. A history of corneal disease may also be of value. The keratitis of herpes simplex infection is often recurrent, but since recurrent erosion is extremely painful and herpetic keratitis is not, these disorders can be differentiated by their symptoms. The patient’s use of topical medications should be investigated, since corticosteroids may have been used and may have predisposed to bacterial, fungal, or viral disease, especially herpes simplex keratitis. Immunosuppression also occurs with systemic diseases, such as diabetes, AIDS, and malignant disease, as well as with specific immunosuppressive therapy. All medications and preservatives can cause contact dermatitis or corneal toxicity.

Laboratory Studies
To select the proper therapy for corneal infections, especially suppurating ulceration, laboratory aid is essential. Bacterial and fungal ulcers, for example, require completely different medications. Since a delay in identifying the correct organism may severely compromise the ultimate visual result, it should be achieved as soon as possible. Examination of corneal scrapings, stained with Gram’s and Giemsa’s stains, may allow identification of the organism, particularly bacteria, while the patient waits. Polymerase chain reaction (PCR) may provide rapid identification of herpes viruses, acanthamoeba, and fungi. Cultures for bacteria are usually obtained in all cases at first presentation. Cultures for fungi, acanthamoeba, or viruses may be undertaken if the clinical features are typical or there is lack of response to treatment for bacterial infection. Appropriate therapy is instituted as soon as the necessary specimens have been obtained. It is important that therapy is not withheld if an organism cannot be identified on microscopic examination of corneal scrapings, although it may have to be empirical based upon the clinical features.

Morphologic Diagnosis of Corneal Lesions

EPITHELIAL KERATITIS
The corneal epithelium is involved in most types of conjunctivitis and keratitis and in rare cases may be the only tissue involved (e.g., in superficial punctate keratitis). The epithelial changes vary widely from simple edema and vacuolation to minute erosions, filament formation, partial keratinization, etc. The lesions vary also in their location on the cornea. All of these features have important diagnostic significance (Figure 6–1), and slitlamp examination with and without fluorescein staining should be a part of every external eye examination.

Figure 6–1.
There are a number of important types of discrete subepithelial lesions, often secondary to epithelial keratitis (eg, the subepithelial infiltrates of epidemic keratoconjunctivitis, caused by adenoviruses 8 and 19).

**STROMAL KERATITIS**

The responses of the corneal stroma to disease include infiltration, representing accumulation of inflammatory cells; edema manifested as corneal thickening, opacification, or scarring; "melting" or necrosis, which may lead to thinning or perforation; and vascularization. The patterns of these responses are less specific for disease entities than those seen in epithelial keratitis, and the clinician often must rely on other clinical information and laboratory studies for clear identification of causes.

**ENDOTHELIAL KERATITIS**

Dysfunction of the corneal endothelium results in corneal edema, initially involving the stroma and later the epithelium. This contrasts with corneal edema due to raised intraocular pressure, in which the epithelium is affected before the stroma. As long as the cornea is not too edematous, it is often possible to visualize morphologic abnormalities of the corneal endothelium with the slitlamp. Inflammatory cells on the endothelium (keratic precipitates [KPs]) are not always an indication of endothelial disease because they are also a manifestation of anterior uveitis, which may or may not accompany stromal keratitis.

**CORNEAL ULCERATION**

Cicatrization due to corneal ulceration is a major cause of blindness and impaired vision throughout the world. Most of this visual loss is avoidable by early diagnosis and prompt appropriate treatment, but also by minimizing predisposing factors.

**INFECTIOUS CORNEAL ULCERS**

Central ulcers usually are infectious ulcers secondary to corneal epithelial damage. The lesion is situated centrally, away from the vascularized limbus. It is often accompanied by hypopyon, a collection of inflammatory cells seen as a pale layer in the inferior anterior chamber that also occurs in severe anterior uveitis (see Chapter 7). Although hypopyon is sterile in bacterial corneal ulcers unless there has been a rupture of Descemet's membrane, in fungal ulcers
it may contain fungal elements.

Central suppurative ulceration was once caused almost exclusively by *S. pneumoniae* infection complicating corneal trauma, particularly occurring in patients with obstructed nasolacrimal ducts. The commonest predisposing factor in developed countries has become contact lens wear, being particularly associated with pseudomonas and acanthamoebae keratitis. More widespread use of compromising systemic and local medications has increased the incidence of corneal ulcers due to opportunistic bacteria, fungi, and viruses.

**Bacterial Keratitis**

Many types of bacterial corneal ulcers look alike and vary only in severity. This is especially true of ulcers caused by opportunistic bacteria (e.g., alpha-hemolytic streptococci, *Staphylococcus aureus*, *Staphylococcus epidermidis*, nocardia, and *M. fortuitum-chelonei*), which cause indolent corneal ulcers that tend to spread slowly and superficially.

**Streptococcus pneumoniae** (pneumococcal) Corneal Ulcer

Pneumococcal corneal ulcer usually manifests 24–48 hours after inoculation of an abraded cornea. It typically produces a gray, fairly well-circumscribed ulcer that tends to spread erratically from the original site of infection toward the center of the cornea (Figure 6–2). The advancing border shows active ulceration and infiltration as the trailing border begins to heal. (This creeping effect gave rise to the term “acute serpiginous ulcer.”) The superficial corneal layers become involved first, and then the deep parenchyma. The cornea surrounding the ulcer is often clear. Hypopyon is common. Scrapings from the leading edge of a pneumococcal corneal ulcer usually contain gram-positive lancet-shaped diplococci. Drugs recommended for use in treatment are listed in Tables 6–1 and 6–2. Concurrent dacryocystitis and nasolacrimal duct obstruction should also be treated.

**Figure 6–2.**

![Pneumococcal corneal ulcer with hypopyon.](image)

**Table 6–1. Treatment of Bacterial, Fungal, or Amebic Keratitis.**

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Initial Therapies²</th>
<th>Alternative Therapies²</th>
</tr>
</thead>
<tbody>
<tr>
<td>No organisms identified; ulcer suggestive of bacterial infection</td>
<td>Moxifloxacin, gatifloxacin, or tobramycin with cefazolin</td>
<td>Ciprofloxacin, levofloxacin, oxfoxacin, gentamicin, ceftazidime, or vancomycin</td>
</tr>
<tr>
<td>Gram-positive cocci: lancet-shaped with capsule = <em>S pneumoniae</em></td>
<td>Moxifloxacin, gatifloxacin, or cefazolin</td>
<td>Levofloxacin, oxfoxacin, penicillin G, vancomycin, or ceftaxidime</td>
</tr>
<tr>
<td>Gram-positive cocci: methicillin-resistant <em>S. aureus</em> (MRSA)</td>
<td>Vancomycin</td>
<td>Other fluoroquinolones</td>
</tr>
<tr>
<td>Gram-positive rods: slender and varying in length—<em>Mycobacterium fortuitum</em>, Nocardia species, Actinomyces species</td>
<td>Amikacine, moxifloxacin, or gatifloxacin</td>
<td>Other fluoroquinolones, penicillin G, vancomycin, or ceftazidime</td>
</tr>
<tr>
<td>Other gram-positive organisms: cocci or rods</td>
<td>Cefazolin, moxifloxacin, or gatifloxacin</td>
<td>Penicillin G, cefazolin, or vancomycin</td>
</tr>
<tr>
<td>Gram-negative cocci³</td>
<td>Ceftriaxone⁴</td>
<td>Other fluoroquinolones, polymyxin B, or carbencillin</td>
</tr>
<tr>
<td>Gram-negative rods: thin = <em>Pseudomonas</em></td>
<td>Moxifloxacin, gatifloxacin, ciprofloxacin, tobramycin, or gentamicin</td>
<td>Tobramycin or getamicin with cefazolin, or penicillin G</td>
</tr>
<tr>
<td>Gram-negative rods: large, square-ended diplobacilli = Moraxella</td>
<td>Moxifloxacin, gatifloxacin, or ciprofloxacin</td>
<td>Ceftazidime, getamicin, or carbencillin</td>
</tr>
<tr>
<td>Other gram-negative rods</td>
<td>Moxifloxacin, gatifloxacin, or tobramycin</td>
<td>Amphotericin B, nystatin, miconazole, or flucytosine</td>
</tr>
<tr>
<td>No organism identified; ulcer suggestive of fungal infection</td>
<td>Natamycin or voriconazole</td>
<td>Amphotericin B, nystatin, miconazole, or flucytosine</td>
</tr>
<tr>
<td>Yeast-like organism = <em>Candida</em> species⁴</td>
<td>Voriconazole or amphotericin B</td>
<td>Amphotericin B or nystatin</td>
</tr>
<tr>
<td>Hyphae-like organisms = fungal ulcer</td>
<td>Natamycin or voriconazole</td>
<td>Amphotericin B or nystatin</td>
</tr>
<tr>
<td>Cyst, trophozoites = <em>Acanthamoeba</em></td>
<td>Propamidine and/or polyhexamethylene biguanide</td>
<td>Chlorhexidine or neomycin</td>
</tr>
</tbody>
</table>

²Intensive topical treatment, every hour during the day and every 2 hours during the night for at least the first 48 hours and then gradually reducing, is essential in all but the mildest cases. Subconjunctival injections are rarely necessary unless there are concerns about compliance with topical therapy or...
Pseudomonas aeruginosa Corneal Ulcer

Pseudomonas corneal ulcer begins as a gray or yellow infiltrate at the site of a break in the corneal epithelium (Figure 6–3). Severe pain usually accompanies it. The lesion tends to spread rapidly in all directions because of the proteolytic enzymes produced by the organisms. Although superficial at first, the ulcer may quickly affect the entire cornea with devastating consequences, including corneal perforation and severe intraocular infection. There is often a large hypopyon that tends to increase in size as the ulcer progresses. The infiltrate and exudate may have a bluish-green color. This is due to a pigment produced by the organism and is pathognomonic of *P aeruginosa* infection.

Change in treatment is only necessary if there is a lack of response and can be guided by antibiotic sensitivity of any organism isolated.

Rarely, *Pityrosporum ovale* or *Pityrosporum orbiculare* may be confused with *Candida* species.

Table 6–2. Drug Concentrations and Dosages for Treatment of Bacterial or Fungal Keratitis.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Topical¹</th>
<th>Subconjunctival</th>
<th>Systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>50–100 mg/mL</td>
<td>25 mg/0.5 mL/dose</td>
<td>10–15 mg/kg/d IV or IM in two doses</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>1.5–3 mg/mL</td>
<td>0.5–1 mg</td>
<td>...</td>
</tr>
<tr>
<td>Carbencillin</td>
<td>4 mg/mL</td>
<td>125 mg/0.5 mL/dose</td>
<td>100–200 mg/kg/d IV in four doses</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>50 mg/mL</td>
<td>100 mg/0.5 mL/dose</td>
<td>15 mg/kg/d IV in four doses</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>50 mg/mL</td>
<td>250 mg (0.5 mL)</td>
<td>1 g IV or IM every 8–12 hours (adult dose)</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>...</td>
<td>...</td>
<td>1–2 g/d IV or IM</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>3 mg/mL</td>
<td>...</td>
<td>500–750 mg orally every 12 hours</td>
</tr>
<tr>
<td>Fluocytosine</td>
<td>1% solution</td>
<td>...</td>
<td>50–150 mg/kg/d orally in four doses</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>3 mg/mL solution</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>10–20 mg/mL (fortified)</td>
<td>20 mg/0.5–1 mL/dose</td>
<td>...</td>
</tr>
<tr>
<td>Miconazole</td>
<td>1% solution or 2% ointment</td>
<td>5–10 mg; 0.5–1 mL/dose</td>
<td>...</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>5 mg/mL solution</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Natamycin</td>
<td>5% suspension</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Neomycin</td>
<td>20 mg/mL</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Nystatin</td>
<td>50,000 units/mL or cream (100,000 units/g)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Paromomycin</td>
<td>10 mg/mL</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>100,000 units/mL</td>
<td>1 million units/dose (painful)</td>
<td>40,000–50,000 units/kg IV in four doses; or continuously, 2–6 million units IV every 4–6 hours</td>
</tr>
<tr>
<td>Polyhexamethylene biguanide</td>
<td>0.01%–0.02% solution</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>1–2 mg/mL</td>
<td>10 mg/0.5 mL dose</td>
<td>...</td>
</tr>
<tr>
<td>Propamidine</td>
<td>0.1 mg/mL solution; 0.15% ointment</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>10–20 mg/mL (fortified)</td>
<td>20 mg/0.5 mL/dose</td>
<td>...</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>50 mg/mL</td>
<td>25 mg/0.5 mL/dose</td>
<td>...</td>
</tr>
</tbody>
</table>

¹Topical: Every hour during the day and every 2 hours during the night for at least 48 hours and then gradually reducing. Many of the preparations listed must be prepared by pharmacists with special training.

**Pseudomonas aeruginosa Corneal Ulcer**

Pseudomonas corneal ulcer begins as a gray or yellow infiltrate at the site of a break in the corneal epithelium (Figure 6–3). Severe pain usually accompanies it. The lesion tends to spread rapidly in all directions because of the proteolytic enzymes produced by the organisms. Although superficial at first, the ulcer may quickly affect the entire cornea with devastating consequences, including corneal perforation and severe intraocular infection. There is often a large hypopyon that tends to increase in size as the ulcer progresses. The infiltrate and exudate may have a bluish-green color. This is due to a pigment produced by the organism and is pathognomonic of *P aeruginosa* infection.
Pseudomonas corneal ulcer is usually associated with soft contact lenses—especially extended-wear lenses. The organism has been shown to adhere to the surface of soft contact lenses. Some cases have been reported following the use of contaminated fluorescein solution or eye drops. It is mandatory that the clinician use sterile medications and sterile technique when caring for patients with corneal injuries.

Scrapings from the ulcer may contain long, thin gram-negative rods that are often few in number. Drugs recommended for use in treatment are listed in Tables 6–1 and 6–2.

**Moraxella liquefaciens Corneal Ulcer**

*M. liquefaciens* (diplobacillus of Petit) causes an indolent oval ulcer that usually affects the inferior cornea and progresses into the deep stroma over a period of days. There is usually no hypopyon or only a small one, and the surrounding cornea is usually clear. *M. liquefaciens* ulcer almost always occurs in a patient with alcoholism, diabetes, or other causes of immunosuppression. Scrapings may contain large, square-ended gram-negative diplobacilli. Drugs recommended for use in treatment are listed in Tables 6–1 and 6–2. Treatment can be difficult and prolonged.

**Group A Streptococcus Corneal Ulcer**

Central corneal ulcers caused by beta-hemolytic streptococci have no identifying features. The surrounding corneal stroma is often infiltrated and edematous, and there is usually a moderately large hypopyon. Scrapings often contain gram-positive cocci in chains. Drugs recommended for use in treatment are listed in Tables 6–1 and 6–2.

**Staphylococcus aureus, Staphylococcus epidermidis, & Alpha-Hemolytic Streptococcus Corneal Ulcers**

Central corneal ulcers caused by these organisms are now being seen more often than formerly, many of them in corneas compromised by topical corticosteroids. The ulcers are often indolent but may be associated with hypopyon and some surrounding corneal infiltration. They are often superficial, and the ulcer bed feels firm when scraped. Scrapings may contain gram-positive cocci— singly, in pairs, or in chains. Infectious crystalline keratopathy (in which the cornea has a crystalline appearance) has been described in patients receiving long-term therapy with topical steroids; the disease is often caused by alpha-hemolytic streptococci as well as nutritionally deficient streptococci. Tables 6–1 and 6–2 show recommended drug regimens.

**Mycobacterium fortuitum-chelonei & Nocardia Corneal Ulcers**

Ulcers due to *M. fortuitum-chelonei* and nocardia are rare. They often follow trauma and are often associated with contact with soil. The ulcers are indolent, and the bed of the ulcer often has radiating lines that make it look like a cracked windshield. Hypopyon may or may not be present. Scrapings may contain acid-fast slender rods (*M. fortuitum-chelonei*) or gram-positive filamentous, often branching organisms (nocardia). See Tables 6–1 and 6–2 for recommended drug regimens.

**Fungal Keratitis**

Fungal corneal ulcers, once seen most commonly in agricultural workers, have become more common in the urban population since the introduction of the corticosteroid drugs for use in ophthalmology. Before the corticosteroid era, fungal corneal ulcers occurred only if an overwhelming inoculum of organisms was introduced into the corneal stroma—an event that can still take place in an agricultural setting or related to soft contact lens wear. The uncompromised cornea seems to be able to handle the small inocula to which urban residents are ordinarily subjected.

Fungal ulcers are indolent and have a gray infiltrate with irregular edges, often a hypopyon, marked inflammation of the globe, superficial ulceration, and satellite lesions (usually infiltrates at sites distant from the main area of ulceration) (Figure 6–4). Underlying the principal lesion—and the satellite lesions as well—there is often an endothelial plaque associated with a severe anterior chamber reaction. Corneal abscesses frequently occur.

**Figure 6–4.**

Most fungal ulcers are caused by opportunists such as candida, fusarium, aspergillus, penicillium, cephalosporium, and others. There are no identifying features that help to differentiate one type of fungal ulcer from another.

Scrapings from fungal corneal ulcers, except those caused by candida, contain hyphal elements; scrapings from candida ulcers usually contain pseudohyphae or yeast forms that show characteristic budding. Tables 6–1 and 6–2 list the drugs recommended for the treatment of fungal ulcers.

**Viral Keratitis**

**Herpes Simplex Keratitis**

Herpes simplex keratitis occurs in two forms: primary and recurrent. It is the most common cause of corneal ulceration and the most common corneal...
cause of blindness in the United States. The epithelial form is the ocular counterpart of labial herpes, with which it shares immunologic and pathologic features as well as having a similar time course. The only difference is that the clinical course of the keratitis may be prolonged because of the avascularity of the corneal stroma, which retards the migration of lymphocytes and macrophages to the lesion. Herpes simplex virus (HSV) ocular infection in the immunocompetent host is often self-limited, but in the immunologically compromised host, including patients treated with topical corticosteroids, its course can be chronic and damaging. Stromal and endothelial disease has previously been thought to be a purely immunologic response to virus particles or virally induced cellular changes. However, there is increasing evidence that active viral infection can occur within stromal and possibly endothelial cells as well as in other tissues within the anterior segment, such as the iris and trabecular endothelium. This highlights the need to assess the relative role of viral replication and host immune responses prior to and during therapy for herpetic disease. Topical corticosteroids may control damaging inflammatory responses but at the expense of facilitation of viral replication. Thus, whenever topical corticosteroids are to be used, antivirals are likely to be necessary. Any patient undergoing topical corticosteroid therapy for herpetic eye disease must be under the supervision of an ophthalmologist.

Serologic studies suggest that almost all adults have been exposed to the virus, although many do not recollect any episodes of clinical disease. Following primary infection, the virus establishes latency in the trigeminal ganglion. The factors influencing the development of recurrent disease, including its site, have yet to be unraveled. There is increasing evidence that the severity of disease is at least partly determined by the strain of virus involved. Most HSV infections of the cornea are still caused by HSV type 1 (the cause of labial herpes), but in both infants and adults, a few cases caused by HSV type 2 (the cause of genital herpes) have been reported. The corneal lesions caused by the two types are indistinguishable. Scrapings of the epithelial lesions of HSV keratitis and fluid from skin lesions contain multinucleated giant cells. The virus can be cultivated on the chorioallantoic membrane of embryonated hens’ eggs and in many tissue cell lines—eg, HeLa cells, on which it produces characteristic plaques. In most cases, however, diagnosis can be made clinically on the basis of characteristic dendritic or geographic ulcers and greatly reduced or absent corneal sensation. PCR methods are used for accurate identification of HSV from tissue and fluid as well as from corneal epithelial cells.

CLINICAL FINDINGS

Primary ocular herpes simplex is infrequently seen but is manifested as a vesicular blepharoconjunctivitis, occasionally with corneal involvement, and usually occurs in young children. It is generally self-limited, without causing significant ocular damage. Topical antiviral therapy may be used as prophylaxis against corneal involvement and as therapy for corneal disease.

Attacks of the common recurrent type of herpetic keratitis (Figure 6–5) are triggered by fever, overexposure to ultraviolet light, trauma, the onset of menstruation, or some other local or systemic source of immunosuppression. Unilaterality is the rule, but bilateral lesions develop in 4–6% of cases and are seen most often in atopic patients.

**Figure 6–5.**


**Symptoms**

The first symptoms of an HSV infection are usually irritation, photophobia, and tearing. When the central cornea is affected, there is also some reduction in vision. Since corneal anesthesia usually occurs early in the course of the infection, the symptoms may be minimal and the patient may not seek medical advice. There is often a history of fever blisters or other herpetic infection, but corneal ulceration can occasionally be the only sign of a recurrent herpetic infection.

**Lesions**

The most characteristic lesion is the dendritic ulcer. It occurs in the corneal epithelium, has a typical branching, linear pattern with feathery edges, and has terminal bulbs at its ends (Figure 6–6). Fluorescein staining makes the dendrite easy to identify, but unfortunately herpetic keratitis can also simulate many corneal infections and must be considered in the differential diagnosis of many corneal lesions.

**Figure 6–6.**
TREATMENT

Debridement

An effective way to treat dendritic keratitis is epithelial debridement, since the virus is located in the epithelium and debridement will also reduce the viral antigenic load to the corneal stroma. Healthy epithelium adheres tightly to the cornea, but infected epithelium is easy to remove. Debridement is accomplished with a tightly wound cotton-tipped applicator. Topical iodine or ether has no value and can cause chemical keratitis. A cycloplegic such as homatropine 5% is then instilled into the conjunctival sac, and a pressure dressing is applied. The patient should be examined daily and the dressing changed until the corneal defect has healed, usually within 72 hours. Adjunctive therapy with a topical antiviral accelerates epithelial healing. Topical drug therapy without epithelial debridement for epithelial keratitis offers the advantage of not requiring patching but involves a hazard of drug toxicity.

Drug Therapy

The topical antiviral agents used in herpetic keratitis are idoxuridine, trifluridine, vidarabine, and acyclovir. (Topical acyclovir for ophthalmic use is not approved in the United States.) Trifluridine and acyclovir are much more effective in stromal disease than the others. Idoxuridine and trifluridine are frequently associated with toxic reactions. Oral acyclovir may be useful in the treatment of severe herpetic eye disease, particularly in atopic individuals who are susceptible to aggressive ocular and dermal (eczema herpeticum) herpetic disease. Dosage for active disease is 400 mg five times daily in nonimmunocompromised patients and 800 mg five times daily in compromised and atopic patients. Prophylactic dosage in recurrent disease is 400 mg twice daily. Famciclovir or valacyclovir may also be used.

Viral replication in the immunocompetent patient, particularly when confined to the corneal epithelium, usually is self-limited and scarring is minimal. It is thus unnecessary and potentially highly damaging to use topical corticosteroids. Regrettably, particularly when there is stromal disease, concerns about permanent scarring due to the corneal inflammation often result in the use of topical corticosteroids, but this is based on the misconception that reducing inflammation reduces disease severity. Even when the inflammatory response is thought to be purely immunologically driven, such as in disciform keratitis, topical corticosteroids are often best avoided if the episode is likely to be self-limited. Once topical corticosteroids have been used, this usually commits the patient to requiring the drug to control further episodes of keratitis, with the potential for uncontrolled viral replication and other steroid-related side effects, such as bacterial and fungal superinfection, glaucoma, and cataract. Topical corticosteroids may also accelerate corneal thinning, thus increasing the risk of corneal perforation. If it becomes necessary to use topical corticosteroids because of the severity of the inflammatory response, it is absolutely essential that appropriate antiviral therapy be used to control viral replication. Problems in the management of HSV keratitis are often due to...
inappropriate use of multiple topical treatments, including antivirals, antibiotics, and corticosteroids, resulting in adverse effects including epithelial toxicity. Frequently, using oral antivirals and tapering the corticosteroids will result in marked improvement.

**Surgical Treatment**

Penetrating keratoplasty may be indicated for visual rehabilitation in patients with severe corneal scarring, but it should not be undertaken until the herpetic disease has been inactive for many months. Postoperatively, recurrent herpetic infection may occur as a result of the surgical trauma and the topical antiviral agents should be used for several months after keratoplasty to cover the use of topical corticosteroids. Corneal perforation due to progressive herpetic stromal disease or superinfection with bacteria or fungi may necessitate emergency penetrating keratoplasty. Cyanoacrylate tissue adhesives can be used effectively to seal small perforations, and lamellar “patch” grafts have been successful in selected cases. Lamellar keratoplasty has the advantage over penetrating keratoplasty of reduced potential for corneal graft rejection. A therapeutic soft contact lens or tarsorrhaphy may be required to heal epithelial defects associated with herpes simplex keratitis, but amniotic membrane transplantation may be more effective.

**Control of Trigger Mechanisms that Reactivate HSV Infection**

Recurrent HSV infections of the eye are common, occurring in about one-third of cases within 2 years after the first attack. A trigger mechanism can often be discovered by careful questioning of the patient. Once identified, the trigger can often be avoided. Aspirin can be used to avoid fever, excessive exposure to the sun or ultraviolet light can be avoided, and aspirin can be taken just prior to the onset of menstruation. Prophylactic topical and/or oral antivirals may be used, for instance, prior to corneal laser refractive surgery.

**Varicella-Zoster Viral Keratitis**

Varicella-zoster virus (VZV) infection occurs in two forms: primary (varicella) and recurrent (herpes zoster). Ocular manifestations are uncommon in varicella but common in ophthalmic zoster. In varicella (chickenpox), the usual eye lesions are poxes on the lids and lid margins, Rarely, keratitis occurs (typically a peripheral stromal lesion with vascularization), and still more rarely, epithelial keratitis occurs with or without pseudodendrites. Disciform keratitis, with uveitis of varying duration, has been reported. In contrast to the rare and benign corneal lesions of varicella, the relatively frequent ophthalmic herpes zoster is often accompanied by keratouveitis that varies in severity according to the immune status of the patient. Thus, although children with zoster keratouveitis usually have benign disease, the aged have severe and sometimes blinding disease. Corneal complications in ophthalmic zoster often occur if there is a skin eruption in areas supplied by the branches of the nasociliary nerve. Unlike recurrent HSV keratitis that usually affects only the epithelium, VZV keratitis affects the stroma and anterior uvea at onset. The epithelial lesions are blotchy and amorphous except for an occasional linear pseudodendrite that only vaguely resembles the true dendrites of HSV keratitis. Stromal opacities consist of edema and mild cellular infiltration and initially are subepithelial. Deep stromal disease can follow with necrosis and vascularization (Figure 6–7). A disciform keratitis sometimes develops and resembles HSV disciform keratitis. Loss of corneal sensation, with the risk of neurotrophic keratitis (see below), is always a prominent feature and often persists for months after the corneal lesion appears to have healed. The associated uveitis tends to persist for weeks or months, but with time it eventually heals. Scleritis (sclerokeratitis) can be a serious feature of VZV ocular disease.

**Figure 6–7.**

![Herpes zoster keratitis](Image)


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Herpes zoster keratitis.

Intravenous and oral antivirals have been used successfully for the treatment of herpes zoster ophthalmicus, particularly in immunocompromised patients. The oral dosage for acyclovir is 800 mg five times daily for 10–14 days; for valacyclovir, 1 g three times daily for 7–10 days; for famciclovir, 500 mg every 8 hours for 7–10 days. Therapy needs to be started within 72 hours after appearance of the rash. The role of topical antivirals is less certain. Topical corticosteroids may be necessary to treat severe keratitis, uveitis, and secondary glaucoma. The use of systemic corticosteroids is controversial. They may be indicated in reducing the incidence and severity of postherpetic neuralgia, but the risk of steroid complications is significant. Unfortunately, systemic acyclovir has little influence on the development of postherpetic neuralgia. However, the condition is self-limited, and reassurance can be helpful as a supplement to analgesics.

**Acanthamoeba Keratitis**
Acanthamoeba is a free-living protozoan that thrives in polluted water containing bacteria and organic material. Corneal infection with acanthamoeba is usually associated with soft contact lens wear, including silicone hydrogel lenses, or overnight wear of rigid (gas-permeable) contact lenses to correct refractive errors (orthokeratology). It may also occur in non–contact lens wearers after exposure to contaminated water or soil.

The initial symptoms are pain out of proportion to the clinical findings, redness, and photophobia. The characteristic clinical signs are indolent corneal ulceration, a stromal ring, and perineural infiltrates, but patients often present with changes confined to the corneal epithelium.

The diagnosis is established by culturing on specially prepared media (nonnutrient agar with an overlay of \textit{E} coli). Better specimens are obtained by corneal biopsy than corneal scrape, since histopathologic examination for amebic forms (trophozoites or cysts) can also be undertaken. Impression cytology and confocal microscopy are newer diagnostic techniques. Contact lens cases and solutions should be cultured. Often the amebic forms can be identified in the contact lens case fluid.

The differential diagnosis includes herpetic keratitis, with which it is frequently confused, fungal keratitis, mycobacterial keratitis, and nocardia infection of the cornea.

In the early stages of the disease, epithelial debridement may be beneficial. Medical treatment is usually started with intensive topical propamidine isethionate (1% solution) and either polyhexamethylene biguanide (0.01–0.02% solution) or fortified neomycin eyedrops (Tables 6–1 and 6–2). Acanthamoeba species may have variable drug sensitivities and may acquire drug resistance. Treatment is also hampered by the organisms’ ability to encyst within the corneal stroma, necessitating prolonged treatment. Topical corticosteroids may be required to control the associated inflammatory reaction in the cornea.

Keratoplasty may be necessary in advanced disease to arrest progression of the infection or after resolution and scarring to restore vision. Amniotic membrane transplants may be helpful for persistent epithelial defects. If the organism reaches the sclera, medical and surgical treatments are usually fruitless.

**NON-INFECTIOUS CORNEAL ULCERS**

**Marginal Infiltrates & Ulcers**

The majority of marginal corneal ulcers are benign but extremely painful. They are secondary to acute or chronic bacterial conjunctivitis, particularly staphylococcal blepharoconjunctivitis and less often Koch-Weeks (\textit{Haemophilus aegyptius}) conjunctivitis. They are not an infectious process, however, and scrapings do not contain the causative bacteria. They are the result of sensitization to bacterial products, antibody from the limbal vessels reacting with antigen that has diffused through the corneal epithelium.

Marginal infiltrates and ulcers (Figure 6–8) start as oval or linear infiltrates, separated from the limbus by a lucid interval, and only later may ulcerate and vascularize. They are self-limited, usually lasting from 7 to 10 days, but those associated with staphylococcal blepharoconjunctivitis usually recur.

Treatment for blepharitis (shampoo scrubs, antimicrobials) usually will clear the problem; topical corticosteroids may be needed for severe cases. Topical corticosteroid preparations shorten their course and relieve symptoms, which are often severe, but treatment of the underlying blepharoconjunctivitis is essential if recurrences are to be prevented. Before starting corticosteroid therapy, great care must be taken to distinguish this entity from marginal herpetic keratitis. Marginal herpetic keratitis is usually almost symptomless because of corneal anesthesia, whereas hypersensitivity-type marginal ulcer is painful.

**Figure 6–8.**

![Marginal ulcer of temporal cornea, right eye.](source)

(Courtesy of P Thygeson.)

**Mooren’s Ulcer (Figure 6–9)**

The cause of Moorén’s ulcer is still unknown, but an autoimmune origin is suspected. It is a marginal ulcer, unilateral in 60–80% of cases and characterized by painful, progressive excavation of the limbus and peripheral cornea that often leads to loss of the eye. It occurs most commonly in old age but does not seem to be related to any of the systemic diseases that most often afflict the aged. It is unresponsive to both antibiotics and corticosteroids. Surgical excision of the limbal conjunctiva in an effort to remove sensitizing substances has recently been advocated. Lamellar tectonic keratoplasty has been used with success in selected cases. Systemic immunosuppressive therapy often is necessary to control moderate or advanced disease.

**Figure 6–9.**
Phlyctenular Keratoconjunctivitis

Phlyctenules are localized accumulations of lymphocytes, monocytes, macrophages, and finally neutrophils. They appear first at the limbus, but in recurrent attacks they may involve the bulbar conjunctiva and cornea. Corneal phlyctenules, often bilateral, cicatrize and vascularize, but conjunctival phlyctenules leave no trace.

Phlyctenular keratoconjunctivitis is a delayed hypersensitivity response, in most cases in developed countries to *S. aureus* or other bacteria that proliferate on the lid margin in association with blepharitis. It may also occur in response to *Mycobacterium tuberculosis*, which was formerly a major cause of visual loss in the United States, particularly among Native Americans. The attack may be triggered by an acute bacterial conjunctivitis but is associated typically with a transient increase in the activity of a childhood tuberculosis. Rare phlyctenules have occurred in San Joaquin Valley fever, a result of hypersensitivity to a primary infection with *Coccidioides immitis*. In this disease they rarely cause visual disability.

Untreated phlyctenules spontaneously regress after 10–14 days. Topical corticosteroid therapy shortens the duration and decreases scarring and vascularization. In the staphylococcal type, the acute staphylococcal infection and chronic blepharitis need to be treated.

Marginal Keratitis in Autoimmune Disease (Figure 6–10)

The peripheral cornea receives its nourishment from the aqueous humor, the limbal capillaries, and the tear film. It is contiguous with the subconjunctival lymphoid tissue and the lymphatic arcades at the limbus. The perilimbal conjunctiva appears to play an important role in the pathogenesis of corneal lesions that arise both from local ocular disease and from systemic disorders, particularly those of autoimmune origin. There is a striking similarity between the limbal capillary network and the renal glomerular capillary network. On the endothelial basement membranes of the capillaries of both networks, immune complexes are deposited and immunologic disease results. Thus, the peripheral cornea often participates in such autoimmune diseases as rheumatoid arthritis, polyarteritis nodosa, systemic lupus erythematosus, scleroderma, midline lethal and Wegener’s granulomatosis, ulcerative colitis, Crohn’s disease, and relapsing polychondritis. The corneal changes are secondary to scleral inflammation, with or without scleral vascular closure (see Chapter 7). The clinical signs include vascularization, infiltration and opacification, and peripheral guttering that may progress to perforation. Mooren’s ulcer may be an example of advanced marginal keratitis. Treatment is directed toward control of the associated systemic disease; topical therapy usually is ineffective, and systemic use of potent immunosuppressive drugs often is required. Corneal perforation may require keratoplasty.

**Figure 6–10.**

[Image of corneal changes due to autoimmune disease]
Corneal Ulcer Due to Vitamin A Deficiency

The typical corneal ulcer associated with avitaminosis A is centrally located and bilateral, gray and indolent, with a definite lack of corneal luster in the surrounding area (Figure 6–11). The cornea becomes soft and necrotic (hence the term "keratomalacia"), and perforation is common. The epithelium of the conjunctiva is keratinized, as evidenced by the presence of a Bitot spot. This is a foamy, wedge-shaped area in the conjunctiva, usually on the temporal side, with the base of the wedge at the limbus and the apex extending toward the lateral canthus. Within the triangle the conjunctiva is furrowed concentrically with the limbus, and dry flaky material can be seen falling from the area into the inferior cul-de-sac. A stained conjunctival scraping from a Bitot spot will show many saprophytic xerosis bacilli (Corynebacterium xerosis; small curved rods) and keratinized epithelial cells.

Avitaminosis A corneal ulceration results from dietary lack of vitamin A or impaired absorption from the gastrointestinal tract and impaired utilization by the body. It may develop in an infant who has a feeding problem; in an adult who is on a restricted or generally inadequate diet; or in any person with a biliary obstruction, since bile in the gastrointestinal tract is necessary for the absorption of vitamin A, or other causes of malabsorption. Lack of vitamin A causes a generalized keratinization of the epithelium throughout the body. The conjunctival and corneal changes together are known as xerophthalmia.

Since the epithelium of the air passages is affected, many patients, if not treated, will die of pneumonia. Avitaminosis A also causes a generalized retardation of osseous growth. This is extremely important in infants; for example, if the skull bones do not grow and the brain continues to grow, increased intracranial pressure and papilledema can result.

Mild vitamin A deficiency should be treated in adults with a dose of 30,000 U/d for 1 week. Advanced cases will require much higher doses initially (20,000 U/kg/d). Sulfonamide or antibiotic ointment can be used locally in the eye to prevent secondary bacterial infection. The average daily requirement of vitamin A is 1500–5000 IU for children, according to age, and 5000 IU for adults. Highly pigmented vegetables are the best source of dietary vitamin A.

Neurotrophic Keratitis

Trigeminal nerve dysfunction, due to trauma, surgery, tumor, inflammation, or any other cause, may result in corneal anesthesia with loss of the blink reflex, one of the cornea's defense mechanisms, as well as lack of trophic factors important for epithelial function. In the early stages of neurotrophic keratitis, there is diffuse blotchy epithelial oedema. Subsequently there is loss of the epithelium (neurotrophic ulcer), which may extend over a large area of the cornea.

In the absence of corneal sensation, even a severe keratitis may produce little discomfort. Patients must be warned to look out for redness of the eye, reduced vision, or increased conjunctival discharge and to seek ophthalmic care as soon as any of these develop. Keeping the cornea moist with artificial tears and lubricant ointments may help to protect it. Swim goggles may be useful at night.

Once neurotrophic keratitis develops, it must be treated promptly. The most effective management is to keep the eye closed by careful horizontal taping of the eyelids, by tarsorrhaphy, or by means of ptosis induced with botulinum toxin. Topical nerve growth factor, if necessary as autologous serum, may be helpful in severe cases. Secondary corneal infection must be treated appropriately.

Exposure Keratitis

Exposure keratitis may develop in any situation in which the cornea is not properly moistened and covered by the eyelids. Examples include exophthalmos from any cause, ectropion, floppy lid syndrome, the absence of part of an eyelid as a result of trauma, and inability to close the lids properly, as in Bell's palsy. The two factors at work are the drying of the cornea and its exposure to minor trauma. The uncovered cornea is particularly subject to drying during sleeping hours. If an ulcer develops, it usually follows minor trauma and occurs in the inferior third of the cornea. Exposure keratitis is sterile but can become secondarily infected.

The therapeutic objective is to provide protection and moisture for the entire corneal surface. The treatment method depends on the underlying condition: eyelid surgery, correction of exophthalmos, an eye shield, or the options mentioned above in the discussion of neurotrophic keratitis. The combination of corneal anesthesia and exposure is particularly likely to result in severe keratitis.

EPITHELIAL KERATITIS

CHLAMYDIAL KERATITIS

All five principal types of chlamydial conjunctivitis (trachoma, inclusion conjunctivitis, primary ocular lymphogranuloma venereum, parakeet or psittacosis...
conjunctivitis, and feline pneumonitis conjunctivitis) are accompanied by corneal lesions. Only in trachoma and lymphogranuloma venereum, however, are they blinding or visually damaging. The corneal lesions of trachoma have been extensively studied and are of great diagnostic importance. In order of appearance, they consist of (1) epithelial microerosions affecting the upper third of the cornea; (2) micropannus; (3) subepithelial round opacities, commonly called trachoma pustules; (4) limbal follicles and their cicatricial remains, known as Herbert's peripheral pits; (5) gross pannus; and (6) extensive, diffuse, subepithelial cicatrization. Mild cases of trachoma may have only epithelial keratitis and micropannus and may heal without impairing vision.

The rare cases of lymphogranuloma venereum have far fewer characteristic changes but are known to have developed blindness secondary to diffuse corneal scarring and total pannus. The remaining types of chlamydial infection cause only micropannus, epithelial keratitis, and, rarely, subepithelial opacities that are not visually significant. Several methods of identifying chlamydia are available through any competent laboratory.

Chlamydial keratoconjunctivitis responds to systemic tetracyclines, eg, doxycycline, erythromycin, and azithromycin (see Chapter 5). Topical sulfonamides, tetracyclines, erythromycin, and rifampin are also effective.

**DRUG-INDUCED EPITHELIAL KERATITIS**

Epithelial keratitis is not uncommonly seen in patients using antiviral medications (idoxuridine and trifluridine) and several of the broad-spectrum and medium-spectrum antibiotics, such as neomycin, gentamicin, and tobramycin. It is usually a coarse superficial keratitis affecting predominantly the lower half of the cornea and interpalastral fissure and may cause permanent scarring. The preservatives in eyedrops, particularly benzalkonium chloride and thimerosal, are a potent cause of toxic keratitis.

**KERATOCONJUNCTIVITIS SICCA (SJÖGREN'S SYNDROME)**

Epithelial filaments in the lower quadrants of the cornea are the cardinal signs of this autoimmune disease, in which secretion of the lacrimal and accessory lacrimal glands is diminished or eliminated. There is also a blotchy epithelial keratitis that affects mainly the lower quadrants. Severe cases develop mucous pseudofilaments that stick to the corneal epithelium.

This keratitis of Sjögren's syndrome must be distinguished from the keratitis sicca of such cicatrizing diseases as trachoma and ocular pemphigoid, in which the goblet cells of the conjunctiva have been destroyed. Such individuals sometimes continue to produce tears, but without mucus the corneal epithelium sheds the tears and remains dry.

Treatment of keratoconjunctivitis sicca calls for the frequent use of tear substitutes and lubricating ointments, of which there are many commercial preparations. When goblet cells have been destroyed, as in the cicatricial conjunctivitides, mucous substitutes must be used in addition to artificial tears. Topical vitamin A may help to reverse the epithelial keratinization. Moisture chambers or swim goggles may be required. Lacrimal punctal plugs and punctal occlusion are important in the management of advanced cases, as are room humidifiers. Cyclosporine (a T cell inhibitor), 0.05% applied topically, can reestablish goblet cell (mucin) density. Preservative-free artificial tears are often indicated.

**ADENOVIRUS KERATITIS**

Keratitis usually accompanies all types of adenoviral conjunctivitis, reaching its peak 5–7 days after onset of the conjunctivitis. It is a fine epithelial keratitis best seen with the slitlamp after instillation of fluorescein. The minute lesions may group together to make up larger ones.

The epithelial keratitis is often followed by subepithelial opacities. In epidemic keratoconjunctivitis (EKC), which is due to adenovirus types 8 and 19, the subepithelial lesions are round and grossly visible. They appear 8–15 days after onset of the conjunctivitis and may persist for months or even (rarely) for several years. Similar lesions occur very exceptionally in other adenoviral infections, eg, those caused by types 3, 4, and 7, but tend to be transitory and mild, lasting a few weeks at most.

Although the corneal opacities of adenoviral keratoconjunctivitis tend to fade temporarily with the use of topical corticosteroids so that the patient is temporarily more comfortable, corticosteroid therapy can prolong the corneal disease and is therefore not recommended.

**OTHER VIRAL KERATITIDES**

A fine epithelial keratitis may be seen in other viral infections, such as measles (in which the central cornea is affected predominantly), rubella, mumps, infectious mononucleosis, acute hemorrhagic conjunctivitis, Newcastle disease conjunctivitis, and verruca of the lid margin. A superior epithelial keratitis can reestablish goblet cell (mucin) density. Preservative-free artificial tears are often indicated.

**DEGENERATIVE CORNEAL CONDITIONS**

**KERATOCONUS**

Keratoconus is an uncommon degenerative bilateral disease that may be inherited as an autosomal recessive or autosomal dominant trait. Unilateral cases of unknown cause occur rarely. Symptoms appear in the second decade of life. The disease affects all races. Keratoconus has been associated with a number of diseases, including Down's syndrome, atopic dermatitis, retinitis pigmentosa, aniridia, vernal catarrh, Marfan's syndrome, Apert's syndrome, and Ehlers-Danlos syndrome. Pathologically, there are disruptive changes in Bowman's layer with keratocyte degeneration and ruptures in Descemet's membrane.

Blurred vision is the only symptom. Many patients present with rapidly increasing myopic astigmatism. Signs include cone-shaped cornea (Figure 6–12); linear narrow folds centrally in Descemet's membrane (Vogt's lines), which are pathognomonic; an iron ring around the base of the cone (Fleischer's ring); and, in extreme cases, indentation of the lower lid by the cornea when the patient looks down (Munson's sign). There is an irregular or scissor reflex on retinoscopy and a distorted corneal reflection with Placido's disk or the keratoscope even early in the disease. Color-coded topography provides more accurate information on the degree of corneal distortion (Figure 2–24). Often, the fundi cannot be clearly seen because of corneal astigmatism.

**Figure 6–12.**
Acute hydrops of the cornea may occur, manifested by sudden diminution of vision associated with central corneal edema. This arises as a consequence of rupture of Descemet's membrane and may be triggered by the patient rubbing the eye. The condition may be mistaken for extreme thinning with impending perforation. Acute hydrops usually clears gradually without treatment but often leaves apical and Descemet membrane scarring.

Rigid contact lenses will markedly improve vision in the early stages by correcting irregular astigmatism. Keratoconus is one of the most common indications for corneal transplantation, traditionally penetrating keratoplasty but possibly deep lamellar keratoplasty (DLK), which avoids the risk of endothelial rejection. Surgery is indicated when a contact lens can no longer be effectively worn or when peripheral thinning will affect the surgery.

Keratoconus is often slowly progressive between the ages of 20 and 60, although an arrest in progression of the keratoconus may occur at any time. If a corneal transplant is done before extreme corneal thinning occurs, the prognosis is excellent; good best-corrected vision is achieved in over 85% of eyes after 4 years and in over 70% of eyes after 14 years.

CORNEAL DEGENERATION

The corneal degenerations are a rare group of slowly progressive, bilateral, degenerative disorders that usually appear in the second or third decades of life. Some are hereditary. Other cases follow ocular inflammatory disease, and some are of unknown cause.

Terrien's Disease

Terrien's disease is a rare bilateral symmetric degeneration characterized by marginal thinning of the upper nasal quadrants of the cornea. Males are more commonly affected than females, and the condition occurs more frequently in the third and fourth decades. There are no symptoms except for mild irritation during occasional inflammatory episodes, and the condition is slowly progressive. The clinical picture consists of marginal thinning and peripheral vascularization with lipid deposition. Perforation is a known complication, especially from trauma. Tectonic (structural) keratoplasty may be required. Histopathologic studies of affected corneas have revealed vascularized connective tissue with fibrillary degeneration and fatty infiltration of collagen fibers. Because the course of progression is slow and the central cornea is spared, the prognosis is good.

Band (Calcific) Keratopathy (Figure 6–13)

Band keratopathy is characterized by the deposition of calcium salts in a band-like pattern in the anterior layers of the cornea. The keratopathy is usually limited to the interpalpebral area. The calcium deposits are noted in the basement membrane, Bowman's layer, and anterior stromal lamellas. A clear margin separates the calcific band from the limbus, and clear holes may be seen in the band, giving the Swiss cheese appearance. Symptoms include irritation, injection, and blurring of vision.
Calcific band keratopathy has been described in a number of inflammatory, metabolic, and degenerative conditions. It is characteristically associated with juvenile idiopathic arthritis. It has been described in long-standing inflammatory conditions of the eye, glaucoma, and chronic cyclitis. Band keratopathy may also be associated with hyperparathyroidism, vitamin D intoxication, sarcoidosis, and leprosy. The standard method of removing band keratopathy consists of removal of the corneal epithelium by curettage under topical anesthesia followed by irrigation of the cornea with a sterile 0.01-molar solution of ethylenediaminetetraacetic acid (EDTA) (edetate calcium) or application of EDTA with a cotton applicator. It can also be achieved with the excimer laser (phototherapeutic keratectomy).

Climatic Droplet Keratopathy (Labrador Keratopathy, Spheroid Degeneration of the Cornea) (Figure 6–14)

Climatic droplet keratopathy affects mainly people who work out of doors. The corneal degeneration is thought to be caused by exposure to ultraviolet light and is characterized in the early stages by fine subepithelial yellow droplets in the peripheral cornea. As the disease advances, the droplets become central, with subsequent corneal clouding causing blurred vision. Treatment in advanced cases is by corneal transplantation.

**Figure 6–14.**

Two photos showing climatic droplet (Labrador) keratodystrophy. Inset at left shows slitlamp view.

(Photo at left courtesy of A Ahmad.)

Salzmann’s Nodular Degeneration

This disorder is usually preceded by corneal inflammation, particularly phlyctenular keratoconjunctivitis or trachoma. Symptoms include redness, irritation, and blurring of vision. There is degeneration of the superficial cornea that involves the stroma, Bowman’s layer, and epithelium, with superficial whitish-gray elevated nodules sometimes occurring in chains.

Rigid contact lenses will significantly improve visual acuity in most cases. Corneal transplantation is rarely required, but superficial lamellar keratectomy or phototherapeutic (excimer laser) keratectomy (PTK) may be necessary.

**ARCUS SENILIS (CORNEAL ANNULUS, ANTERIOR EMBRYOTOXON)**

Arcus senilis is an extremely common, bilateral, benign peripheral corneal degeneration. Its prevalence is strongly associated with age. It is also associated with hypercholesterolemia and hypertriglyceridemia. Blood lipid studies should be performed in people under age 50.

Pathologically, lipid droplets involve the entire corneal thickness but are more concentrated in the superficial and deep layers, being relatively sparse in the corneal stroma.

There are no symptoms. Clinically, arcus senilis appears as a hazy gray ring about 2 mm in width and with a clear space between it and the limbus (Figure 6–15). No treatment is necessary, and there are no complications.

**Figure 6–15.**
HEREDITARY CORNEAL DYSTROPHIES

This is a group of rare hereditary disorders of the cornea of unknown cause characterized by bilateral abnormal deposition of substances and associated with alteration in the normal corneal architecture that may or may not interfere with vision. These corneal dystrophies usually manifest themselves during the first or second decade but sometimes later. They may be stationary or slowly progressive throughout life. Corneal transplantation, when indicated, improves vision in most patients with hereditary corneal dystrophy.

Anatomically, corneal dystrophies may be classified as epithelial, stromal, and posterior limiting membrane dystrophies.

Epithelial Corneal Dystrophies

MEESMANN DYSTROPHY

This slowly progressive disorder is characterized by microcystic areas in the epithelium. The onset is in early childhood (first 1–2 years of life). The main symptom is slight irritation, and vision is slightly affected. The inheritance is autosomal dominant.

EPITHELIAL BASEMENT (ANTERIOR) MEMBRANE DYSTROPHY

Microcysts, dots, or map or fingerprint patterns, hence the older names Cogan’s microcystic dystrophy and map-dot-fingerprint dystrophy, are seen at the level of the epithelial basement membrane. In vivo confocal microscopy demonstrates abnormal epithelial basement membrane protruding into the epithelium, as well as epithelial cell abnormalities and microcysts. Recurrent erosion is common. Vision usually is not significantly affected.

OTHERS

Reis-Bückler dystrophy is a dominantly inherited dystrophy affecting primarily Bowman’s layer. The disease begins within the first decade of life with symptoms of recurrent erosion. Opacification of Bowman’s layer gradually occurs, and the epithelium is irregular. No vascularization is usually noted. Vision may be markedly reduced.

Vortex dystrophy, or cornea verticillata, is characterized by pigmented lines occurring in Bowman’s layer or the underlying stroma and spreading over the entire corneal surface. Visual acuity is not markedly affected. Such a pattern of radiating pigmented lines may also be seen in patients treated with chlorpromazine, chloroquine, indomethacin, or amiodarone as well as in Fabry’s disease.

Stromal Corneal Dystrophies

There are three primary types of stromal corneal dystrophies.

GRANULAR DYSTROPHY

This usually asymptomatic, slowly progressive corneal dystrophy most often begins in early childhood. The lesions consist of central, fine, whitish "granular" lesions in the stroma of the cornea. The epithelium and Bowman’s layer may be affected late in the disease. Visual acuity is slightly reduced. Histologically, the cornea shows uniform deposition of hyaline material. Corneal transplant is not needed except in very severe and late cases. The inheritance is autosomal dominant.

MACULAR DYSTROPHY

This type of stromal corneal dystrophy is manifested by a dense gray central opacity that starts in Bowman’s layer. The opacity tends to spread toward the periphery and later involves the deeper stromal layers. Recurrent corneal erosion may occur, and vision is severely impaired. Histologic examination shows deposition of acid mucopolysaccharide in the stroma and degeneration of Bowman’s layer. Penetrating keratoplasty is often required. The inheritance is autosomal recessive.

LATTICE DYSTROPHY

Lattice dystrophy starts as fine, branching linear opacities in Bowman’s layer in the central area and spreads to the periphery. The deep stroma may become involved, but the process does not reach Descemet’s membrane. Recurrent erosion may occur. Histologic examination reveals amyloid deposits in the collagen fibers. Corneal transplantation, usually penetrating keratoplasty but possibly deep lamellar keratoplasty, is common, as is recurrence of the dystrophy in the graft. The hereditary pattern for lattice dystrophy is autosomal dominant.

Posterior Corneal Dystrophies

FUCHS’ DYSTROPHY

This disorder begins in the third or fourth decade and is slowly progressive throughout life. Women are more commonly affected than men. There are central wart-like deposits on Descemet’s membrane, thickening of Descemet’s membrane, and defects of size and shape of the endothelial cells. Decompensation of the endothelium may occur, particularly after cataract surgery, and leads to edema of the corneal stroma and epithelium, causing blurring of vision. Corneal haze is slowly progressive. Histologic examination of the cornea reveals the wart-like ex crescences, which are secreted by the...
endothelial cells, over Descemet's membrane. Thinning and pigmentation of the endothelium and thickening of Descemet's membrane are characteristics. Penetrating keratoplasty, generally combined with cataract surgery if this has not been performed previously, is often needed once corneal decompensation has developed, but overall has become required less frequently with improvements in cataract surgery. Deep lamellar endothelial keratoplasty (DLEK), in which the endothelium with only a thin layer of stroma is transplanted, is a promising new technique.

**POSTERIOR POLYMORPHOUS DYSTROPHY**
This is a common disorder with onset in early childhood. Polymorphous plaques of calcium crystals are observed in the deep stromal layers. Vesicular lesions may be seen in the endothelium. Edema occurs in the deep stroma. The condition is asymptomatic in most cases, but in severe cases, epithelial and total stromal edema may occur. The inheritance is autosomal dominant.

**MISCELLANEOUS CORNEAL DISORDERS**

**THYGESON'S SUPERFICIAL PUNCTATE KERATITIS**
Superficial punctate keratitis is an uncommon chronic and recurrent bilateral disorder more common in females. It is characterized by discrete and elevated oval epithelial opacities that show punctate staining with fluorescein, mainly in the pupillary area. The opacities are not visible grossly but can be easily seen with the slit lamp or loupe. Subepithelial opacities underlying the epithelial lesions (ghosts) are often observed as the epithelial disease resolves. No causative organism has been identified, but a virus is suspected. A varicella-zoster virus has been isolated from the corneal scrapings of one case. Mild irritation, slight blurring of vision, and photophobia are the only symptoms. The conjunctiva is not involved. Epithelial keratitis secondary to staphylococcal blepharoconjunctivitis is differentiated from superficial punctate keratitis by its involvement of the lower third of the cornea and lack of subepithelial opacities. Epithelial keratitis in trachoma is ruled out by its location in the upper third of the cornea and the presence of pannus. Many other forms of keratitis involving the superficial cornea are unilateral or are eliminated by their histories. Short-term instillation of corticosteroid drops will often cause disappearance of the opacities and subjective improvement, but recurrences are the rule. The ultimate prognosis is good since there is no scarring or vascularization of the cornea. Untreated, the disease runs a protracted course of 1–3 years. Long-term treatment with topical corticosteroids may prolong the course of the disease for many years and lead to steroid-induced cataract and glaucoma. Therapeutic soft contact lenses have been used to control symptoms in especially bothersome cases. Cyclosporine topical drops, 1% or 2%, have been effective as a substitute for corticosteroids.

**RECURRENT CORNEAL EROSION**
This is a fairly common and serious mechanical corneal disorder that presents some classic signs and symptoms but may be easily missed if the physician does not look for it specifically. The patient is usually awakened during the early morning hours by a pain in the affected eye. The pain is continuous, and the eye becomes red, irritated, and photophobic. When the patient attempts to open the eyes in the morning, the lid pulls off the loose epithelium, resulting in pain and redness. Three types of recurrent corneal erosions can be recognized:

1. **Acquired recurrent erosion (traumatic):** The patient usually gives a history of a previous corneal injury. It is unilateral, it occurs with equal frequency in males and females, and the family history is negative. The recurrent erosion occurs most frequently in the center below the pupil no matter where the site of the previous corneal injury was.
2. **Recurrent erosion associated with corneal disease:** After corneal ulceration heals, the epithelium may break down in a recurrent fashion (as in HSV "metaherpetic" ulcer).
3. **Recurrent erosion associated with corneal dystrophies:** Recurrent erosions of the cornea may be observed in patients with epithelial basement membrane dystrophy, lattice dystrophy, and Reis-Bückler corneal dystrophy.

Recurrent corneal erosion is due to a defect in anchoring of the corneal epithelium, either between the basal layer of the corneal epithelium and the basement membrane because of abnormal hemidesmosomes or between the basement membrane and Bowman's layer. The epithelium is loose and vulnerable to separation. Instillation of a local anesthetic relieves the symptoms immediately, and fluorescein staining will show the eroded area, typically a small area in the lower central cornea. Healed erosions often exhibit subepithelial debris. Treatment consists of a pressure bandage on the eye to promote healing. Mechanical denuding of the loose corneal epithelium may be necessary. The other eye should be kept closed most of the time to minimize movement of the lid over the affected eye. Bed rest is desirable for 24 hours. The cornea usually heals in 2–3 days. To prevent recurrence and to promote continued healing, it is important for these patients to use a bland ophthalmic ointment at bedtime for several months. In more severe cases, artificial tears are instilled during the day. The use of hypertonic ointment (glucose 40%) or 5% sodium chloride drops is often of value. Therapeutic soft contact lenses, needle micropuncture of Bowman's layer, and excimer laser phototherapeutic keratectomy have been useful in cases that do not respond to more conservative management.

**INTERSTITIAL KERATITIS DUE TO CONGENITAL SIPHILIS**
This self-limited inflammatory disease of the cornea, also known as immune stromal keratitis, characteristically is a late manifestation of congenital syphilis, but overall other causes are now more prevalent (see below), partly because of the reduction in incidence of congenital syphilis. Interstitial keratitis rarely occurs in acquired syphilis, of which the incidence has increased markedly in association with HIV infection. Interstitial keratitis due to congenital syphilis occasionally starts unilaterally but almost always becomes bilateral weeks to months later. It affects all races and is more common in females than males. Symptoms appear between the ages of 5 and 20. Pathologic findings include edema, lymphocytic infiltration, and vascularization of the corneal stroma. It is probably a delayed immune response to stromal antigen retained from passage of Treponema pallidum organisms through the cornea before or at birth, because the organisms are not found in the cornea during the acute phase.

**Clinical Findings**

**SYMPTOMS AND SIGNS**
Hutchinson's triad comprises interstitial keratitis, deafness, and notched upper central incisors. Saddle nose is another sign of congenital syphilis. The patient complains of pain, photophobia, and blurring of vision. Physical signs include conjunctival injection, corneal edema, vascularization of the deeper corneal layers, and miosis. There is an associated severe anterior granulomatous uveitis and blepharospasm due to photophobia. The grayish-pink appearance of the cornea (due to edema and vascularization) that occurs in the acute phase is sometimes referred to as a "salmon patch."

**LABORATORY FINDINGS**
Serologic tests for syphilis are positive.

**Complications & Sequelae**
Corneal scarring and vascularization occur if the process has been particularly severe and prolonged. Secondary glaucoma may result from the uveitis.

**Treatment**

Topical cycloplegics to dilate the pupils are important to prevent formation of posterior synechiae. Corticosteroid drops often relieve the symptoms dramatically but must be continued for long periods to prevent recurrence of symptoms. Dark glasses and a darkened room may be necessary if photophobia is severe. Treatment should be given for systemic syphilis, even though this usually has little effect on the ocular condition. Corneal scarring may necessitate corneal transplant, and glaucoma, if present, may be difficult to control.

**Course & Prognosis**

The severity of corneal disease is not affected by treatment, which is aimed at prevention of complications. The inflammatory phase lasts 3 or 4 weeks. The cornea then gradually clears, leaving ghost vessels and scars in the corneal stroma.

**INTERSTITIAL KERATITIS DUE TO OTHER CAUSES**

In the United States, unilateral interstitial (immune stromal) keratitis is usually due to herpes simplex virus and occasionally due to varicella-zoster virus. Commonly no cause is found for active bilateral interstitial keratitis, but congenital syphilis remains the most commonly identified cause of inactive bilateral disease. Tuberculosis, leprosy, cytomegalovirus, measles virus, mumps virus, and Lyme disease are rare causes of interstitial keratitis. Treatment is usually symptomatic, but it is important to establish the cause whenever possible.

Cogan syndrome is a rare disorder generally believed to be a vascular hypersensitivity reaction of unknown origin. It is a disease of young adults and is characterized by nonsyphilitic interstitial keratitis and a vestibulolauditory disturbance, usually sudden hearing loss. Corticosteroids are reputed to be of value, but some degree of visual impairment and complete nerve deafness usually supervene. Rarely patients die due to vasculitis, such as aortitis.

**CORNEAL PIGMENTATION**

Pigmentation of the cornea may occur with or without ocular or systemic disease. There are several distinct varieties.

**Krukenberg Spindle**

In pigment dispersion syndrome, brown uveal pigment is deposited bilaterally upon the central endothelial surface in a vertical spindle-shaped fashion (Krukenberg spindle). It occurs in a small percentage of people over age 20, usually in myopic women. It can be seen grossly but is best observed with the slitlamp. The visual acuity is only slightly affected, and the progression is extremely slow. Pigmentary glaucoma must be ruled out by yearly intraocular pressure measurements.

**Blood Staining**

This disorder occurs occasionally as a complication of traumatic hyphema with secondary glaucoma and is due to hemosiderin in the corneal stroma. The cornea is golden brown, and vision is decreased. In most cases the cornea gradually clears in 1–2 years.

**Kayser-Fleischer Ring**

This is a bilateral pigmented ring whose color varies widely from ruby red to bright green, blue, yellow, or brown. Composed of fine granular deposits of copper, each ring is 1–3 mm in diameter and located just inside the limbus at the level of Decemet's membrane. In exceptional cases, there is a second ring.

Kayser-Fleischer rings are almost always due to Wilson's disease (hepatolenticular degeneration) and are an important clinical finding as their presence may obviate the need for liver biopsy in patients with suggestive clinical features and abnormal copper studies. They have been described in chronic liver disease not due to Wilson's disease. In Wilson's disease, the intensity of the pigmentation can be reduced by treatment of the abnormal copper metabolism.

**Iron Lines (Hudson-Stähl line, Fleischer's Ring, Stocker's Line, Ferry's Line)**

Localized deposits of iron within the corneal epithelium may occur in sufficient quantity to become visible clinically. The Hudson-Stähl line is a horizontal line at the junction of the middle and lower thirds of the cornea, corresponding to the line of lid closure, in otherwise normal elderly patients. Fleischer's ring surrounds the base of the cone in keratoconus. Stocker's line is a vertical line associated with pterygia, and Ferry's line develops adjacent to limbal filtering blebs. Similar iron deposits are seen at the site of corneal scars.

**CONTACT LENSES**

Glass contact lenses were first described in 1888 by Adolf Fick and were then used for the treatment of keratoconus by Eugene Kalt. Poor results were achieved until 1945, when Kevin Tuohy of Los Angeles produced a plastic precorneal lens with a diameter of 11 mm. Since that time, advances in contact lens technology have produced several different varieties of lenses, which are broadly divided into two types: rigid and soft lenses. The basic requirement for success of contact lenses is to overcome the effect on oxygen supply to the cornea from wearing an occlusive lens. The optical features of contact lenses are discussed in Chapter 21.

**Rigid Lenses**

**STANDARD HARD LENSES**

These direct descendants of Tuohy's lens are made of polymethylmethacrylate (PMMA) (Perspex), are impervious to oxygen, and thus rely on pumping of tears into the space between the lens and the cornea during blinking to provide oxygen to the cornea. They are smaller than the corneal diameter. Always for daily wear, these lenses are easy to care for, are relatively inexpensive, and correct vision efficiently, particularly if there is significant astigmatism. Unfortunately, many persons cannot tolerate them. Corneal edema due to corneal hypoxia and spectacle blur (poor vision with spectacle correction after a period of contact lens wear) are common complaints, and they are now rarely used.

**RIGID GAS-PERMEABLE LENSES**

These are rigid lenses made from cellulose acetate butyrate, silicone acrylate, or silicone combined with polymethylmethacrylate. They have the advantage of high oxygen permeability, thus improving corneal metabolism, and greater comfort while retaining the optical properties of rigid lenses, although they are not as easy to tolerate as soft lenses. They are generally used on a daily-wear basis but can be used on an extended-wear (24-hour) basis in exceptional circumstances. Gas-permeable lenses are particularly suitable for correction of keratoconus and astigmatism and when bifocal or multifocal lenses are required.

**Orthokeratology** is the overnight wear of rigid gas-permeable lenses to correct myopia or astigmatism by reshaping the cornea. It is advocated as a safer, less expensive alternative to refractive surgery, but there is risk of corneal infection. Most ophthalmologists recommend not wearing any type of refractive contact lens through the night.

**Soft Lenses**

**COSMETIC SOFT LENSES**

Hydrogel lenses, either based on hydroxymethyl methacrylate (HEMA) or silicone, of which the latter provides greater oxygen permeability, are
considerably more comfortable than rigid lenses but are flexible and thus conform to the surface of the cornea. Regular astigmatism can be partially corrected by incorporating cylinder into the soft lens; irregular astigmatism is poorly corrected. They are cheaper to purchase but are less durable.

Complications are more common than with rigid lenses and include ulcerative keratitis (particularly if the lenses are worn overnight), immune corneal reactions to deposits on the lenses, giant papillary conjunctivitis, reactions to lens-care solutions (especially those containing the preservative thimerosal), corneal edema, and corneal vascularization.

Cosmetic soft contact lenses are usually removed each day, to be cleaned, disinfected, and then stored overnight in solution. With care, a pair of such lenses will last for 1 year but then should be discarded. Disposable soft contact lenses for daily wear but replacement each month probably reduce the risk of corneal infection. Daily disposable soft contact lenses, a new pair being worn each day, completely remove the need for cleaning and disinfecting, as well as reducing the risk of corneal infection, but are more expensive. Disposable soft contact lenses for overnight (extended) wear, usually to be worn for 1 week and then replaced to be worn for up to 30 days, are being strongly promoted by contact lens manufacturers but generally are not recommended by ophthalmologists because of the increased risk of corneal infection. For aphakic correction, it is occasionally necessary to resort to extended wear because of difficulties with insertion, removal, and care of the lenses. This has become much less frequent in adults because of the availability of intraocular lenses but continues to be a consideration in babies and children after cataract surgery.

**Therapeutic Soft Lenses**

The use of therapeutic soft contact lenses has become an indispensable part of the ophthalmologist’s management of external eye disease. The lenses form a soft barrier between the outside and the cornea, providing protection against trichiasis and exposure. Lenses with high water content can act as a “stent” for epithelial healing, such as in the treatment of recurrent erosions. Patients with pain due to epithelial disease, such as in bullous keratopathy, particularly benefit from therapeutic soft contact lenses. Lenses with low water content can be used to seal small corneal perforations or wound leaks. In all cases of therapeutic contact lens wear, infection can occur. Antimicrobial coverage may be indicated if there is an epithelial defect.

**Contact Lens Care**

It is essential that all contact lens wearers be made aware of the risks associated with contact lens wear—particularly those patients choosing the high-risk varieties such as extended-wear lenses for cosmetic optical correction purely on the grounds of convenience. All wearers must be under the regular care of a contact lens practitioner. Many of the chronic complications of contact lens wear are asymptomatic in their early and easily treated stages. Any contact lens should be removed immediately if the eye becomes uncomfortable or inflamed, and ophthalmic attention must be sought immediately if symptoms do not rapidly resolve.

Except for daily disposables, contact lenses require regular cleaning and disinfecting, and particularly in the case of soft lenses, removal of protein deposits is required. Disinfection regimens include heat, chemical soaking, and hydrogen peroxide solutions. All are effective if used according to the manufacturer’s instructions, although heat systems may be preferable for combating resistant organisms such as acanthamoeba.

For contact lens wearers who have developed hypersensitivity reactions to preservatives in their contact lens solutions, there are contact lens care systems that do not contain preservatives. It is important that such individuals are aware of the ability of organisms such as pseudomonas and acanthamoeba to survive in nonpreserved saline solutions. The use of nonpreserved contact lens solutions requires much greater vigilance in the regular disinfection of lenses and lens storage cases. Even with standard contact lens care systems, deposits in contact lens storage cases may prevent effective disinfection. Tap water, which may harbor organisms such as acanthamoeba, should not be used for rinsing contact lenses or contact lens storage cases. Contact lenses should not be worn when bathing in a hot tub or swimming.

**CORNEAL TRANSPLANTATION**

Corneal transplantation (keratoplasty) is indicated for a number of serious corneal conditions, eg, scarring, edema, thinning, and distortion. Penetrating keratoplasty (PK) means full-thickness corneal replacement. Lamellar keratoplasty is a partial-thickness procedure to replace the anterior cornea with a variable amount of stroma, extending to deep lamellar keratoplasty (DLK), in which almost all of the cornea except the endothelium is replaced. The reverse procedure is deep lamellar endothelial keratoplasty (DLEK), in which the endothelium with only a thin layer of stroma is transplanted.

Younger donors are preferred for penetrating and deep lamellar endothelial keratoplasties, because there is a direct relationship between age and the health and number of the endothelial cells, but older corneas (50–65 years) are acceptable if the endothelial cell count is adequate. Because of the rapid endothelial cell death rate, the eyes should be enucleated soon after death and refrigerated immediately. Whole eyes should be used within 48 hours, preferably within 24 hours. Modern storage media allow for longer storage. Corneoscleral caps stored in nutrient media may be used up to 6 days after donor death, and preservation in tissue culture media allows storage for as long as 6 weeks.

For lamellar and deep lamellar keratoplasty, corneas can be frozen, dehydrated, or refrigerated for several weeks; the endothelial cells are not important in these partial-thickness procedures involving the anterior cornea.

Diseases, such as chemical injuries (see Chapter 19), in which loss of limbal stem cells leads to failure of corneal epithelialization, may benefit from limbal stem cell transplants, from the fellow eye or a donor eye, or amniotic membrane transplants, particularly in preparation for corneal transplantation. For severe corneal disease unsuitable for corneal transplantation, various artificial corneas (keratoprostheses) have been tried but with little long-term success.

**Techniques**

For penetrating or lamellar keratoplasty, the recipient eye is prepared by a partial-thickness cutting of a circle of diseased cornea, such as with a suction trephine (cookie-cutter action), and full-thickness removal with scissors or partial-thickness removal with dissection. For deep lamellar endothelial keratoplasty, the recipient endothelium is removed using instruments inserted into the posterior stroma and anterior chamber.

For penetrating keratoplasty, the donor corneoscleral cap is placed endothelium up on a suction Teflon block; the trephine (Figure 6–16) is pressed down into the cornea, and a full-thickness button is punched out. For lamellar, deep lamellar, and deep lamellar endothelial keratoplasty, the process is adapted, using mechanical or possibly laser-cutting devices, to remove the required portion of cornea from a corneoscleral cap or whole globe.

**Figure 6–16.**
Developments in sutures (Figure 6–17), instruments, and microscopes, as well as changes in surgical techniques, have significantly improved the prognosis in all patients requiring corneal transplants. Reducing and managing postoperative astigmatism and corneal graft rejection continue to be major problems, particularly after penetrating keratoplasty (see Chapter 16). In contrast to other forms of transplantation, such as renal and cardiac transplantation, it is still not clear whether HLA tissue-type matching or ABO blood-group matching reduces the incidence of rejection after corneal transplant surgery.

A popular vacuum corneal punch and trephine. (Manufactured by Barron-Katena.)

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**Figure 6–17.**

REFRACTIVE CORNEAL SURGERY

The inconvenience of spectacles to many wearers and the complications associated with contact lenses have resulted in a search for surgical solutions to the problem of refractive error.

Radial Keratotomy

Developed initially by Sato of Japan and later by Fyodorov of the USSR, the central cornea is flattened by almost full-thickness radial incisions. The procedure is now rarely performed.

Keratomileusis

In 1961, Barraquer of Colombia reported on the technique of myopic keratomileusis in which a lamellar corneal autograft is removed, shaped with a cryolathe (flattened), and sutured back into position. The procedure, also now rarely performed, was a precursor to laser in situ keratomileousis (LASIK).

Procedures to Correct Astigmatism

Astigmatism continues to be a problem following most corneal operations, especially penetrating keratoplasty, and after cataract surgery. Astigmatism after keratoplasty may be improved by various surgical procedures, including relaxing incisions, compression sutures, and wedge resections. Laser procedures, such as LASIK or surface ablation techniques (LASEK, PRK, Epi-LASIK) (see below), may be helpful. Refinements of incision, including adjustment of location according to preoperative corneal astigmatism, are useful in preventing postoperative astigmatism after cataract surgery.

Alloplastic Corneal Implants

Various plastic discs and rings (eg, Intacs) have been placed in the corneal stroma to correct refractive errors but with limited success.

Clear Lens Removal & Phakic Lens Implants

Removal of the crystalline lens (clear lens removal) is widely advocated for treatment of high myopia and presbyopia, but there are significant risks, notably retinal detachment in highly myopic eyes. Insertion of an intraocular lens without removal of the crystalline lens (phakic lens implant) is also undertaken, but corneal endothelial damage and development of cataract are likely.
Lasers

A further approach to refractive corneal surgery involves the use of lasers (see Chapter 24). The excimer laser has received the most publicity, but the femtosecond laser is also proving useful.

In LASIK, a motorized microkeratome or the femtosecond laser (all-laser LASIK, IntraLase) is used to cut a thin lamellar corneal disk, which is folded back. Laser of the stromal bed produces the desired carefully programmed reshaping of the cornea, and then the flap is repositioned. The surface ablation techniques are photorefractive keratectomy (PRK), laser epithelial keratectomy (LASEK), and epi-LASIK. In PRK, only the corneal epithelium is removed prior to the laser treatment. In LASEK and epi-LASIK, the epithelium is removed, with dilute alcohol and a microkeratome respectively, and replaced after the laser treatment. When necessary, the laser delivery can be further refined by wavefront guided technology to take account of the optical aberrations of individual eyes.

Laser refractive surgery is mostly used for myopia but can also treat astigmatism or hyperopia. Long-term visual results are about the same for the various techniques, but each has its advantages and disadvantages. In general, PRK is used for low (≤6.00 PD or less) and LASIK for moderate myopia, clear lens removal being advocated for high myopia. LASIK produces the most rapid recovery, both visually and in terms of discomfort. The surface ablation techniques are particularly indicated for thin corneas and patients at risk of corneal trauma. Complications of laser refractive corneal surgery include unexpected refractive outcome, fluctuating refraction, irregular astigmatism, regression, epithelial, flap, or interface problems, stromal haze, corneal ectasia, and infection. Previous laser refractive corneal surgery results in particular difficulties when determining intraocular lens power for cataract surgery.

Other Refractive Techniques

Conductive keratoplasty (CK) shows promise along with safety in the treatment of hypermetropia and possibly presbyopia. Laser thermokeratoplasty (LTK) is also being studied for the treatment of low hyperopia.

REFERENCES


