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CORNEA AND EXTERNAL DISEASE

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I. Normal anatomy and physiology**A. *Conjunctiva: anatomy***

1. **Gross anatomy.** The conjunctiva is a thin, transparent mucous membrane lining the inner surface of the eyelid (palpebral conjunctiva) and covering the anterior sclera (bulbar conjunctiva). The palpebral portion is designated as marginal, tarsal, and orbital and merges with the conjunctiva of the superior and inferior fornices in loose folds. The bulbar conjunctiva is adherent to the underlying Tenon capsule and therefore to sclera, with the tightest adhesion occurring in a narrow band at the corneoscleral limbus. A delicate vertical crescent, the semilunar fold (plica semilunaris), separates the bulbar conjunctiva from the lacrimal caruncle at the medial canthus. The conjunctiva tends to be a mobile tissue and is capable of great distention with edema fluid, as is often seen with trauma or inflammation.
2. **Microscopically,** the conjunctiva is composed of (a) an anterior stratified columnar epithelium that is continuous with the corneal epithelium, and (b) a lamina propria composed of adenoid and fibrous layers. The epithelium is from two to seven layers thick and contains numerous unicellular mucous glands (goblet cells) that secrete the inner mucoid layer of the tear film. Although the healthy epithelium is never keratinized, it may become keratinized in certain disease states. The lamina propria is composed of connective tissue housing blood vessels, nerves, and glands. The accessory lacrimal glands of Krause are located deep in the substantia propria in the superior and inferior fornices. The accessory lacrimal glands of Wolfring are situated near the upper margin of the superior tarsal plate. The adenoid layer of the lamina propria, which develops particularly after 3 months of age, contains lymphocytes enmeshed in a fine reticular network without the presence of true lymphoid follicles. The fibrous layer of the lamina propria surrounds the smooth palpebral muscle of Müller.
3. The **blood supply** of the palpebral conjunctiva originates from peripheral (bulbar and fornix) and marginal arterial arcades of the eyelid. Within 4 mm of the limbus the vascular supply is derived from the anterior conjunctival branches of the anterior ciliary arteries (superficial plexus), which anastomose with the posterior conjunctival vessels from the peripheral arcade. Conjunctival vessels move with the conjunctiva and constrict with instillation of 1:1,000 epinephrine—a point of differentiation from the deeper episcleral and ciliary vessels.
4. **Innervation** of the bulbar conjunctiva is via the sensory and sympathetic nerves from the ciliary nerves. The remaining palpebral and fornix conjunctiva is innervated by

the ophthalmic and maxillary divisions of the trigeminal nerve (cranial nerve V).

5. **Lymphatic** drainage of the conjunctiva parallels that of the lid, with lateral drainage to the preauricular nodes and medial drainage to the submandibular nodes.

B. Cornea

1. **Gross anatomy.** The cornea represents the anterior 1.3 cm² of the globe and is the main refracting surface of the eye. Although the cornea is continuous with the sclera at the limbus, the anterior corneal curvature (radius equal to 7.8 mm) is greater than that of the sclera, with the central 4-mm optical zone almost spherical and the periphery gradually flattening toward the scleral curve. The horizontal diameter of the anterior

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surface of the cornea (11.6 mm) is longer than the vertical diameter (10.6 mm), so that the anterior aspect of the cornea forms a horizontal ovoid. Viewed from the posterior surface, the cornea is circular (with a diameter of 11.6 mm). A corneal diameter greater than 12.5 mm is termed *megalocornea*; a corneal diameter less than 11.0 mm is termed *microcornea*. The height of the cornea from the basal plane of the visible limbus to the apex is 2.7 mm. The central thickness of the cornea is 0.52 mm, which increases to 0.70 mm in the far periphery.

2. **Microscopically**, the cornea consists of five strata: the epithelium and its basement membrane, Bowman's layer, stroma, Descemet's membrane, and endothelium.
 - a. The corneal **epithelium** is a uniform five- to six-layer structure 50 to 100 μm thick and is composed of (a) a basal cell layer of replicating cylindrical cells, 18 μm high and 10 μm wide, (b) a wing cell layer with superior convex–inferior scalloped cells interdigitating between the apices of the basal cells, and (c) surface cells composed of flat cells in two or three layers culminating in a smooth corneal surface that is studded with ultrastructural microplicae and microvilli. Corneal **nerves** passing from the corneal stroma through Bowman's layer terminate freely between the epithelial cells, thus accounting for the great sensitivity of the cornea. The epithelium is firmly attached to the underlying Bowman's layer by a continuous basement membrane that is a very important source of firm epithelial adhesion.
 - b. **Bowman's layer** is a homogeneous condensation of the anterior stromal lamellae continuous with the corneal stroma. Its termination at the corneal periphery marks the anterior margin of the corneoscleral limbus.
 - c. The **stroma** represents 90% of the corneal thickness, with bundles of collagen fibrils of uniform thickness enmeshed in mucopolysaccharide ground substance. These bundles form 200 lamellae arranged parallel to the corneal surface but with alternate layers crisscrossing at right angles. This regular lattice structure, coupled with the deturgescent state of the stroma, has been credited with providing the extreme transparency of the cornea necessary for

optical clarity.

- d. **Descemet's membrane** is the basement membrane of the endothelial cells and can be easily stripped from the stroma. When torn or traumatized, the ends will tend to retract, indicating an inherent elasticity. Gradual thickening of this layer with age is noted, with the thickness approximately 3 to 4 μm at birth but increasing to 10 to 12 μm in adulthood. Peripheral dome-shaped excrescences of Descemet's membrane (Hassall-Henle warts) occur in persons over age 20 years. Histologically, the membrane is a homogeneous glass-like structure, but ultrastructurally is composed of stratified layers of very fine collagenous filaments in the anterior layer (anterior banded layer) with an amorphous posterior layer that increases with age.
 - e. The **endothelium** is a single layer of approximately 500,000 polygonal cells, 5 to 18 μm in size, that spread uniformly across the posterior surface of the cornea. Although mitotic activity can be seen in very young endothelial cells in the adult, repair most often occurs by amitotic enlargement of the central endothelial cells. These cells maintain deturgescence and contribute to the formation of Descemet's membrane.
3. The **blood supply** of the cornea arises predominantly from the conjunctival, episcleral, and scleral vessels that arborize about the corneoscleral limbus. The cornea itself is avascular.
 4. The **innervation** of the cornea is that of a rich sensory supply mostly via the ophthalmic division of the trigeminal nerve. This innervation is via the long ciliary nerves that branch in the outer choroid near the ora serrata region. These nerves pass via the sclera into the middle third of the cornea as 70 to 80 large nerve trunks that lose their myelin sheaths approximately 2 to 3 mm from the limbus, but can be visualized as fine

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filaments beyond. There is significant dichotomous and trichotomous branching, and the subsequent passage of nerve fibers through Bowman's layer ends freely between the epithelial cells.

C. Physiology: precorneal tear film

1. The **physiology** of the cornea and conjunctiva is best introduced in a discussion of the **precorneal tear film**. This film, which is 6 to 10 μm thick, is composed of three layers: (a) superficial lipid layer, (b) middle aqueous layer, and (c) inner mucous layer. The normal tear volume in the conjunctival sac is about 3 to 7 μL and can increase to the conjunctival sac capacity of 25 μL before overflow occurs. Tear flow rate is approximately 1 μL /per minute and comes from the secretion of the main and accessory lacrimal glands. After their release in the superotemporal region, the tears are distributed by the blinking action of the lids with the tear meniscus forming superior and inferior marginal tear strips before draining into the lacrimal puncta

located near the medial canthus. With a pH of 7.6 and an osmolarity comparable to sodium chloride 0.9%, there is a low glucose concentration and an electrolyte distribution similar to plasma, with the exception of a slightly greater potassium content. Oxygen dissolves readily in the tear film, and the dissolved protein content of the tear film includes immunoglobulins and lysozyme. These characteristics allow the tear film to provide a smooth surface for refraction, to mechanically wash and protect the cornea and conjunctiva, to provide oxygen exchange for the epithelium, to lubricate the surface during a blink, and to provide bacteriostasis.

2. **Corneal function.** The primary physiologic function of the cornea is to maintain an optically smooth surface and a transparent medium while protecting the intraocular contents of the eye. This duty is fulfilled by the effective interaction of the epithelium, stroma, and endothelium. The epithelium, endothelium, and Descemet's membrane are transparent because of the uniformity of their refractive indices. The transparency of the stroma is conferred by the special physical arrangement of the component fibrils. Although the refractive index of collagen fibrils differs from that of the interfibrillar substance, the small diameter of the fibril (300 Å) and the small distance between them (300 Å) provide a separation and regularity that causes little scattering of light despite the optical inhomogeneity. The relative state of deturgescence is provided by the barrier functions of the epithelium and endothelium as well as by the dehydrating function of the endothelium. Disturbance of this equilibrium, such as occurs in corneal edema, will increase light scattering and the opacity of the stroma.
 - a. The **anterior epithelial surface** with its microplacae and microvilli provides the scaffold for a smooth and continuous precorneal tear film. In addition, the epithelium serves as a relatively impermeable barrier to water-soluble materials. The epithelium also provides an effective barrier to many infectious agents. The epithelium is the most mitotically active layer of the cornea, and because of its high cellular density consumes considerable glucose and oxygen. The major source of oxygen for the epithelium is atmospheric oxygen dissolved in the tear film, which explains the sensitivity to hypoxia that occurs with improperly fitted or overworn contact lenses. Glucose for the epithelium is obtained from the aqueous humor by diffusion through the corneal stroma. The substance is either used or stored as glycogen. Epithelial metabolism occurs through the hexose monophosphate shunt or tricarboxylic acid cycle in the presence of oxygen, or via the anaerobic glycolysis pathway in the absence of oxygen. With these metabolic capabilities, the turnover of the epithelium is rapid, occurring approximately once every 7 days, and explains the ability of the epithelium to heal itself rapidly.
 - b. **Stroma.** There is little turnover of the stromal matrix, and the keratocytes may survive as long as 2 years under normal conditions.

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Glucose is obtained from the aqueous humor and oxidized via the Embden-Meyerhof tricarboxylic acid cycle. Interaction of the interfibrillar substances, particularly the acid mucopolysaccharides, generates a swelling pressure for

the stroma both in vivo and in vitro. This tendency to imbibe fluid results in light scattering if it is not kept in check by the dehydrating function of the endothelium.

- c. **Endothelium.** The major function of the endothelium is the maintenance of proper corneal hydration. The endothelium requires oxygen and glucose to maintain the metabolically active process, but the exact nature of the endothelial pump is not completely clear. Impairment of the pump function can occur in dystrophic conditions (Fuchs dystrophy), injury (postsurgical or traumatic), and in some inflammatory conditions (anterior segment necrosis).

II. Acute traumatic conditions

A. Abrasions and lacerations

(see Chapter 2, sec. V. and sec. VI.).

B. Perforations

1. **Etiologically,** corneal perforation can result from any corneal ulceration, either infectious (bacterial, fungal, or viral), inflammatory (rheumatoid arthritis or collagen disease), posttraumatic (burn), or trophic defects of degenerations, neurotrophic ulcer, or postherpetic ulcer. Use of topical *nonsteroidal antiinflammatory drugs (NSAIDs)* such as diclofenac in at-risk patients may trigger or worsen thinning and perforation.
2. **Treatment.** Occasionally, these perforations will seal with a small knuckle of iris and rarely can be self-sealing, but they usually result in partial or complete loss of the anterior chamber. Thus, they represent an urgent situation to be treated in most cases. Small, noninfectious perforations can often be splinted by use of a therapeutic **soft contact bandage lens** (Permalens, Kontur). Such treatment will sometimes allow healing of the perforation, but often is a stabilizing or interim treatment that requires further definitive therapy. **Medical adhesive** is of great use in helping to seal small perforations. **Cyanoacrylate tissue adhesive** (Dermabond Ethicon; not U.S. Food and Drug Administration [FDA] approved for ocular use) can successfully seal a perforation without excess ocular toxicity. It is essential that epithelium and necrotic stroma be débrided to allow firm adhesion of the cyanoacrylate glue to surrounding healthy basement membrane. A thin application of this glue will often remain intact for several months and is tolerated by the patient if covered with a continuously worn soft contact lens (Plano T). Healing of the corneal defect will often occur beneath the glue. Even if spontaneous healing of the leak is not expected, the glue will provide adequate time to obtain corneal donor material if keratoplasty becomes necessary. It is essential to observe the patient closely to ensure that the anterior chamber has reformed and there is no associated superinfection. Topical antibiotic coverage is advisable after gluing and with the use of a soft contact lens. When contact lens or adhesive therapy is inadequate, **surgical**

patch grafting will usually be successful. For moderate-size perforations, a small lamellar button may be sutured into the débrided defect. In the event of large central perforations, it may be preferable to perform penetrating keratoplasty.

C. Burns

Anterior segment burns may be chemical, thermal, radiation, or electric (see Chapter 2, sec. I., sec. II., sec. III. and sec. IV.).

D. Subconjunctival hemorrhage

Subconjunctival hemorrhage may be induced with major, minor, or no detectable trauma to the front of the eye. Occasionally, a patient will wake up with a “spontaneous” hemorrhage. Clinically, it presents as a striking flat, deep-red hemorrhage under the conjunctiva and may become sufficiently severe to cause a dramatic chemotic “bag of blood” to protrude over the lid margin. Occasionally, pneumococcal or adenoviral conjunctivitis may be associated, in which case there will be discomfort and discharge. In the absence of infection or significant trauma to the eye, **treatment** is unnecessary. The

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patient should be reassured that the blood will clear over a 2- or 3-week period.

III. Conjunctival infection and inflammation

A. Conjunctivitis

Conjunctivitis is an inflammation of the conjunctiva characterized by vascular dilation, cellular infiltration, and exudation. The differential features of bacterial conjunctivitis versus those caused by virus, allergy, or toxic factors are listed in Table 5.1. **Floppy eyelid syndrome** is an often-overlooked cause of *chronic conjunctivitis*. Unrecognized eversion of the “loose” upper lid during sleep is associated with papillary conjunctivitis and red eye. Treatment is horizontal lid shortening.

<p>Table 5.1. CLINICAL FEATURES OF CONJUNCTIVITIS</p>
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B. Bacterial conjunctivitis

Bacterial conjunctivitis can be acute or chronic. The **acute** stage classically is recognized by vascular engorgement and mucopurulent discharge, with the associated symptoms of irritation, foreign body sensation, and sticking together of the lids. Occasionally, a severe reaction with purulent conjunctivitis and corneal involvement can occur. The **chronic** infection is more innocuous in its onset, runs a protracted course, and is often associated with involvement of the lids or lacrimal system by low-grade inflammatory reaction. A wide variety of bacterial organisms can infect the conjunctiva. Although the bacterial etiology is often clinically apparent, the identity of the causative organism may not be obvious. Certain

clinical features determined by the pathogenicity of the infectious agent, however, may provide an accurate clinical diagnosis.

1. Acute bacterial conjunctivitis

- a. ***Staphylococcus aureus*** is probably the single most common cause of bacterial conjunctivitis and blepharoconjunctivitis in the Western world. The aerobic Gram-positive coccus is often harbored elsewhere on the skin or in the nares. It may affect any age group. Although usually not aggressively invasive, the organism is very toxigenic and can provide corneal infiltrates, eczematous blepharitis, phlyctenular keratitis, and angular blepharitis.
- b. ***Staphylococcus epidermidis*** is usually considered an innocuous inhabitant of the lids and conjunctiva, but in some instances it can cause blepharoconjunctivitis. The organism is capable of producing necrotic exotoxin and has been shown to colonize eye cosmetics, with subsequent production of blepharoconjunctivitis.
- c. ***Streptococcus pneumoniae*** (pneumococcus) is an aerobic encapsulated Gram-positive diplococcus that is often present in the respiratory tracts of asymptomatic carriers. This organism more commonly affects the conjunctiva of children and can run a self-limiting course of 9 to 10 days.
- d. ***Streptococcus pyogenes*** is an aerobic Gram-positive coccus. Although an infrequent cause of conjunctivitis, the organism is invasive and toxigenic, and thus is capable of producing a pseudomembranous conjunctivitis. The pseudomembrane consists of a fibrinous layer entrapping inflammatory cells and is attached to the conjunctival surface. Removal of this pseudomembrane is possible with minimal bleeding of the underlying tissue.
- e. ***Haemophilus influenzae (H. aegyptius)***, Koch-Weeks bacillus) is a fastidious aerobic Gram-negative pleomorphic organism often seen as a slender rod or a coccobacillary form. It is frequently isolated from upper respiratory tracts of healthy carriers and most commonly causes conjunctivitis in children rather than in adults. It is a toxigenic organism and can be accompanied by patchy conjunctival hemorrhages during an acute infection. An untreated case can last for 9 to 12 days, occurring as a self-limited infection, but occasionally can be part of a more ominous periorbital cellulitis associated with respiratory infection that can lead to bacteremia in young children. Accompanying the acute infection and probably a manifestation of the toxigenic potential is the presence of *inferior corneal limbal infiltrates*.

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- f. ***Moraxella lacunata*** is an aerobic Gram-negative diplobacillus once considered the most common cause of **angular blepharoconjunctivitis**. Although angular blepharoconjunctivitis is now more commonly the result of staphylococcal infection, *Moraxella* sp can produce an acute conjunctivitis that

occasionally results in a chronic conjunctivitis with follicular reaction.

2. Hyperacute conjunctivitis (acute purulent conjunctivitis)

- a. ***Neisseria*** sp (gonococcus, meningococcus) are Gram-negative diplococci. Like *Haemophilus* sp, *Streptococcus* sp, and *Corynebacterium diphtheriae* are aggressively invasive bacteria that can produce a severe conjunctivitis that is often bilateral. Occurring in the child as an infection from the maternal genital tract, in adolescents via fomite transmission, or in via inoculation from infected genitalia, the conjunctivitis can start as a routine mucopurulent conjunctivitis that rapidly evolves into a severe inflammation with copious exudate and marked chemosis and lid edema. This clinical appearance demands laboratory confirmation, immediate therapy, and occasionally, hospitalization.
- b. **Neonatal conjunctivitis (ophthalmia neonatorum)**. Conjunctivitis of the newborn deserves special mention because of the severity and threatening potential of this condition. Conjunctivitis caused by *Neisseria* sp usually becomes symptomatic in the newborn 2 to 4 days following inoculation of the conjunctival mucosa at the time of birth. Clinically, a yellow purulent discharge with prominent lid edema and conjunctival chemosis appears. This condition needs to be distinguished from the neonatal conjunctivitis caused by inclusion conjunctivitis agents, chemical keratoconjunctivitis, nasolacrimal obstruction with other bacterial superinfection, or trauma. The differential points in diagnosis are listed in Table 5.2 (see sec. III.C.2. and Chapter 11, sec. II.B.).

<p>Table 5.2. NEONATAL CONJUNCTIVITIS</p>
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3. Chronic bacterial blepharoconjunctivitis

- a. ***S. aureus*** is the most common cause of chronic bacterial conjunctivitis or blepharoconjunctivitis, with *S. epidermidis*, *Propionibacterium acnes*, *Corynebacterium* sp, and the yeast *Pityrosporum* being other etiologic agents. Often this conjunctivitis is associated with **rosacea** of the skin, a low-grade inflammation of the lid margins, and colonization of the meibomian orifices and lash follicles with *Staphylococcus*. **Anterior blepharitis** has crusty, red, thickened lids with prominent blood vessels, and **posterior blepharitis** (meibomitis) has inspissated oil glands with fluorescein staining along the palpebral conjunctival margin. *Staphylococcus* can produce a variety of exotoxins, which probably accounts for the clinical manifestations. An ulcerative blepharitis

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can occur as well as an eczematoid scaling, and sometimes weeping inflammation of the lids occurs. **Eczematoid** blepharitis is usually distinguishable from the less severe seborrheic blepharitis, which is often accompanied by scaling and greasy deposits on the eyelid, as well as from frequently associated seborrheic dermatitis. An **angular**

blepharoconjunctivitis with maceration of the tissue at the lateral canthus, at one time most commonly associated with *Moraxella* sp, is now most commonly produced by *Staphylococcus*. The cornea also can be involved, with an inferior superficial punctate keratitis or by limbal infiltrates. **Marginal corneal ulcers** can be produced by chronic staphylococcal blepharoconjunctivitis.

- b. **Chronic conjunctivitis** can also be produced by Gram-negative rods including *Proteus mirabilis*, *Klebsiella pneumoniae*, *Serratia marcescens*, and *Escherichia coli*. Gram-negative diplobacilli (*M. lacunata*) can produce a chronic blepharoconjunctivitis (angular conjunctivitis) as previously mentioned and may be present with a chronic follicular reaction.
- c. **Parinaud ocular glandular syndrome (cat scratch disease, bartonellosis)** is a febrile illness caused by the bacillus, *Bartonella henselae*, and is usually contracted through cat or flea exposure. Eye findings include unilateral conjunctival redness, often with epithelial ulceration, foreign body sensation, epiphora, mild lid swelling, serous to purulent discharge, and the disease hallmark: *regional lymphadenopathy*. Neuroretinitis and focal chorioretinitis are not uncommon (2%) (see sec. III.D.4., below).

C. Laboratory diagnosis in bacterial conjunctivitis is not routine

However, when clinical findings are insufficient to diagnose confidently the etiology of an infection, or in those situations in which the reaction is severe or has not responded to routine therapy, conjunctival scrapings for microscopic examination and cultures are indicated. These should also be performed in cases of neonatal conjunctivitis, hyperacute conjunctivitis, and chronic recalcitrant conjunctivitis.

1. **Conjunctival cultures** should be taken prior to the use of topical anesthetics, because these agents and their preservatives will reduce the recovery of certain bacteria. Cultures are taken by moistening a sterile alginate (*not cotton*) swab with sterile saline and wiping the lid margin or conjunctival cul-de-sac. The culture medium is then inoculated directly with the swab tip. Inoculation of solid media can be made in the shape of the letter *R* for the right lid and *L* for the left lid margin. On the same plate, a conjunctival culture may be inoculated at a different site using a zigzag pattern. In this way, the site of culture may be distinguished by the pattern of growth on the plate. After inoculating solid media, the tip of the applicator may be broken off and dropped into a tube of liquid culture medium if it is available.
2. For **bacterial isolation and identification**, the most widely used and generally available **media** are blood agar and chocolate agar. Meat broth has a significantly higher growth rate for most common organisms, but must be secondarily plated for identification. Chocolate agar is well suited for growth of any organism that can be isolated on blood agar and has the added advantage of isolating *Haemophilus*, the fastidious *Neisseria* organisms, and fungi. Thayer-Martin medium is a chocolate agar

medium containing vancomycin, colistimethate, and nystatin, and is of use in culture and isolation of gonococcus. Thioglycolate medium is a commonly used medium in cultivating anaerobic organisms from ocular infection. Liquid Sabouraud medium may be useful in isolating fungal organisms when solid agar medium has failed. Table 5.3 summarizes the culture media of use in specific ocular infectious states. Cultures for *B. henselae* (cat scratch disease) are difficult. Diagnosis is usually based on polymerase chain reaction (PCR) testing on local tissue biopsy and serology.

Table 5.3. CULTURE MEDIA

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3. **Scrapings for microscopic examination** are made after cultures have been taken. Local anesthetic is instilled. A platinum spatula is flamed and allowed to cool to room temperature. The spatula can then be used to scrape gently the involved conjunctival surface, and the material obtained can be spread in a thin layer on a pre-cleaned glass slide. If possible, two or three such slides are made and stained for microscopic examination (Table 5.4). Because scrapings are only about 70% *reliable* and may be traumatic to the patient, cultures take priority and, in appropriate situations, scrapings are omitted.

Table 5.4. CYTOLOGIC FEATURES OF CONJUNCTIVITIS

4. **Stains** most useful for identifying organisms and inflammatory cell type are the Gram, Giemsa, or Wright stain. The Hansel stain is also a useful technique for rapid identification of any eosinophilic response. The Giemsa and Wright stains are most useful in revealing the condition and character of epithelial cells and inflammatory cells. The Giemsa stain is most effective in showing the presence or absence of viral cytoplasmic or intranuclear inclusion bodies and in outlining the morphology of bacteria. The Gram stain is useful in revealing whether an organism is Gram positive or negative; it also provides some information about the morphology of the organism.
5. The **cytologic features** of each type of conjunctivitis are helpful in diagnosis. As a rule, a *polymorphonuclear leukocyte* response occurs with bacterial conjunctivitis (with the exception of diplobacillus). Acute Stevens-Johnson syndrome may produce a polymorphonuclear response, as will the early stages of a viral infection. A mixed outpouring of polymorphonuclear leukocytes and lymphocytes is commonly noted with adult and neonatal inclusion conjunctivitis. Such a mixed response with the added presence of plasma cells and macrophages (Leber cells) are almost diagnostic of trachoma. Chemical conjunctivitis can also produce a polymorphonuclear response. A predominantly *lymphocytic* response is most commonly seen in viral infections, but can also be seen in drug-induced toxic follicular conjunctivitis. Numerous **eosinophils** are indicative of vernal conjunctivitis or allergic

conjunctivitis. The appearance of eosinophils and polymorphonuclear leukocytes in conjunction with a hyperacute conjunctivitis may be indicative of early erythema multiforme, particularly if associated with systemic symptoms. *Basophils*, rarely seen in conjunctival scrapings, are equivalent in interpretation to eosinophilic reaction. *Epithelial cells* may demonstrate cytoplasmic **inclusions** that, if basophilic, suggest inclusion conjunctivitis and, if

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eosinophilic, suggest pox virus. Pink intranuclear inclusions on Giemsa stain are diagnostic of herpesvirus infection (either simplex or zoster). Multinucleate giant cells are suggestive of a viral disorder.

6. When **organisms** are identified, Gram-positive cocci in pairs or chains may indicate *S. pyogenes*. The Gram-negative diplococci, appearing within polymorphonuclear leukocytes and having the “coffee bean” shape, indicate *Neisseria* sp. Large Gram-negative diplobacilli characterize *Moraxella* sp. *H. influenzae* is a pleomorphic organism variably appearing as Gram-negative coccobacillus or slender rods. Gram-negative rods may also be noted, but are difficult to differentiate as to species.

D. Treatment of bacterial conjunctivitis and blepharitis

(see Chapter 3, sec. I.1.).

1. Acute mucopurulent conjunctivitis

- a. **Topical antibiotic therapy.** Acute mucopurulent conjunctivitis will typically respond to topical antimicrobial therapy in solution or ointment form. If treatment is based on clinical diagnosis alone, topical antibiotics should be broad spectrum, i.e., anti-*Staphylococcus* sp, *Streptococcus* sp, and anti-Gram-negative organisms such as *Moraxella*, *Serratia*, *Haemophilus*, and *Pseudomonas*. Erythromycin or bacitracin ointment or sodium sulfacetamide 10% to 15% solution or ointment effectively covers only the more common Gram-positive infections. About 50% of staphylococci are resistant to the sulfonamides. There has been a significant increase in resistance to ciprofloxacin and cefazolin. Neomycin–polymyxin–bacitracin (Neosporin, Ocutricin, AK-Spore) is a very effective broad-spectrum antimicrobial (Gram-positive and negative organisms are covered), but there is a 6% to 8% allergic sensitivity to neomycin. Polymyxin B–bacitracin (Polysporin, AK Poly-Bac) ointment and polymyxin B–trimethoprim drop (Polytrim) have excellent broad-spectrum coverage. Gentamicin (generics), tobramycin (Tobrex), netilmicin (Nettacin) drops or ointment are very good broad-spectrum agents, but are usually reserved for suspected Gram-negative organisms. They are poorly effective against *Streptococcus* sp, and there is increasing incidence of resistance to *Staphylococcus* sp. The **quinolones**, ciprofloxacin (Ciloxan), ofloxacin (Ocuflox), levofloxacin (Quixin), and norfloxacin (Chibroxin), have very broad and potent Gram-positive and negative antibacterial activity with low, but unfortunately increasing, Gram-positive and -negative rates of

resistance. The first two are also approved for corneal ulcers and the latter are pending approval.

- b. **Systemic therapy.** For particularly *acute* staphylococcal blepharitis, oral dicloxacillin or, if penicillin allergy exists, erythromycin are very effective adjuncts (see Appendix B).
 - c. **Local measures** are of great value in treatment, particularly when blepharitis is present and chronic. Warm wet compresses improve circulation, mobilize meibomian secretions, and help cleanse crusting deposits of the lashes. Thick or inspissated lid secretions may require the physician to express the lids between cotton-tipped applicators after topical anesthesia, followed by daily lid margin scrubs with commercial cleansing pads (Eye Scrub, Lid Wipes SPF) or baby shampoo scrubs (using fingertips) performed by the patient. Seborrhic blepharitis is often improved by use of **dandruff shampoo** to the scalp and eyebrows. Daily application of **steroid** ointment to lid margins for 10 to 14 days often controls the pronounced lid inflammation.
2. **Hyperacute bacterial conjunctivitis** (acute purulent conjunctivitis) is a more serious situation and demands more vigorous therapy. After the patient is examined and the necessary cultures and scrapings are obtained, it is important to institute treatment prior to obtaining the culture results.

- a. **Systemic therapy** is indicated for *Neisseria gonorrhoeae*, *N. meningitidis*, and *H. influenzae*, and is far **more critical than topical**

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therapy. Because more than 20% of *N. gonorrhoeae* cases are resistant, **penicillin and tetracycline are no longer adequate as first-line treatment.** Recommended therapy that covers antimicrobial-resistant strains is any of the following: (a) norfloxacin 1.2 g orally (p.o.) qd for 5 days or other quinolone (for penicillin-allergic patients); (b) cefotaxime intravenously (i.v.) or intramuscularly (i.m.) or 50 mg per kg, or ceftriaxone 125 mg i.m., q8 to 12h all for 7 days; or (c) spectinomycin 2 g i.m. for 3 days. All of the above regimens should then be followed by a 1-week course of either doxycycline 100 mg p.o. bid or erythromycin 250 to 500 mg p.o. qid. An alternative combination is ceftriaxone 1 g or 50 mg per kg i.v. once on an outpatient basis, followed by a week of doxycycline or erythromycin p.o. Doses are adjusted per Appendix B, in consultation with a pediatric or infectious disease consultant. For patients who may only be treated with oral medication, norfloxacin, levofloxacin, or other quinolone, and cefaclor with probenecid are recommended (see Appendix B).

- b. **Prophylactic** therapy for intimate contacts of *N. gonorrhoeae* patients is 1 g of ceftriaxone i.v. once or, for *N. meningitidis*, rifampin 600 mg p.o. q12h for 4 days. Isolation of *H. influenzae* in children warrants therapy with ampicillin 100 to 200 mg per kg i.m. or i.v. for 7 to 10 days or 50 to 100 mg per kg q6 to 8h p.o. for 10 to 14 days; neonates receive 50 to 200 mg per kg q12h i.m. or i.v. for 10 days (see Appendix B). Adult dosage is 2 to 4 g p.o., i.m., or i.v. q6 to

8h for 10 to 14 days. If the *Haemophilus* strain is *ampicillin resistant* or the patient is *penicillin allergic*, a quinolone, e.g., levofloxacin or norfloxacin, in the dosages described in Appendix B, is given for 10 to 14 days. The **quinolones should not be used in neonates** or children without consultation with a pediatrician or infectious disease consult.

- c. **Topical** bacitracin or erythromycin ointment is instilled every 2 hours for the first 2 to 3 days for *N. meningitidis*, *Streptococcus* sp, *C. diphtheriae*, and *N. gonorrhoeae* in the neonate, child, or adult, and then five times daily for 7 days. *Haemophilus* or *Moraxella* infections are treated with topical ciprofloxacin, ofloxacin, gentamicin, or tobramycin in the same dosage schedule as that for *Neisseria*. Frequent *irrigation* with sterile saline is very therapeutic in washing away infected debris.

3. **Chronic conjunctivitis** and **blepharitis** (see sec. III.C., above, and sec. VII.I., below, and Chapter 3 for anterior and posterior blepharitis review) are especially common in patients with acne **rosacea**. It is rarely cultured and only if there is no response to standard treatment, and is then re-treated in accordance with the sensitivities obtained after the pathogen is cultured. The presence of recalcitrant blepharitis or meibomitis in association with chronic staphylococcal conjunctivitis requires not only topical treatment with bacitracin or erythromycin, but also intensive *hygiene of the lid margins*. This hygiene may be initiated in the office by expression of the lid meibomian glands (using topical anesthesia) with cotton-tipped applicators. Daily lid hygiene with 5-minute warm compresses and lid margin massage with Eye Scrub or baby shampoo by the patient using the lathered fingertips are important in completely eradicating the inflammation. *Certain antibiotics* inhibit the abnormal fatty acid metabolism, which invites lid margin inflammation. Doxycycline 100 mg p.o. qd for 1 month, then 50 to 100 mg qd 3 to 6 *months* with a meal; or (less convenient) tetracycline 250 mg p.o. qd on an empty stomach; erythromycin 250 mg p.o. qd; or minocycline 100 mg qd, in the same multimonth regimen, is generally very effective. Daily hand and face scrubs with pHisoHex for 2 to 3 weeks and then three to four times weekly will lower the facial germ count and reduce acneiform eruptions and styes. Metronidazole 0.75% gel (Metro Gel) bid to the facial skin for 6 months is highly effective adjunctive

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therapy. Infectious **eczematoid dermatitis** occurring with staphylococcal blepharitis is an indication for erythromycin or bacitracin ointment bid for 10 days, or antimicrobial–steroid combination. Sulfacetamide–prednisolone combinations are particularly effective. Acne **rosacea** patients should use steroids with caution, however, because they are more prone to corneal ulceration with these drugs. Sterile **corneal marginal infiltrates** and ulcerations that occur with chronic staphylococcal blepharoconjunctivitis also respond to topical steroids, usually within 4 or 5 days. **Phlyctenular keratoconjunctivitis** will resolve on treatment with topical antibiotic–steroid agents qid for 10 to 14 days (see sec. VII.H., below; for chalazia, see Chapter 3, sec. I.I.3.).

4. **Catscratch fever (Parinaud ocular glandular syndrome, bartonellosis)** responds

well to doxycycline 100 mg p.o. Erythromycin p.o. is effective in children and may be combined with rifampin 300 mg p.o. bid for more severe infections. Duration of treatment is 2 to 4 weeks in immunocompetent patients and 4 months in immunocompromised patients (see sec. III.B.3.c., above).

IV. Corneal infections and inflammation (keratitis and keratoconjunctivitis)

A. Superficial keratitis

Superficial keratitis includes inflammatory lesions of the corneal epithelium and adjacent superficial stroma. Although some of the changes described in this section can be produced by noninflammatory conditions and therefore would more appropriately be considered keratopathy, they are considered here because of their diagnostic importance. The etiologies of this clinical condition include numerous *infective, toxic, degenerative, and allergic* conditions that can often be characterized by the morphology and distribution of the lesions produced. These conditions may occur with bacterial, viral, and fungal infections. Degenerative states resulting from dry eye, neurotrophic defects, or in association with systemic disease can also produce ulceration of the cornea. When accompanied by infiltration or significant ocular anterior chamber reaction, infection must be excluded or diagnosed and treated.

1. **Morphologically**, the lesions include punctate **epithelial erosions** that are focal defects in the corneal epithelium, best visualized by rose bengal and fluorescein staining and slitlamp biomicroscopy. Punctate **epithelial keratitis** is characterized by focal inflammatory infiltration of the epithelium, resulting in minute opaque epithelial lesions observed in focal illumination or with the slitlamp. Although they may occur without staining, they often do stain with rose bengal or fluorescein because of associated punctate epithelial erosion. Punctate **subepithelial infiltrates** are nonstaining focal areas that occur as semiopaque spots in the superficial stroma.
2. **Identification** of the morphology and distribution of the lesions is greatly enhanced by the use of vital *clinical stains*, most notably rose bengal and fluorescein. **Rose bengal** stains dead or degenerating cells and presently is available as sterile paper strips (wet with saline). Prior instillation of proparacaine 0.5% will relieve the smarting sensation produced by rose bengal, but tetracaine and cocaine should be avoided, because they will often produce an artifactual rose bengal staining pattern. Rose bengal is also an excellent stain for mucus and filaments. Fluorescein from a 2% solution or from a Fluri-strip wet with saline will stain epithelial defects or bared basement membrane, and is also used when highlighting corneal filaments.
3. The **distribution** of the epithelial and subepithelial lesion is of *diagnostic value*. Figure 5.1 summarizes the **six** clinical patterns and their respective etiologies. *Diffuse* and nonspecific *punctate epithelial erosions* may occur with early bacterial or viral infections of many types. Breakdown of microcystic areas of epithelial edema can also produce this pattern, and such areas of edema will also demonstrate areas

of

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negative staining in the fluorescein film corresponding to intact epithelial microcysts. Any toxic reaction to topical medications, chemicals, or aerosol sprays can produce this pattern. Mechanical trauma from a foreign body or eye rubbing must also be considered. The epithelial erosions secondary to molluscum contagiosum of the lids will occur in areas *contiguous* to the lesion. *Inferior* punctate epithelial erosions frequently result from staphylococcal blepharitis or blepharoconjunctivitis and are often accompanied by epithelial keratitis and subepithelial infiltrates. Trichiasis or incomplete lid closure (*exposure keratopathy*) can produce this distribution of erosion, and the pattern is also occasionally seen in

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dry eye patients. The *interpallebral* distribution is typical of keratitis sicca, ultraviolet radiation exposure, chronic exposure, or incomplete blinking. Conjunctival staining usually will accompany the corneal lesion. Episodic recurrent erosions frequently will occur in the inferior area or interpallebral area. The *superior* distribution of epithelial erosion is typical of superolimbic keratoconjunctivitis, but can also be seen in vernal conjunctivitis and with trachoma. Corneal epithelial filaments consisting of coiled epithelial remnants and adherent mucous strands may be associated with any of these patterns, but most typically appear with superolimbic keratoconjunctivitis or keratoconjunctivitis sicca. *Central* lesions, with or without some peripheral punctate, suggest contact lens malfit or overwear, and *linear* lesions suggest a foreign body on the lid rubbing the cornea.

Fig. 5.1. Staining patterns of the cornea and conjunctiva in various disease states. TRIC, trachoma-inclusion conjunctivitis.

4. The **etiology of punctate epithelial erosion** is often local desiccation. Instability of the tear film results in focal dry spots and epithelial breakdown. Epithelial membrane damage from detergent chemicals, liquid solvents, quaternary amines, and a variety of drugs also results in erosions. Superficial viral and chlamydial infections can produce focal erosions, as can the epithelial hypoxia of contact lens overwear. **Punctate epithelial keratitis** with minute focal opacities is typical of viral keratitis, especially that associated with epidemic keratoconjunctivitis of adenovirus, but may also be seen with staphylococcal and chlamydial infections. The infiltrates also occur with vaccinia, Reiter syndrome, and acne rosacea. The coarse, granular infiltrates of punctate epithelial keratitis are quite characteristic of Thygeson superficial punctate keratitis.
5. **Nonstaining punctate subepithelial infiltrates** in the superficial stroma are sometimes seen after such entities as adenoviral, herpes simplex, herpes zoster, Epstein-Barr viral, vaccinia, chlamydial, Reiter, Lyme disease, and rosacea keratitis. Staphylococcal infection must be considered when this pattern appears in a marginal infiltrate distribution. Inferior peripheral limbal infiltrates can accompany acute *H.*

influenzae conjunctivitis.

B. Bacterial corneal ulcers

1. **Central ulcer.** Predominant causes of central bacterial keratitis are *Staphylococcus*, e.g., *S. aureus*, and *S. epidermidis*; *Streptococcus*, such as *S. pneumococcus* and groups A–G *Streptococcus*; other **Gram-positive organisms**, such as *Bacillus* and *Propionibacterium* sp; the **Gram-negative organisms** *Haemophilus*, *Pseudomonas*, and *Moraxella*; and other **Enterobacteriaceae** (*Proteus*, *Serratia*, *E. coli*, and *Klebsiella*). *Mycobacterium chelonae* keratitis may follow laser-assisted in situ keratomileusis (LASIK) surgery. Gram-negative diplococci are an uncommon cause of corneal ulceration except in inadequately treated cases of hyperacute gonococcal conjunctivitis. Infection of the cornea usually tends to occur after injury to the epithelium or in compromised hosts, except for *Neisseria* and *Corynebacterium*, which may invade intact epithelium. Stromal infiltration in an area of an epithelial defect with surrounding edema and folds associated with endothelial fibrin plaques or anterior chamber reaction is usually indicative of microbial infection. Staphylococcal ulcers are often more localized, whereas pneumococcus may produce a shaggy undermined edge of an ulcer that is associated with a hypopyon. A destructive keratitis with rapid necrosis and adherent mucopurulent discharge is highly suggestive of *Pseudomonas*, *Streptococcus*, or anaerobic infection. **Infectious crystalline keratopathy** is an indolent, noninflammatory branching crystalline growth commonly associated with *Streptococcus viridans*, but also reported with *Peptostreptococcus* sp, *S. epidermidis*, *H. influenzae*, and two fungal species. There is also often a history of local ocular trauma, contact lens use, steroid use, and/or chronic antibiotic administration. Response to antibiotic therapy is very slow and may fail. Surgical

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intervention with neodymium:yttrium, aluminum, garnet (Nd:YAG) **laser disruption**, e.g., 3.2 mJ × 30, creates diffuse haze of the protective glycocalyx matrix within the intrastromal crystals making the bacteria drug-susceptible. This should be considered before more extensive surgical steps are taken.

2. **Marginal ulcers.** Ulceration with superficial white infiltrates in the corneal periphery is seen most commonly with *staphylococcal* bacterial disease. There is concurrent blepharoconjunctivitis. The ulceration may be caused by hypersensitivity reaction, because culture of the ulcer is often sterile. The ulceration must be distinguished from Mooren ulcer and the peripheral ulceration seen with collagen vascular diseases such as rheumatoid arthritis. *Moraxella* sp has been described as producing ulcers that extend to the limbus, especially inferiorly.
3. **Laboratory tests** are similar to those for hyperacute conjunctivitis (see sec. III.C., above) apply also to bacterial corneal disease.
 - a. **Cultures** are performed after instillation of topical proparacaine 0.5% (tetracaine, benoxinate, and cocaine are more likely to interfere with recovery

of the organisms) and should obtain as much material as feasible, particularly from the deeper areas and the margin of the ulcer, using a sterile broth or saline-moistened calcium alginate or dacron–rayon swab. *Organism recovery is much higher when alginate swabs are used* rather than spatulas. Cultures are done on meat broth, blood agar plates (at room temperature and 38°C), chocolate agar, thioglycolate broth, and Sabouraud agar–broth (fungus), and Page medium (*Acanthamoeba*), if suspected. Scrapings taken from a nonnecrotic area may be examined microscopically with Gram and Giemsa stains. Because 30% to 40% will be negative even if infection is present, these scrapings may be judiciously omitted.

- b. **Corneal biopsy** is often diagnostic in cases that progress despite seemingly adequate treatment; even if an organism has been identified, another may have been missed. In the minor operating room or at the slitlamp, after local anesthesia (drops or xylocaine block), a 2 to 3 mm sterile disposable dermatologic trephine is advanced to partial depth into the anterior corneal stroma, taking both clinically infected and adjacent clear cornea. The base is then undermined with a surgical blade to complete the lamellar keratectomy.
4. **Initial treatment** is based on clinical impression and results, if any, of the scraping. Coverage should be broad, intensive, and amenable to change when final culture and sensitivity reports are available. Contact lens wearers with central corneal ulcers should particularly be covered for *Pseudomonas* (tobramycin, netilmicin, and/or a quinolone). Antibiotic treatment of infectious corneal ulcers must be aggressive using fortified solutions, and patients should be kept under close observation to prevent serious scarring or frank perforation. Initial antibiotic therapy may be guided by the results of the Gram stain of the corneal scraping, but broad-spectrum therapy should be used (**see** Table 5.5, Table 5.6, **and** Table 5.7 **and** Appendix B for detailed lists of drug indications, dosage, and routes of administration).

Table 5.5. INITIAL TOPICAL ANTIBIOTIC THERAPY OF BACTERIAL KERATITIS BASED ON GRAM-STAIN FINDINGS^a

Table 5.6. SUBSEQUENT THERAPY FOR CULTURE-IDENTIFIED BACTERIAL ULCERS^a

Table 5.7. PREPARATION OF ANTIBIOTICS FOR FORTIFIED TOPICAL AND SUBCONJUNCTIVAL USE

- a. **Gram-positive cocci.** In mild to moderate infections, frequent topical therapy alone may be used, but it may be advisable to give subconjunctival therapy as well in severe infections, or apply a collagen contact lens soaked 10 minutes

in fortified antibiotic solution (see sec. IV.B.6.).

1. **Coupled fortified cephalosporin–aminoglycoside therapy** is common. Topical cefazolin solution, 100 mg per mL, should be used *q1min for 5 doses to achieve high stromal levels quickly* and then q60min 24 hours per day or 16 times per day with a polymyxin–bacitracin ointment HS depending on severity of disease. Tobramycin is often effective against *Staphylococcus*, but poorly effective against pneumococcus or other *Streptococcus*. Fortified drops of one of these aminoglycosides are used in

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the same regimen as cefazolin to cover any Gram-negative organisms that may be revealed only by culture. Vancomycin (14 to 25 mg per mL) or bacitracin (10,000 units per mL) is effective in Gram-positive coccal and bacillus infections, and especially *methicillin-resistant Staphylococcus*, where cephalosporins would fail. Drops are tapered over a 1- to 2-week period to qid for 3 weeks more as indicated. For **methicillin-resistant organisms**, vancomycin is the drug of choice.

2. **Single-agent broad-spectrum drops** of the quinolones, (ciprofloxacin, ofloxacin, levofloxacin, or norfloxacin) are commercially available. More severe ulcers should probably be treated at least initially with double agents (sec. IV.B.), but either quinolone may be substituted when the situation is under control and organism(s) known. Organisms covered are similar to those for cefazolin or vancomycin and an aminoglycoside, and include the microbes listed in sec. III.B.1., above.
 3. **Subconjunctival therapy** is usually used only in severe cases, or for uncooperative or unreliable patients. Because a 10% cross sensitivity between cephalosporins and penicillin has been reported in **penicillin-allergic patients**, it is usually safer to proceed with vancomycin therapy. Subconjunctival injections are **painful** and are best preceded by topical anesthetic (or general anesthetic when treating children) and adequate postinjection analgesics.
- b. **Gram-negative cocci** (*N. meningitidis*, *N. gonorrhoeae*) and *Haemophilus* require **systemic** and **topical** therapy and are discussed under hyperacute conjunctivitis (see sec. III.D.2., above). Topical therapy should be q1h for 2 to 4 days with taper over 2 to 4 weeks.
 - c. **Gram-positive rods**. These uncommon agents of ocular infection usually respond to systemic penicillin (see Appendix B). *Bacillus* sp are susceptible to moderate doses of penicillin; clostridial organisms require higher doses. *Bacillus cereus* infections may be extremely hard to treat, even using gentamicin, ofloxacin, norfloxacin,

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ciprofloxacin, or clindamycin. **Topical drops** and **subconjunctival** injections are used q1h. Tetracycline topically and orally is a useful adjunctive.

d. **Gram-negative rods**

1. **Topical** therapy initially should be fortified tobramycin ophthalmic solution q1min for 5 doses, then q60min for 3 to 6 days before starting slow taper. Important adjunctive therapy is topical ticarcillin 6 mg per mL, or carbenicillin 4 mg per mL, q60min. Treat *Pseudomonas* at least 1 month or rebound infection may occur. **Aminoglycoside-resistant** strains are increasing. If *Pseudomonas* is gentamicin-resistant, a quinolone drop should be coupled with ticarcillin or carbenicillin, as above. If the strain is **quinolone-resistant**, *amikacin* is often effective.
2. **Subconjunctival therapy**, if used, should include tobramycin or amikacin 40 mg, and carbenicillin 100 mg, each injected in a different area of the conjunctiva.

e. **Anaerobic Gram-positive filaments** (*Actinomyces*, *Nocardia* [formerly *Streptothrix*]) are sensitive to penicillins and tetracyclines.

- f. ***Mycobacterium chelonae*** ulcers are treated with a combination of topical amikacin (50 mg per mL, commercial ciprofloxacin, and either clarithromycin (10 mg per mL) or azithromycin (2 mg per mL) hourly around the clock to start with, then taper over weeks. Oral doxycycline 100 mg bid is additive therapeutically.

g. **When no organisms are identified**, but bacterial etiology is strongly suspected on clinical grounds:

1. **Topical** therapy should be with fortified cefazolin q1min for 5 doses, then coupled with tobramycin 14 mg per mL q60 min, for 3–6 days before taper over 4–6 weeks. Use vancomycin in severe cases and suspected methicillin-resistant or penicillin-allergic patients.
2. **Subconjunctival therapy**, if used, should be cefazolin 100 mg, plus tobramycin 40 mg, until culture results are available. A fortified-antibiotic-soaked collagen lens (see sec. IV.B.6.) may also be effective adjunctively.

h. **Systemic antibiotics** are used if there is scleral extension of the infection or a threatened perforation. Levofloxacin 500 mg p.o. q24h or ofloxacin 200 to 400 mg p.o. q12h for 7 days both have excellent aqueous and vitreous penetration after oral dosing. A cephalosporin or vancomycin and an aminoglycoside may also be used p.o. or i.v., with doses given as in Appendix B. In cases of *vancomycin resistance*, which is an emerging problem, linezolid 600 mg i.v. or p.o. q12h may be indicated. Table 5.5, Table 5.6 and Table 5.7, and Appendix B summarize the recommended therapy. Therapy may be refined when culture and sensitivities return.

- i. The **antibiotic regimen is altered**, if necessary, when final culture and

sensitivity information is available. Fortified vancomycin and bacitracin are used if *methicillin-resistant staphylococci* are recovered. In the event that a suspected Gram-negative coccus infection was initially treated with penicillin and the subsequent culture results disclose *Acinetobacter* sp, penicillin should be discontinued because these organisms are often not sensitive to penicillin.

5. Other treatment modalities

- a. **Dilation.** Long-acting cycloplegics such as atropine 1% or scopolamine 0.25% should be used if significant anterior chamber reaction is present. Initial instillation is usually required at least three times a day. If significant synechiae are forming at the pupillary margin, one or two doses of topical 2.5% phenylephrine are often indicated to ensure mobility of the pupil.
- b. **Corticosteroid** use in treatment of infectious corneal ulcers is less controversial than in past years. It is probably unwise to use steroids

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until at least 24 to 48 hours of antibacterial treatment has been completed, or until the etiologic agent has been identified and shown to be sensitive to the antibiotics being used. Corticosteroid use is *contraindicated* if *fungus* is at all suspected. Low-dose topical corticosteroids (e.g., prednisolone 0.12% qid) have a place in limiting the inflammatory reaction once the clinician is satisfied that the antibiotic treatment is effective.

6. **Collagen shields** (Surgilens, Bausch & Lomb), are contact lenses initially developed to enhance corneal epithelial healing after surgery, trauma, or dystrophic erosions and filaments, but are also used as effective high-dose drug delivery systems (the lenses are not FDA approved as drug delivery systems). The lenses come in two sizes and dissolve spontaneously over 24 to 72 hours. Soaking the lenses in antibiotics, such as tobramycin 40 mg solution for 10 minutes, results in a 30-fold increase in antibiotic penetration into the aqueous compared to subconjunctival injection or a regular therapeutic soft contact lens (TSCL) and q1h drops. The high level of drug may be maintained with q4h drops using the collagen shields.
7. **Special pediatric considerations.** Subconjunctival therapy is usually not feasible unless the child is under general anesthesia at the time of a corneal culture and scraping. Should systemic medication be considered necessary, it is best done with the consultation of a pediatrician or internist. See Appendix B for dosages and organism indications.

C. Chlamydial (trachoma-inclusion conjunctivitis) organisms

Chlamydial (trachoma-inclusion conjunctivitis) organisms are intracellular “parasites” but not true viruses, having enzyme systems similar to bacteria. They can produce acute inflammatory diseases of the conjunctiva and cornea that will often progress to a more chronic follicular conjunctivitis. Infection with inclusion conjunctivitis usually takes different

forms in children and adults.

1. **Neonatal inclusion conjunctivitis (inclusion blennorrhoea)** has an acute onset 5 to 12 days after birth, presenting as an acute conjunctivitis with purulent discharge.
 - a. **Diagnosis** of this *Chlamydia trachomatis* infection is facilitated by the presence of **intracytoplasmic inclusion bodies** apparent in epithelial cells obtained by conjunctival scraping. Giemsa stain is the most effective method for demonstrating the individual elementary bodies or larger initial bodies as basophilic inclusions with, at times, small eosinophilic opacities. It is obviously important to distinguish this infection from *N. gonorrhoeae*. Although the infection can resolve without sequelae, a membranous conjunctivitis may develop and result in conjunctival scarring, and a definite keratitis may supervene with superficial corneal vascularization.
 - b. **Treatment** is **systemic antibiotics** with the topical being adjunctive. Erythromycin 12 mg per kg p.o. daily in four divided doses for 2 to 3 weeks is the preferred therapy in newborns. Sulfisoxazole is the alternative drug (see Appendix B). *Children under 8 years of age should not receive systemic tetracyclines*. In infants, the usual topical treatment is sulfacetamide 10% or erythromycin ointment qid for at least 3 weeks. Because the condition is acquired by the presence of *Chlamydia* in the birth canal, it should be assumed that the parents are infected and probably require treatment with systemic tetracycline to eliminate the source of the infection. If the mother is *breast-feeding*, erythromycin 250 mg p.o. qid, or sulfonamides 500 mg p.o. qid should be used for 21 days (see sec. IV.C.2.b., below).
2. **Adult inclusion conjunctivitis** usually presents as an acute follicular conjunctivitis with mucopurulent discharge occurring after an incubation period of 4 to 12 days. The disease usually occurs in sexually active young adults, but may occur in senior citizens as well, often after having acquired a new sexual partner in the preceding 2 months. The acute conjunctivitis

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often evolves into a chronic follicular conjunctivitis. An epithelial keratitis may develop, as well as marginal and more central corneal infiltrates accompanied by superficial vascularization as an *inferior* limbal pannus. Iritis has been reported later in the condition, as well as Reiter syndrome.

- a. **Diagnosis** by Giemsa-stained scraping of the epithelium is less likely to show inclusion bodies, but these may be seen in a number of patients with the acute disease. Microtrak assay of scrapings is far more reliable diagnostically, but any culture or immune laboratory test may still have false positives or negatives.
- b. **Treatment.** Systemic azithromycin is more effective and efficient than either erythromycin or tetracycline and is given as 1 g p.o. for 2 days. Alternative first-line therapies are doxycycline 100 mg p.o. bid with a meal, or tetracycline 250 to 500 mg p.o. qid 30 minutes before meals or 2 hours after meals for 21

days. Erythromycin or sulfonamides are also effective, as are the quinolones ofloxacin and ciprofloxacin (but not norfloxacin) in bid dosing. Topical antibiotics are relatively ineffective in treating the eye disease, but may modify a conjunctivitis. Because the condition may be associated with an asymptomatic venereal infection *partners* should also be *treated systemically* and the possibility of *other venereal disease* must be excluded. Tetracyclines should not be used in women who are pregnant or breast-feeding. Azithromycin 1 g p.o. qd for 2 days, erythromycin 250 mg p.o. qid, or sulfisoxazole 500 mg p.o. qid for 21 days, are effective alternatives. High-dose amoxicillin may be used in pregnancy (Appendix B).

3. **Trachoma.** The initial manifestation of trachoma is a chronic follicular conjunctivitis that is classically more marked on the upper tarsal plate, with progressive disease scarring of the conjunctiva occurring on the superior tarsal conjunctiva as fine linear scars and often as a transverse band of scar (**Arlt line**). When marked, this scarring can lead to entropion and trichiasis, with secondary ocular surface breakdown, including corneal ulceration. Primary corneal involvement occurring with the conjunctivitis can include an epithelial keratitis, marginal and central corneal infiltrates, and superficial vascularization. This is usually more pronounced on the upper half of the cornea and can appear as a fibrovascular pannus. Follicle formation at the limbus regresses to sharply defined depressions (**Herbert pits**) at the base of the pannus.
 - a. **The disease**, as classically described by **MacCallan**, considers the *conjunctival* changes according to the following classification:
 1. **Trachoma I.** Immature follicles on the upper tarsal plate including the central area, but without scarring.
 2. **Trachoma II.** Mature (necrotic or soft) follicles on the upper tarsus obscuring tarsal vessels, but without scarring.
 3. **Trachoma III.** Follicles present on the tarsus and definite scarring of the conjunctiva.
 4. **Trachoma IV.** No follicles on the tarsal plate but marked scarring of the conjunctiva. This infection is not commonly seen in developed countries, but only the United Kingdom and some parts of Europe are totally free of endemic disease.
 - b. **Treatment.** Azithromycin 1 g p.o. qd for 2 days is efficient, effective, but expensive therapy. Individual patients with trachoma will also respond to a 3-week course of either tetracycline or erythromycin p.o. in full dosages (250 mg qid). Clinical response may be slow, and prolonged treatment may be required. When large groups are treated, topical tetracycline or erythromycin ointments may be given twice daily for 2 months. When systemic treatment is used, tetracycline should be used in preference to oral sulfonamides due to the lower incidence of side effects with tetracycline (see sec. IV.C.1. and sec. C.2., above, for further therapy information).

D. Herpes simplex virus (HSV) keratoconjunctivitis and iritis

Ocular infections with herpesvirus represent a challenge to diagnosis and treatment.

Primary ocular herpes is rare and usually occurs as an acute follicular keratoconjunctivitis with regional lymphadenitis, with or without vesicular ulcerative blepharitis or cutaneous involvement. The keratitis can occur as a coarse punctate or diffuse branching epithelial keratitis that does not usually involve the stroma. The condition is self-limited, but the virus establishes a latent infection in the trigeminal ganglion. It may *reactivate* under various forms of physical stress (recent fever, flu, or surgical or dental procedures), with the prostaglandin analog latanoprost used in glaucoma therapy, as well as with any form of ocular laser treatment, and cause recurrence of the disease in a host who has both competent cellular and humoral immunity. **Recurrent disease** of the anterior segment may occur as one or a combination of the following: epithelial infectious ulcers, epithelial trophic ulcers, stromal interstitial keratitis (IK), stromal immune diskiform keratitis, and iridocyclitis. Management of this disease, with its chronic recurring and often progressive nature, can be difficult and must be tailored to minimize permanent ocular damage.

1. **Epithelial infection.** Dendritic or geographic ulceration of the cornea is caused by live virus present in intracellular and extracellular locations, particularly in the basal epithelium. The use of steroids in purely infectious epithelial disease serves only to make the ulceration spread and to prolong the infectious phase of the disease. Fluorescein or rose bengal staining make the ulcers easier to see.
 - a. **Topical antiviral chemotherapy** with topical **trifluridine 1%** solution nine times a day for 5 days, then five time per day for 9 to 21 days, **or vidarabine 3%** ointment four to five times a day arrests viral replication until infected cells slough from the eye. **Idoxuridine** 0.1% drops are given hourly by day and q2h at night or as just antiviral ointment at bedtime. With treatment, the infectious epithelial disease resolves 80% to 90% of the time without complication and without the need for antiinflammatory drugs. **Limbal ulcers** are more resistant to healing, but eventually close without much scarring. HSV infections in **human immunodeficiency virus-positive (HIV positive)** patients show a predilection for peripheral versus central involvement, moderately prolonged course with mean healing time of 3 weeks with topical antivirals, rare stromal involvement, and tendency to frequent recurrence (more than two times per year). With prolonged treatment, the antivirals can produce a **toxic** punctate keratopathy, retardation of epithelial healing, superficial stromal opacification, follicular conjunctivitis, or lacrimal punctal occlusion.
 - b. **Systemic antiviral acyclovir.** A dosage of 400 mg p.o. tid for 14 days delivers high-titer therapeutic doses in tear film and aqueous for treatment of acute infectious epithelial HSV in those patients for whom topical therapy is difficult (those with severe arthritis or in children). Pediatric dosing ranges from 20 to 40 mg/kg/day. Post-HSV **keratoplasty** dosage of 400 mg bid for 12 to 18 months is indicated therapy and may successfully prevent recurrent infection

and graft rejection. Both *epithelial and stromal recurrences* are inhibited by 400 mg bid. This **long-term prophylaxis** is recommended for use in patients at risk of recurrent epithelial or stromal disease more than two times yearly. Treatment is usually given for 1 year, but may go significantly longer (genitourinary HSV prophylaxis goes for 5 years or longer). Acyclovir is equivocally effective in iritis and not generally used.

- c. **Systemic antiviral famciclovir** and **valacyclovir** are highly effective alternatives to acyclovir. In **acute** first infections, dosage is famciclovir 250 mg p.o. tid for 7 days or valacyclovir 1 g p.o. bid for 7 days. For **recurrent** infection, the dosage is famciclovir 125 mg p.o. bid or valacyclovir 500 mg p.o. bid for 7 days. For **long-term**

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suppression dosages are 125 mg p.o. qd to bid and 500 mg p.o. qd to bid, respectively. Valaciclovir should *not* be used long term in *immunosuppressed* patients because of myelosuppression.

- d. Acyclovir 3% ophthalmic ointment, applied five times a day, is available outside of the United States.
2. **Epithelial sterile trophic ulceration (metaherpetic, postinfectious, persistent epithelial defect)**. An indolent linear or ovoid epithelial defect with heaped-up borders can occur at the site of a previous herpetic ulcer and be confused with infectious geographic ulcer. These persistent epithelial defects are mechanical healing problems similar to recurrent traumatic erosion and are caused by damage to the basement membrane sustained during the acute infectious epithelial stage. Damaged basement membrane heals extremely slowly over 8 to 12 weeks. During this period, epithelial cells are unable to maintain their position after migrating across the bed of the ulcer.
- a. Because of the mechanical nature of the problem, **treatment** is designed to protect the damaged basement membrane. Ointments and artificial tears may affect healing, but often a high-water-content plano therapeutic soft contact lens (TSCL) (Permalens, Kontur) worn for 2 to 6 months is needed (see sec. XI., below). Patching, lid taping, partial tarsorrhaphy, or, infrequently, a surgically placed conjunctival flap are alternatives. Stromal inflammatory disease may interfere with the healing of the basement membrane. Mild corticosteroid such as 1/8% prednisolone bid to qid is useful. Antibiotic solution once or twice a day should be used when treatment includes continuously worn therapeutic contact lenses, along with frequent lubrication with artificial tears for several months even after the lens has been removed.
 - b. If active **corneal thinning** (melting) occurs, sealing off the ulcer with **cianoacrylate tissue adhesive** (Dermabond; not FDA approved for ocular use) should be considered. With the patient under topical anesthesia, the physician débrides and dries the ulcer and periulcer area of debris and loose cells with Weckcell sponges, and applies the liquid adhesive in short strokes or concentric spots. It polymerizes almost instantly to the tissue. Sterile saline

is dripped on the eye to complete polymerization, a *Plano-T* TSCL is applied, and antibiotic drops are given bid. If needed for inflammation, steroids may now be used with greater safety. The cornea should heal and dislodge the glue in 1 to 3 months, usually leaving the eye quiet but scarred, and it is hoped that it will be amenable to transplant if vision is significantly compromised.

3. **Stromal IK, immune rings, and limbal vasculitis** result from antigen–antibody complement-mediated immune reaction in the stroma. Viral IK presents as *necrotic*, blotchy, white infiltrates that may lie under ulcers or appear independently. Immune rings are gray anterior stromal Wessley rings, and limbal vasculitis is a local Arthus reaction. These lesions must be distinguished from secondary bacterial or fungal infections, which are usually much less indolent. After several weeks of smoldering inflammation, dense leashes of stromal vascularization may begin to advance into the cornea.
 - a. **Therapy** is suppression of immune damage. If the inflammatory infiltrates do not involve the visual axis or there is no active necrosis or neovascularization, steroid therapy may be avoided because the process often burns itself out spontaneously in weeks to months and, with the exception of limbal vasculitis, scars form despite steroid therapy. The vascularization regresses to leave ghost vessels. Treatment may be limited to **lubricants**.

Generally, if **corticosteroids** have *never been used* in an eye, the clinician should try to do without them, because subsequent recurrences will then require reinitiation of steroids and treatment is

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prolonged over a taper period. If the inflammatory reaction is moderate to severe, however, if steroids have been used previously, if the visual axis is threatened, or if there is active necrosis or neovascularization, the use of steroids will speed resolution of the inflammation and decrease formation of scar tissue and deep vessel invasion that could later compromise success of surgery. The **corticosteroid dosage** is whatever controls the disease and may range from dexamethasone 0.1% q3h to prednisolone 0.12% every other day. Once hyperemia and edema begin to decrease, steroids should be tapered downward over several weeks to several months. *Prophylactic antiviral agents* such as trifluridine qid or acyclovir 400 mg p.o. bid should be used, and daily *antibiotics* continued until steroid dose is reduced to the equivalent of prednisolone 1% bid unless the patient is prone to infectious recurrences.

4. **Diskiform keratitis** results from a delayed hypersensitivity reaction characterized by sensitized T lymphocytes and macrophages reacting to viral antigen in the cornea. Clinically there is a focal or diffuse, nonnecrotic disk-shaped area of stromal edema often with focal keratic precipitates (**endotheliitis**). With progressive severity, more diffuse edema with folds in Descemet's membrane, neovascularization, and iritis may appear.

Therapeutically, the same rules apply to treatment of diskiform keratitis as to viral IK (see sec. IV.D.3., above).

5. **If diskiform stromal disease** is present with an HSV- **infected epithelial ulcer**, gentle débridement of the epithelium and full antiviral therapy should be started a day or two before steroids. If the ulcer progresses despite antiviral therapy, steroid dosage should be reduced until the ulcer is under control and is healing. If diskiform keratitis is combined with **trophic ulceration**, control of underlying stromal edema with low-dose topical steroids and the application of a TSCL will aid healing. A **persistent epithelial defect** carries the added risk of collagenase release, and steroids may enhance **melting**, with ultimate corneal perforation. Cyanoacrylate adhesives (see sec. II.B., above) or surgical intervention by conjunctival flap or penetrating keratoplasty may be necessary before perforation actually occurs.
6. **Iridocyclitis, retinitis**, and occasionally **panuveitis** may occur with herpes simplex infection. Intraocular inflammation may occur without concomitant keratitis, but almost invariably accompanies active keratitis. Uveitis in an eye with previous herpetic keratitis should be considered herpetic until proved otherwise. Therapy is discussed in Chapter 9, sec. VIII.A.2. Prophylactic antivirals and antibiotic agents should be used with topical steroids. If ulcerative keratitis supervenes, particularly if the cornea is melting, **systemic steroids** such as oral prednisone 60 to 80 mg per day, may be substituted for part or all of the topical steroid regimen.
7. **Oral antivirals** will have no effect on active immune keratitis, but acyclovir 400 mg p.o. bid for 1 year inhibits recurrence of stromal inflammation. Famciclovir 125 mg p.o. bid or valacyclovir (in the nonimmunosuppressed patient) 500 mg p.o. qd for 1 year are alternatives.
8. **Steroid tapering.** Special comment should be made regarding the gradual reduction and termination of steroid treatment. Because too rapid a steroid taper or abrupt cessation of treatment can often be accompanied by recrudescence of the inflammation, it is essential to carefully control the steroid dose. The rule of thumb is **never taper steroids by more than 50% at any given time**. Each level should be maintained for several days or, at lower doses, for several weeks depending on the severity of inflammation at the initiation of treatment and the therapeutic response. One method uses progressively decreasing strengths of glucocorticoid such that, from the dexamethasone 0.1% or prednisolone 1% daily, tapered from four times down to once, prednisolone 0.12% solution can

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be used qid with gradual reduction to tid, bid, once a day, every 2 days, and so forth, until cessation of treatment. Occasionally, patients will require chronic low-dose (once or twice weekly) prednisolone to maintain a quiet eye. Coverage with antiviral medication need not be continued after reduction to less than 1% prednisolone bid except in patients with epithelial HSV infection within 6 months.

9. **Penetrating keratoplasty (corneal transplant)** of the herpes simplex scarred eye has about 85% 5-year success rate on first procedure in the *quiet* eye. Emergency surgery on inflamed eyes has a success rate of between 40% and 60%. Interrupted 10-0 sutures, intensive topical steroids for several weeks, and acyclovir 400 mg p.o. bid for 12 to 18 months are factors favoring success. Antivirals are also critical if steroids are being used to treat an allograft rejection. See also sec. IX.B.4., below,

for management of graft rejection.

E. Herpes zoster ophthalmicus

Herpes zoster is an acute infection of a dorsal root ganglion by the varicella-zoster virus (VZV, chickenpox) characterized by severe pain and vesicular skin lesions distributed over the sensory dermatome innervated by the affected ganglion. Regional lymphadenopathy with dermatomal pain is common. The ophthalmic (trigeminal ganglion, Vth cranial nerve) form of the disease usually presents as a combination of two or more of the following: conjunctivitis, episcleritis, scleritis, keratitis, iridocyclitis, and glaucoma. Chorioretinitis, V¹ dermatomal vesicular dermatitis, extraocular muscle palsies, retinitis, and optic neuritis may also be seen (see Chapter 9, sec. VIII.A.3.). Herpes zoster is increasing in frequency due to the acquired immunodeficiency syndrome (AIDS) epidemic and aging population, but may soon decrease due to **vaccination of adults** (*Varivax*) to reboot the immune system.

1. **Conjunctivitis, episcleritis, and scleritis** occur in about half of the cases. Conjunctival involvement is common and may occur as watery hyperemia with petechial hemorrhages, follicular conjunctivitis with regional adenopathy, or severe necrotizing membranous inflammation. Scleritis or episcleritis may be diffuse or focal nodular. On resolution, scleritis can leave scleral thinning and staphyloma.
2. **Keratitis** occurs acutely in about 40% of all patients and may precede the neuralgia or skin lesions. Keratitis may occur as a fine or coarse punctate epithelial keratitis with or without stromal edema, or as actual vesicle formation with ulceration in a **dendritiform** pattern that can be mistaken for herpes simplex keratitis. VZV DNA is present from 2 to 34 days after acute onset, especially in patients over 66 years old (HIV negative). Delayed mucoid plaques resembling dendrites may occur months later and also contain VZV DNA. **Corneal sensation** is usually greatly reduced in herpes zoster keratitis due to ganglion damage. Trophic neuroparalytic ulcers may occur with melting and corneal perforation if the epithelial defect persists. Stromal keratitis, either immune diskiform or white necrotic IK, may occur with or independent of epithelial disease.
3. **Iridocyclitis** is a frequent occurrence (50%) and may appear independent of corneal activity. After resolution of the acute perineuritis and vasculitis, there may be focal or sector atrophy of the iris. Hypopyon, hemorrhage into the anterior chamber (anterior segment necrosis), and phthisis bulbi may result from zoster vasculitis and ischemia.
4. **Glaucoma** may occur acutely or months later due to inflammatory trabeculitis. In later stages, synechial closure of the angle may also occur (see Chapter 10, sec. XVIII.).
5. **Therapy.** Systemic antivirals (famciclovir, valacyclovir, and acyclovir) decrease acute pain, stop viral progression, and significantly reduce the incidence and severity of keratitis and iritis if started within 72 hours of rash onset. Inhibition of **postherpetic neuralgia (PHN)** is established for famciclovir and valacyclovir.

Systemic steroids are currently controversial because of the increased incidence of zoster in HIV-positive patients.

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The following regimen is presently recommended for ocular management. Therapy is most effective if started within 72 hours of onset of rash using both **antiviral** and **tricyclic antidepressant (TCA) therapy**. If used in acute disease, the latter greatly inhibits development of PHN.

- a. **Antiviral famciclovir** (Famvir) 500 mg p.o. tid for 7 days or **valacyclovir** (Valtrex) 1 g p.o. tid for 7 days are equal to acyclovir in acute disease and better in **reducing late neuralgia**. **Acyclovir** (Zovirax) 800 mg tablet p.o. five times a day (4,000 mg per day total) for 7 days in the immunocompetent patient, or in the immunosuppressed patient, 5 to 10 mg per kg or 500 mg per m² i.v. q8h for 5 to 7 days, followed by 2 to 3 weeks of oral dosing is recommended. **Brivudine** 125 mg qd for 7 days is as effective as the above acyclovir regimen, but currently is available only in Europe.
- b. **TCAs** are highly effective in inhibiting acute and long-term pain. Desipramine, imipramine, amitriptylene, or other TCA dosage **is started during acute illness** at 10 to 25 mg p.o. HS with increase over 1 to 2 weeks to 50 mg bid for 2 to 4 months, if tolerated. These same dosages are used for long-term therapy of PHN if it does develop.
- c. **Topical steroids** are prescribed only if needed for corneal **diskiform** immune edema or **iritis**, e.g., 1/8% (.012%) prednisolone qd to qid with gradual taper. Use cycloplegia and steroids for iritis.
- d. **Vidarabine** 3% antiviral ointment is prescribed 5 id for 7 to 14 days for recurring dendritic ulcers if they persist without therapy. Alternatives are trifluridine drops or p.o. antivirals. Response is variable.
- e. **Topical antibiotic** is prescribed if epithelium is ulcerated or topical steroids are in use.
- f. **Lateral tarsorrhaphy** can be performed if cornea is anesthetic, with frequent artificial tear lubrication to prevent neurotrophic ulceration.
- g. **TSCLs** are used if epithelium is unhealthy or has sterile trophic ulceration; antibiotic drops bid for prophylaxis and artificial tears for lubrication are prescribed. Neovascular pannus may heal ulcerated corneas and should not be blocked with steroid therapy. Nerve growth factor improved sensitivity and healed ulcers in human studies.
- h. Cyanoacrylate **tissue adhesive** (glue, Dermabond, not FDA approved for the eye) is used if there is corneal ulcer melting (thinning). Cover with a soft contact lens, and administer prophylactic antibiotics and lubricants (see sec. IV.D.2., above).
- i. For **secondary glaucoma** beta-adrenergic blockers, adrenergic agonists, antiprostaglandins, carbonic anhydrase inhibitors, and other nonmiotic agents

are used to control pressure. Mydriatic cycloplegics prevent synechiae (see Chapter 10).

- j. **Nonnarcotic or narcotic analgesics for neuralgia** during the first 10 to 30 days should be used to control pain. Patients *over 55 years* or those presenting *with severe pain at onset* regardless of age are at greatest risk for permanent or prolonged neuralgia. Young patients rarely have sustained pain; 85% of neuralgias resolve spontaneously over several months.
- k. **PHN** is often relieved by TCAs, such as in sec. **IV.F.5.b.** above. Therapy may last for years. The anticonvulsant, *Gabapentin (Neurontin)* 300 mg up to 600 mg p.o. qid, is one of the most effective anti-PHN therapies available and may be coupled with all other anti-PHN treatments. *Capsaicin* 0.025% (Zostrix) topical skin cream qd to bid d