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INFECTIOUS SYNDROMES OF THE HEAD
AND NECK

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The Red Eye

Infectious Conjunctivitis, Keratitis, Endophthalmitis, and Periocular Cellulitis

*Kirk R. Wilhelmus, MD**

BASIC CONSIDERATIONS

Anatomy of the Eye and Orbit

An understanding of ocular anatomy is necessary to recognize the various structures and tissue planes of the eye and its adnexa that may become involved as a result of microbial invasion. With appropriate examination techniques, several clinical syndromes of ocular and periocular infections can be distinguished.

The fine-textured skin of the *eyelids* is loosely attached to the underlying connective tissue. Within the eyelid, the *orbital septum* connects the fibrous *tarsus* and levator aponeurosis to the orbital periosteum, dividing the orbit into preseptal and orbital compartments (Fig. 1). Individual eyelid structures—including the ciliary follicles, the sebaceous glands of Zeis, the sweat glands of Moll, and the *meibomian glands*—are potential foci for acute and chronic inflammation.

The transition from eyelid skin to conjunctival mucous membrane, with its underlying *Tenon's capsule* on the globe, occurs at the mucocutaneous junction just behind the meibomian gland orifices. The *palpebral conjunctiva* covers the posterior aspect of the eyelid; the *conjunctival fornix* reflects onto the globe and contains *lacrimal gland* tissue superiorly. The *bulbar conjunctiva* covers the anterior portion of the eye, blending into the corneoscleral *limbus*. At the limbus, conjunctival, episcleral, and superficial scleral blood vessels anastomose with the iris circulation. Intraocular inflammation can thereby produce hyperemia of the limbal vasculature, known as ciliary flush. Lymphatic channels from the eyelids and conjunctiva drain predominantly to the ipsilateral *preauricular lymph node* that may enlarge with certain infectious agents.

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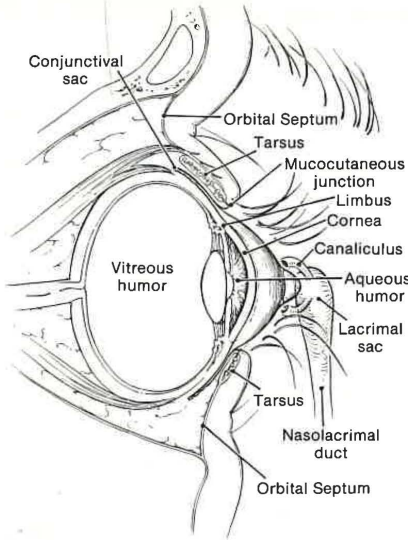


Figure 1. Anatomy of the eye and orbit.

The *cornea* is covered by nonkeratinized, stratified epithelium, and the abundant nerve supply makes it one of the most sensitive structures of the body. Corneal sensitivity is a selective measure of the function of the ophthalmic division of the trigeminal cranial nerve; certain viral infections, such as herpes simplex and herpes zoster, may lead to corneal hypesthesia.

The *tear film* covers the conjunctival and corneal surface and is composed of three principal layers: the mucous layer produced by the conjunctival goblet cells, the aqueous layer produced by the lacrimal glands, and the superficial oily layer produced by the meibomian glands. Reflex tearing is produced by the lacrimal gland, located in the superotemporal angle under the superior orbital rim. With blinking, the tears drain via the *lacrimal puncta* and *canaliculi* into the *lacrimal sac*, located directly behind the bony lacrimal crest at the *medial canthus*.

The globe is constructed of a thin wall containing connective tissue (cornea and sclera), uveal blood vessels (iris, ciliary body, and choroid), and retina. Occupying about 20 per cent of the adult orbit, the eye is protected within the confines of the orbital bones. The major venous drainage from the orbit is into the cavernous sinus by the superior and inferior ophthalmic veins.

The close proximity of the various ocular tissues may produce overlapping signs of a red eye, but a careful examination usually permits accurate anatomic localization of inflamed structures.

Examination Technique

By following a stepwise examination pattern, following the surface anatomy, specific distinctive signs of the principal entities producing a red eye can be determined.

1. *Facial inspection.* An overall evaluation of the facial anatomy should be performed to determine any obvious changes. Some skin disorders such as rosacea dermatitis may be detected to account for eyelid and eye inflammation.

2. *Palpation for regional lymphadenopathy.* Normally, the preauricular lymph nodes are not palpable. The presence of a node just anterior to the tragus suggests the possibility of viral or chlamydial conjunctivitis or chronic granulomatous disease.

3. *Globe position.* Forward displacement of the globe can be detected by measuring the distance from the lateral orbital rim to the anterior corneal surface, by perpendicular siting along a millimeter ruler, or by comparing the position of both globes when viewed from above. The presence of proptosis generally means orbital inflammation or a mass lesion.

4. *Eyelid inspection.* The skin of the eyelids, the number and direction of the eyelashes, and the integrity of the eyelid margins should be examined.

5. *Conjunctival discharge.* The presence and type of any conjunctival discharge should be determined (Table 1). Because many patients wrongly interpret mucous or watery discharge as "pus," this may be an important step in evaluating patients with a red eye. Many forms of ocular diseases, including acute glaucoma and uveitis, may produce reflex tearing but no apparent discharge. The presence of a white mucoid discharge may mean allergic conjunctivitis or tear deficiency, whereas a mucopurulent or purulent discharge generally implies infectious conjunctivitis.

6. *Conjunctival examination.* Both eyes should be assessed and compared for the presence and type of conjunctival injection. By pulling down on the lower eyelids, the lower tarsal and bulbar conjunctiva can be evaluated. The upper tarsal conjunctiva is best seen by everting the upper lid by applying a blunt instrument just above the tarsal margin and folding over the lid for brief examination. Con-

Table 1. *Clues to the Cause of Acute Conjunctivitis Based on Type of Conjunctival Discharge*

ETIOLOGY	CONJUNCTIVAL DISCHARGE			
	Serous	Mucoid	Mucopurulent	Purulent
Viral	+	+	-	-
Chlamydial	-	+	+	-
Bacterial	-	-	+	+
Toxo-allergic	+	+	-	-
Dry eye syndrome	-	+	-	-

junctival edema, or chemosis, and dilatation of the conjunctival and episcleral vessels may occur with a variety of diseases and does not necessarily imply infectious conjunctivitis. Similarly, subconjunctival or intraconjunctival hemorrhages may occur not only with bacterial or viral conjunctivitis but also with hematologic and vascular disorders, as well as following trauma. Papillae are capillary tufts of the palpebral conjunctiva, and follicles are enlarged lymphoid germinal centers. Membrane formation and conjunctival ulceration can be extremely important signs.

7. *Corneal inspection.* The detection of corneal abnormalities substantially influences decision-making in the evaluation of an inflamed eye. The clarity of the cornea can be judged by the ability to visualize iris details while shifting an examination light across the eye. A magnifying lens can be very helpful. A convenient technique is to use the high-plus lenses in a direct ophthalmoscope held at arm's length to detect the presence of corneal opacities by their interference with the normal reddish-orange fundus reflex. Pathologic processes in the cornea generally produce one of two major structural alterations: an epithelial defect or stromal opacification. Loss of the corneal epithelium can easily be seen by instilling fluorescein eye-drops. Opacification may be either focal or diffuse; of the many causes of corneal inflammation, herpes simplex virus is one of the leading agents in developed countries.

8. *Vision.* Using an eye chart at 20 feet (6 meters), best-corrected visual acuity is determined in each eye. If lenses are not available, a pinhole will do.

CLINICAL SYNDROMES

Blepharitis and Conjunctivitis

Etiology. Among the several dermatologic conditions that can involve the eyelids, many cases of anterior marginal blepharitis are attributed to chronic bacterial infection by staphylococci.¹⁹ However, the cause of "staphylococcal blepharitis" remains uncertain. *Staphylococcus aureus* can be isolated from the eyelid margins of many patients with blepharitis, but these same species are also found on normal eyelid margins as well. Various other microorganisms, such as *Moraxella*, *Haemophilus*, and *Proteus*, have also been incriminated, but the differentiation between normal commensal and pathogenic flora may be difficult.

Acute conjunctivitis can be caused by several microorganisms, including *Staphylococcus aureus*, group A streptococci, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria gonorrhoeae*.²³ Gram-negative organisms such as *Pseudomonas aeruginosa*, *Moraxella*, and others are unusual except in immunocompromised individuals or neonates (Fig. 2). Bacterial conjunctivitis is much less common than other causes of acute conjunctivitis such as adenoviral infection and allergic reactions.



Figure 2. Eyelid ecchymosis (left) and purulent conjunctival discharge (right) in a newborn with *Neisseria flavescens* conjunctivitis.

Clinical Manifestations. Chronic redness and irritation, usually bilateral, may occur with staphylococcal blepharitis.²⁶ Typical signs include hyperemia and edema of the eyelid margins with focal suppuration, or hordeolum, along with secondary nonspecific conjunctival injection. Crusting and scaling of the anterior eyelid margin with loss of the eyelashes are typical findings. Peripheral corneal inflammation is sometimes present.

The acute onset of eyelid edema and discomfort is typical of acute bacterial conjunctivitis. There is diffuse conjunctival injection with a purulent discharge. Preauricular lymphadenopathy is usually not present, except with gonococcal conjunctivitis. Some microorganisms may induce a pseudomembrane or subconjunctival hemorrhage.

Complications. Chronic blepharitis may lead to eyelid malposition, eyelash loss, and conjunctival scarring. Although bacterial conjunctivitis is generally self-limited, invasive bacteria such as *N. gonorrhoeae* can lead to corneal ulceration and even endophthalmitis.

Differential Diagnosis. Eyelid margin changes may be due to other skin conditions. For example, staphylococcal blepharitis may be confused with seborrheic blepharitis; it is important to distinguish anterior eyelid margin involvement from posterior lid margin changes caused by meibomian gland dysfunction. Viral blepharitis due to herpes simplex virus generally begins with eyelid vesicles, and an eyelid nodule may be found with molluscum contagiosum or verruca. Some parasites such as *Phthirus pubis*, the pubic louse, can infest the eyelid margins and lashes. Neoplasms may also occur on the eyelid margin. In particular, meibomian gland carcinoma should be considered as a cause of recurrent or chronic blepharoconjunctivitis as diagnostic delay risks increased mortality.

Conjunctival hyperemia frequently is a nonspecific sign of ocular disease, occurring with most forms of eye inflammation. In addition,

because the conjunctiva is closely adherent to the underlying episclera and superficial scleral vessels, episcleritis or scleritis may be initially misdiagnosed as conjunctivitis. *Chlamydia trachomatis* is becoming increasingly recognized as an important cause of both neonatal and adult conjunctivitis. Several viruses may also cause acute conjunctivitis, including adenovirus, herpes simplex virus, and enterovirus. Parinaud's oculoglandular syndrome is a granulomatous conjunctivitis with marked preauricular lymphadenopathy; various causative agents include the cat-scratch disease bacillus.

Laboratory Investigations. Laboratory evaluation usually is not in the workup of blepharitis. Smears of the conjunctival discharge associated with blepharoconjunctivitis generally show inflammatory cells with only a few microorganisms.

Specimens are mandatory, on the other hand, from patients suspected of having acute bacterial conjunctivitis (Table 2). After the purulent discharge is removed, a cotton-tipped swab is used to collect a conjunctival specimen by swabbing the entire area of the upper and lower palpebral conjunctivae. Gram-stained smears may not always be reliable in determining the responsible microorganisms but may be the most rapid way to detect virulent bacteria such as gonococci. Giemsa staining is used to assess the cytologic pattern and to detect intracytoplasmic chlamydial inclusions within conjunctival epithelial cells. For cultures, the specimen should be inoculated onto a chocolate agar plate, blood agar plate, Thayer-Martin medium, and possibly an anaerobic medium as well. The laboratory should be asked to identify and to perform sensitivity and beta-lactamase testing on the isolates. In addition, swabbings may also be inoculated into a chlamydial transport medium if chlamydial conjunctivitis is suspected. Rapid immunochemical tests are now available for chlamydial and gonococcal infections.

Therapy. Eyelid margin cleansing may be all that is required in controlling the symptoms of staphylococcal blepharitis. As a controlled clinical trial or an adequate animal model is lacking, the use of antibiotic therapy remains unproved. Based on previous susceptibility testing of staphylococcal isolates, an appropriate initial choice would be erythromycin or bacitracin ophthalmic ointment, rubbed onto the eyelid margins.²

Although bacterial conjunctivitis can be a self-limited disease, a placebo-controlled study showed that topical antibiotic therapy sig-

Table 2. Steps in Evaluation of Acute Conjunctivitis

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1. Check for eyelid changes, such as vesicular eruption.
 2. Determine type of conjunctival discharge.
 3. Assess conjunctival inflammatory pattern: hyperemia, papillae, follicles, membrane, ulceration.
 4. Examine cornea.
 5. Obtain conjunctival swabbings for smears and cultures.
-

nificantly shortens the duration of symptoms and enhances bacterial eradication.⁹ A broad-spectrum agent, such as erythromycin ointment, or an aminoglycoside antibiotic solution, such as gentamicin or tobramycin, is preferred. For gonococcal conjunctivitis, parenteral therapy should be administered based on beta-lactamase production. Severe, purulent conjunctivitis in a child or neonate may also require systemic therapy. The treatment of chlamydial conjunctivitis is systemic erythromycin or tetracycline.

Prevention. Many forms of infectious blepharitis and conjunctivitis may not be preventable, even by adequate hygiene. Prophylactic application of silver nitrate, erythromycin, or tetracycline to newborns' eyes after birth can prevent many cases of neonatal conjunctivitis. In adults, any eyedrops that could be contaminated should be avoided, and contact instrumentation such as tonometers should be sterilized regularly.

Keratitis

Etiology. Multiple microorganisms are capable of producing corneal infection.³⁵ The principal responsible bacteria include *S. aureus*, *S. epidermidis*, streptococci, *Pseudomonas* species, and members of the family *Enterobacteriaceae*. Less commonly encountered species include *Corynebacterium*, *Neisseria*, *Moraxella*, *Azotobacter*, *Nocardia*, *Peptococcus*, *Peptostreptococcus*, *Actinomyces*, and *Bacteroides*, as well as atypical mycobacteria. Various fungi have also been encountered, including filamentous organisms such as *Fusarium*, *Aspergillus*, *Curvularia*, and others, and yeasts such as *Candida albicans* (Fig. 3). More recently *Acanthamoeba* species have also been found to be capable of infecting the cornea.

Prior to bacterial infection, generally an alteration in the defense mechanisms of the outer eye occurs.²⁰ Rarely do microorganisms penetrate intact corneal epithelium, although *Neisseria gonorrhoeae*,

Figure 3. *Candida albicans* keratitis related to poor eyelid closure in an elderly, debilitated woman.



N. meningitidis, *Corynebacterium diphtheriae*, and *Shigella* species may do so directly. In addition, except in syphilis, tuberculosis, and onchocerciasis, pathogens do not generally invade the cornea by a hematogenous route. More commonly, microorganisms gain entry through a corneal epithelial defect produced by mechanical, thermal, or chemical injury, or from a preexisting ocular condition. The responsible microorganisms may be part of the indigenous microflora of the conjunctiva or an exogenous contaminant from a foreign body or contact lens.

Using specialized organelles and molecular adhesins, microbial attachment is initiated by the interaction of bacterial lectins with glycolipid receptors of the ocular surface. In the cornea, sialic acid has been identified as one of these receptors for *P. aeruginosa*. Fibronectin has also been found to selectively bind lipoteichoic acid present in the cytoplasmic membrane of gram-positive cocci. Following local production of a bacterial adherence factor, pit-like depressions are formed in the corneal epithelial cell, subsequently leading to corneal stromal invasion and ocular damage by bacterial products.¹⁶

Clinical Manifestations. The hallmark of microbial keratitis is polymorphonuclear leukocytic suppuration, distinguished by a dense yellow-white or gray-white infiltrate with epithelial and stromal ulceration. A ring-shaped infiltrate may also be present, located between the infectious focus and the corneoscleral limbus, that may represent a complement-mediated immune reaction. With progression, peripheral corneal neovascularization, increasing stromal edema, and anterior uveitis with hypopyon can appear.

Complications. Intraocular inflammation typically follows keratitis. Anterior uveitis may, in turn, lead to iris adhesions and secondary glaucoma. Rarely, microbial invasion may extend into the eye's anterior chamber, leading to endophthalmitis. Progressive stromal ulceration may lead to corneal thinning with descemetocoele formation and subsequent perforation. Even with adequate antimicrobial therapy, residual corneal scarring may produce severe visual loss.

Differential Diagnosis. Suppurative keratitis may also be caused by severe toxic or chemical injuries. Viral keratitis, initiated by an immunogenic reaction to herpes simplex virus, varicella-zoster, or Epstein-Barr virus, may also lead to necrotizing corneal inflammation. Less frequently, systemic conditions such as connective tissue disorders or vasculitis may produce peripheral corneal disease.

Laboratory Investigations. Although swabbings are useful to assess the ocular flora of the conjunctiva, corneal scrapings are necessary in the etiologic investigation of microbial keratitis³³ (Table 3). Following application of a topical anesthetic, a heat-sterilized spatula is used to perform corneal scrapings using slit-lamp biomicroscopic magnification. Several smears should be obtained so that different staining techniques can be employed. Gram staining is useful for the identification of various microorganisms, and Giemsa staining is useful for fungal identification. Calcofluor white can stain the poly-

Table 3. *Steps in Evaluation of Microbial Keratitis*

-
1. Evaluate predisposing factors. Consider possible contamination of contact lens solutions or eyelid cosmetics.
 2. Assess severity of keratitis: progression, area, depth, structural damage.
 3. Obtain corneal scrapings for smears and cultures (blood agar plate, chocolate agar plate, thioglycolate broth, brucella agar plate, Sabouraud agar plate, brain-heart infusion broth).
 4. Review gram-stained smear and previous microbial isolates from similar patients of that geographic location.
 5. Prepare appropriate concentration of topical antimicrobial agents. Consider cycloplegia.
-

saccharide polymers of fungal and amoebic cell walls, and other supplemental stains and immunofluorescent techniques are also becoming available.

Material is also obtained for inoculation onto various media, including a blood agar plate, chocolate agar plate, thioglycolate broth tube, brucella blood agar plate, Sabouraud agar plate, and brain-heart infusion broth.¹⁴ A corneal biopsy may be needed to obtain sufficient tissue for culture and histopathology. Culture media are incubated at 35°C in a candle jar or other system to maintain a 3 to 10 per cent carbon dioxide concentration. Additional plates may be incubated anaerobically, and fungal media should be maintained at room temperature (25°C). Laboratory personnel should examine the media, preferably with a dissecting microscope, on a daily basis to detect early bacterial or fungal colonies or the meandering trails of amoebic trophozoites. Antimicrobial susceptibility testing for both minimal inhibitory concentrations (MIC) and minimal bactericidal concentrations (MBC) may be performed for each isolate, although clear correlations between in vitro sensitivity results and achievable drug concentrations in the cornea are not available.

Therapy. Because of the wide variety of microorganisms that can cause suppurative keratitis, specific antimicrobial therapy should be initiated based on appropriate microbiologic evaluation.¹³ Initially, antibiotics can be chosen according to the smear morphology of corneal scrapings. If no microorganisms are seen, broad-spectrum therapy should be instituted,² such as with combined cephalosporin and aminoglycoside agents; to avoid any biophysical interaction, they should not be mixed together in the same eyedropper dispenser. Commercially available preparations of ophthalmic antibiotics may be "fortified" to achieve a higher dosage level. Most antimicrobial agents that are available for parenteral administration may be formulated as a topical preparation.

Fungal keratitis is treated with natamycin or other antifungal agents, including amphotericin B and imidazoles such as miconazole and ketoconazole.³⁰ Optimal medical therapy has not yet been established for *Acanthamoeba* keratitis.

For microbial keratitis, subconjunctival antibiotic injection is now considered optional. Parenteral therapy is also not usually necessary, although intravenous administration can be considered for

scleral extension or threatened perforation. With appropriate antimicrobial therapy and judicious steroid use, permanent central corneal scarring can be minimized.

Prevention. The reduction of blinding corneal disease in developed countries is largely due to improvements in hygiene and prevention, rather than treatment, of infectious ocular diseases. Thus, although appropriate diagnostic and therapeutic management is essential for individuals with microbial keratitis, only by identifying specific risk factors and designing preventive measures can an overall beneficial impact be made. For example, appropriate care and disinfection of contact lenses may be able to prevent some cases of microbial keratitis.¹ Many foreign body eye injuries could potentially be prevented by protective spectacles. Also, specific corneal conditions such as dry eye syndrome and exposure keratopathy should be properly managed with lubricants, patching, or tarsorrhaphy, particularly in comatose patients. The role of prophylactic antibiotics has not yet been substantiated as a preventive measure following corneal trauma, and the biophysical alteration of microbial adherence to the corneal surface remains to be assessed.

Endophthalmitis

Etiology. Multiple microorganisms are capable of causing endophthalmitis. Gram-positive cocci account for approximately 80 per cent of cases, gram-negative bacilli for 15 per cent, and smaller numbers are caused by other bacteria and various fungi. Responsible pathogens of exogenous endophthalmitis include *S. epidermidis*, *S. aureus*, streptococci, *Proteus*, *Pseudomonas* and *Bacillus*,⁴ among others. *Candida albicans* is the leading cause of endogenous endophthalmitis from hematogenous spread.

Microbial endophthalmitis begins with microorganisms circumventing the eye's natural defense mechanisms.³⁴ Exogenous endophthalmitis occurs after about 2 per cent of perforating eye injuries, with an increased risk in those with an intraocular foreign body. Following intraocular surgery, the risk of postoperative endophthalmitis is currently estimated to be approximately 1 in 1500 cataract extractions and 1 in 500 corneal transplants. Presumably, inoculation of the normal conjunctival flora into the eye may occur from intraocular surgery⁶ (Fig. 4). However, epidemics of fungal and bacterial endophthalmitis have occurred related to contaminated solutions and intraocular lenses. Delayed-onset postsurgical endophthalmitis has occurred after suture removal, in the presence of wound dehiscence or vitreous strands to the wound, with filtering blebs, and from low-virulent organisms such as *S. epidermidis* and *Propionibacterium acnes*.¹⁷

Endogenous endophthalmitis may be a complication of sepsis from an indwelling catheter, hyperalimentation, immunosuppressive therapy, or intravenous drug addiction.^{8,10} Less frequently, contiguous spread from an adjacent infected tissue may occur.

Following a brief incubation period with bacterial proliferation in the vitreous cavity, leukocytes are usually recruited within a few



Figure 4. Pneumococcal endophthalmitis presenting two months after cataract surgery, possibly related to suture abscess.

hours. The virulence of different microorganisms, the release of microbial toxins, and the influx of inflammatory cells can rapidly lead to irreversible, blinding changes.

Clinical Manifestations. The onset of bacterial endophthalmitis is generally rapid, within 48 to 72 hours after inoculation of microorganisms. Visual loss and increasing pain occur along with eyelid swelling, conjunctival chemosis, and redness. The hallmark of endophthalmitis is the presence of intraocular inflammation: anterior chamber inflammation with hypopyon and vitreous inflammatory cells. Less fulminant, chronic vitreitis may be produced by anaerobic bacteria such as *Propionibacterium acnes* and fungi. Endogenous endophthalmitis may begin with a fluffy, white lesion in the retina, subsequently leading to posterior vitreous inflammation.

Complications. Progressive intraocular inflammation may lead to permanent structural damage, including glaucoma, cataract, and retinal detachment, as well as phthisis. Even with adequate antimicrobial therapy, retinal necrosis may result in a poor visual outcome. Overall, approximately one half of patients with exogenous endophthalmitis have loss of usable vision.²²

Differential Diagnosis. Multiple other causes of intraocular inflammation exist. Following ocular surgery or trauma, sterile iritis may lead to initial diagnostic confusion. In addition, various uveitis syndromes can selectively produce anterior, intermediate, or posterior inflammatory changes. For example, retinal toxoplasmosis or ocular toxocariasis can produce acute intraocular inflammation.

Laboratory Investigations. After a complete eye evaluation, appropriate microbiologic testing is essential (Table 4). Conjunctival swabbings may sometimes help if postoperative wound suppuration or filtering bleb necrosis is present. All patients with microbial endophthalmitis need appropriate sampling of the intraocular fluids. Aqueous humor aspiration may be obtained using sterile technique via a keratocentesis site at the limbus, but it is even more important to obtain a vitreous specimen. If aphakic, the same keratocentesis

Table 4. *Steps in Evaluation of Endophthalmitis*

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1. Determine route of infection (exogenous, endogenous) and pace of inflammation.
 2. Test vision and pupils.
 3. Assess intraocular structures and localize foreign body, if present; consider B-scan echography and CT scan.
 4. Obtain intraocular fluids (aqueous humor and vitreous) for smears and cultures. Blood and tissue for other cultures are also obtained if endogenous endophthalmitis is suspected.
 5. Decide whether therapeutic vitrectomy is indicated.
-

site may be used, directing the needle through the pupil. Alternatively, the pars plana is entered for a diagnostic vitrectomy. Blood cultures should also be obtained if an endogenous origin is suspected.

Material should be prepared for smears and cultures, including a blood agar plate, chocolate agar plate, thioglycolate broth tube, Sabouraud dextrose agar plate (without cycloheximide but with gentamicin, 15 µg per ml), and brain-heart infusion broth (with gentamicin, 50 µg per ml). Vitreous washings collected during vitrectomy can be concentrated onto sterile filter paper with an aseptic vacuum technique. If previous antimicrobial therapy has already been given, an antimicrobial removal device may be useful to selectively bind residual antibiotics from the specimens.

Therapy. Antibiotic selection is largely dependent on rapid microbial identification and sensitivity testing from aqueous humor and vitreous specimens. An initial regimen could include a semisynthetic penicillin or cephalosporin and an aminoglycoside such as gentamicin or tobramycin. An effective antimicrobial regimen should be instituted as soon as possible by multiple routes, including topical application, subconjunctival or periocular injection, and intravenous infusion.⁷ Because of the difficulty in achieving adequate drug levels within the vitreous cavity, intravitreal injection has also been advised, but additional clinical experience is needed to assess the roles of vitrectomy and intravitreal antibiotics in the therapy of endophthalmitis.^{5,21} Systemic and local corticosteroid therapy is sometimes started early to minimize postinflammatory structural changes contributing to sight-threatening complications.

Prevention. Before ocular surgery, prophylactic antibiotics have been recommended. Preoperative topical administration is effective in reducing the normal ocular flora, but a consensus is lacking on the use and choice of antibiotic prophylaxis for ophthalmic surgery.²⁸ Subconjunctival injections of antibacterial drugs are also given by some surgeons at the time of intraocular surgery and during the repair of penetrating eye injuries. Proper antiseptic technique should be routine at all times.

Ocular Adnexal Infections (Dacryocystitis, Preseptal Cellulitis, and Orbital Cellulitis)

Etiology and Pathogenesis. Infection of the lacrimal sac may result from impaired drainage of the nasolacrimal duct. Frequently

encountered microorganisms in acute dacryocystitis include streptococci, especially *S. pneumoniae*, staphylococci, and gram-negative rods, including *H. influenzae*, *Escherichia coli*, and *Proteus* species.

Preseptal and orbital cellulitis are generally preceded by trauma or sinusitis with upper respiratory tract inflammation and otitis media.^{24,32} The close proximity of the paranasal sinuses to the orbital walls can permit microbial invasion through various vascular anastomoses (Fig. 5). Staphylococci, streptococci, and *H. influenzae* are the most common organisms causing preseptal and orbital cellulitis. Most gram-negative organisms are infrequently encountered, but *H. influenzae* remains one of the leading causes of nontraumatic preseptal and orbital cellulitis in young children (Fig. 6). Infantile maxillary osteomyelitis is an uncommon condition characterized by bacterial, usually staphylococcal, infection of the maxilla in the newborn infant with surrounding necrosis and sequestration.³⁷ Orbital zygomycosis and other fungal infections should be considered in immunocompromised and diabetic patients.³

Clinical Manifestations. The level of involvement in eyelid infection determines the clinical findings (Fig. 7). Marked eyelid edema and ecchymosis with localized tenderness occur with dacryocystitis. Lacrimal sac enlargement can be visible beneath the medial canthal tendon; pressure in this area may produce purulent material through the lacrimal puncta. With obstruction of the common canaliculus, canaliculitis with hyperemia and punctal edema may ensue.

Figure 5. Anatomical relationships of the paranasal sinuses to the orbit.

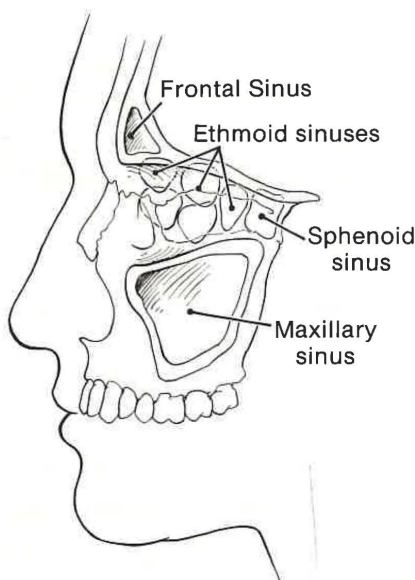




Figure 6. *Haemophilus influenzae* preseptal cellulitis in a young boy with upper respiratory tract and otic symptoms.

Preseptal cellulitis generally causes diffuse eyelid swelling that may even spread across the nasal bridge. It is mandatory to open the eyelids to ensure that the globe is not affected. With orbital cellulitis, additional eye findings are also present, including conjunctival edema, proptosis, limitation of ocular motility, and decreased vision. Optic disc edema and vascular engorgement may be detected by ophthalmoscopy. Systemic changes include fever and leukocytosis.

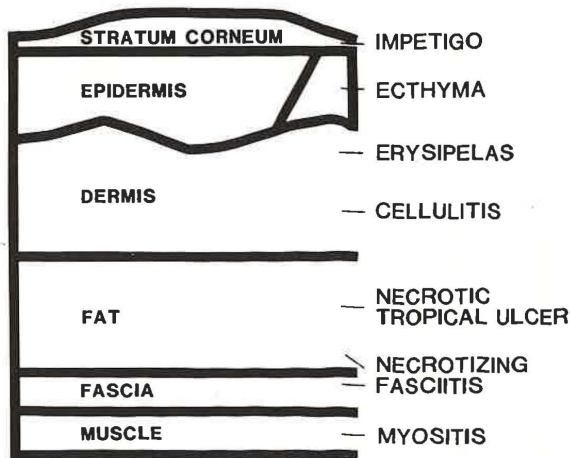


Figure 7. Tissue plane involvement of staphylococcal and streptococcal infections leading to various clinical syndromes.

Complications. Recurrent dacryocystitis can occur with persistent lacrimal duct obstruction. With chronic inflammation, a fistula may form from the lacrimal sac to the overlying skin surface. A subcutaneous abscess may occur from either dacryocystitis or preseptal cellulitis.

As a result of the loose connective tissue between the eyelid skin, orbicularis oculi muscle, and orbital septum, preseptal cellulitis is able to expand and produce marked swelling of the eyelid tissues. Orbital inflammation, on the other hand, is limited in humans by the bony orbital walls and the inelastic orbital septum. An intraorbital or subperiosteal abscess may form that can contribute to visual loss by a precipitous increase in the orbital pressure. Posterior extension may produce an orbital apex syndrome, and multiple cranial nerves passing through the superior orbital fissure may become involved. Without appropriate therapy, cavernous sinus thrombophlebitis, meningitis, and brain abscess may ensue.

Differential Diagnosis. Acute dacryocystitis can mimic preseptal cellulitis, and severe conjunctivitis may produce similar changes. Diagnostic considerations for rapidly progressive, unilateral proptosis would include pseudotumor, orbital myositis, thyroid orbitopathy, and, in children, rhabdomyosarcoma and other tumors.

Laboratory Investigations. The collection of diagnostic specimens depends on the level of tissue involvement (Table 5). If possible, material should be expressed from the lacrimal puncta for smears and cultures. Discharge from any open wound or drainage site should be obtained as well. With preseptal cellulitis, aspiration of material is not performed routinely because of the risk of inadvertently perforating the orbital septum, unless abscess formation is identified. In the evaluation of orbital cellulitis, conjunctival, nasopharyngeal, and blood cultures should be obtained. X-ray studies, including sinus films and orbital computed tomography or magnetic resonance imaging, can be very helpful.^{18,38} Lumbar puncture may be indicated if there are meningeal signs. Diagnosis of zygomycosis or aspergillosis may require sinus or orbital biopsy; an enzyme immunoassay has been described recently.

Therapy. Systemic antimicrobial therapy should be administered based on the likely responsible microorganisms and the results

Table 5. Steps in Evaluation of Ocular Adnexal Infection

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1. Determine route of infection. If trauma or sinusitis is not present, search for a more distant site of infection. Perform complete physical examination, including otorhinolaryngologic and neurologic evaluations. Consider sinus x-rays, CT scan or MRI, and orbital ultrasonography.
 2. Determine level of tissue involvement: preseptal, orbital.
 3. Assess spread of inflammation, and determine whether surgical drainage of abscess is justified.
 4. Monitor frequently for ophthalmologic and neurologic complications.
 5. Obtain smear and cultures from wound, blood, conjunctival, and nasopharyngeal specimens. Be aware of potential risk of inadvertent perforation through orbital septum if tissue aspiration performed.
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Table 6. Common Microorganisms Capable of Causing Ocular Infection

MORPHOLOGY	AEROBIC	ANAEROBIC
Gram-positive cocci	Micrococcaceae <i>S. aureus</i> <i>S. epidermidis</i> <i>Micrococcus</i> spp. Streptococcaceae <i>S. pneumoniae</i> <i>S. pyogenes</i> <i>S. faecalis</i> <i>Aerococcus viridans</i> <i>Pediococcus</i> spp.	Peptococcaceae <i>Peptococcus</i> spp. <i>Peptostreptococcus</i> spp.
Gram-negative cocci	Neisseriaceae <i>N. gonorrhoeae</i> <i>N. meningitidis</i> <i>Moraxella</i> spp. <i>Acinetobacter calcoaceticus</i>	Veillonellaceae <i>Veillonella</i> spp.
Gram-positive rods	Bacillaceae <i>B. cereus</i> <i>Corynebacterium</i> spp.	Bacillaceae <i>Clostridium</i> spp.
Gram-positive filaments	Nocardiaceae <i>N. asteroides</i> Mycobacteriaceae <i>M. fortuitum</i> <i>M. chelonae</i>	Propionibacteriaceae <i>P. acnes</i> Actinomycetaceae <i>A. israelii</i> <i>A. viscosus</i> <i>Arachnia propionica</i>
Gram-negative rods	Pseudomonadaceae <i>P. aeruginosa</i> <i>P. fluorescens</i> <i>P. cepacia</i> Enterobacteriaceae <i>Escherichia coli</i> <i>Klebsiella</i> spp. <i>Enterobacter</i> spp. <i>Serratia</i> spp. <i>Proteus</i> spp. <i>Morganella morganii</i> Pasteurellaceae <i>Haemophilus influenzae</i> Azotobacteriaceae <i>Azotobacter</i> spp.	Bacteroidaceae <i>B. fragilis</i>
Yeasts	<i>Candida</i> spp.	
Filamentous fungi	<i>Fusarium</i> spp. <i>Aspergillus</i> spp. <i>Curvularia</i> spp. <i>Drechslera</i> spp.	
Amoeba	Hartmannellidae <i>Acanthamoeba</i> spp.	

of laboratory investigations. Warm compresses and massage of the lacrimal sac may be useful to permit drainage for acute dacryocystitis. Systemic antibiotics such as ampicillin are administered, and an antibiotic can be irrigated directly into the lacrimal drainage system. With persistent nasolacrimal duct obstruction, probing or dacryocystorhinostomy, or both, may be necessary.

For preseptal and orbital cellulitis, systemic antibiotics are necessary. The first clinical use of penicillin was in a 43 year old British policeman with combined staphylococcal and streptococcal orbital cellulitis. A current regimen could include a semisynthetic penicillin such as methicillin or nafcillin, an aminoglycoside such as tobramycin, and an agent effective against anaerobes such as clindamycin. Agents that have activity against both gram-positive cocci and *H. influenzae*, such as ampicillin, cefuroxime, or cefotaxime, could be substituted.^{25,31} Surgical intervention may be indicated for abscess formation,¹¹ and sinus drainage may need to be considered.¹² Systemic antifungal therapy is indicated for orbital zygomycosis¹⁵; surgical debridement may also be necessary.

Prevention. Nasolacrimal probing is sometimes required in infants with persistent tearing due to congenital obstruction to prevent dacryocystitis. Early treatment of sinusitis may prevent preseptal and orbital cellulitis. Prophylactic antibiotics are probably helpful after orbital trauma; for example, oral cephalexin would be appropriate for a dog or human bite. Tetanus prophylaxis would also be warranted. Children should be vaccinated against *H. influenzae* type b disease.

SUMMARY

Patients presenting with a red eye may have a minor, self-limited inflammation of the ocular surface or a vision-threatening infection such as endophthalmitis or orbital cellulitis. Careful evaluation of distinctive clinical signs is necessary to determine the level of ocular involvement. A knowledge of the common microorganisms causing various eye infections (Table 6) can provide the basis to guide appropriate laboratory investigation and initial therapy. Detailed reference textbooks on ocular infection should be available,^{27,29,36} and ophthalmologic consultation should be considered in these cases to assist in diagnostic investigations and to monitor potential ocular complications.

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