Preseptal and Orbital Cellulitis

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Learning Objectives

Upon completion of this module, the reader should be able to:

- Delineate the similarities and differences between preseptal and orbital cellulitis
- Identify the likely pathogens involved in infectious periorbital disease
- Formulate a multidisciplinary medical and surgical treatment plan to manage preseptal and orbital cellulitis
- Understand the evolving complexities of antibiotic-resistant infections of the ocular adnexa

Financial Disclosures

The authors, reviewers, and consultants disclose the following financial relationships. John Bryan Holds, MD: (C) QLT Phototherapeutics. Ronald W. Pelton, MD: (L) AO-ASIF. Steven I. Rosenfeld, MD, FACS: (L) Allergan. Albert T. Vitale, MD: (C) Bausch & Lomb.

The following contributors state that they have no significant financial interest or other relationship with the manufacturer of any commercial product discussed in their contributions to this module or with the manufacturer of any competing commercial product: Richard C. Allen, MD, PhD. Thomas L. Beardsley, MD; Keith D. Carter, MD, FACS; William S. Clifford, MD; Kathleen M. Duerksen, MD, FACS; Bradley S. Foster, MD; Stephen R. Klapper, MD, FACS; Christie Morse, MD; Anil D. Patel, MD; Eric P. Purdy, MD; Ramana S. Moorthy, MD; George A. Stern, MD; C. Gail Summers, MD.

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Introduction

Preseptal cellulitis describes an infection or inflammation of the eyelids anterior to the orbital septum. Orbital cellulitis occurs posterior to the orbital septum and involves the soft tissues within the bony orbit. These processes occur most commonly following the spread of infection from adjacent structures. Preseptal cellulitis occurs more frequently than orbital cellulitis. Dermato-blepharitis, conjunctivitis, dacrocystitis, dacryoadenitis, endophthalmitis, and trauma can all lead to infection of the eyelids and orbit. The most common cause of orbital infection and inflammation is sinusitis. Although the clinical presentation varies, the hallmark of both preseptal and orbital cellulitis is periorbital edema and erythema (Figure 1). While these two signs of preseptal and orbital infection may be similar, orbital cellulitis generally has greater potential for significant morbidity and even mortality. Preseptal infections do not cause
proptosis, motility deficits, or vision loss—signs that define orbital cellulitis. Therefore, it is imperative that the treating physician distinguish between pre- and post-septal infections. Recognition of patient risk factors and distinguishing clinical characteristics, as well as high-quality computed tomography (CT) or magnetic resonance imaging (MRI) studies, can lead to vision-sparing or even life-saving treatment.

Anatomic Considerations

The orbital septum is a thin yet strong fibrous membrane that separates the orbital from the preseptal compartments. In the upper eyelid, the septum extends from the bony orbital rim to the levator aponeurosis just superior to the tarsal plate. In the lower eyelid, it fuses with the inferior border of the tarsal plate. It anatomically divides the anterior preseptal eyelid tissues (skin and orbicularis) from the posterior orbital compartment. Chandler’s classification system, described more than 35 years ago, provides a guideline to anatomically categorize periorbital infections (Figure 2). Group 1 refers to periorbital edema or preseptal cellulitis, group 2 to orbital cellulitis, group 3 to subperiosteal orbital abscess, group 4 to diffuse orbital infection or abscess, and group 5 to cavernous sinus thrombosis (albeit not an actual periorbital process). Although there may be overlapping findings in this arbitrary and historical classification schema, it is important to recognize that one type of infection does not inevitably lead into the next group.

Extension of bacterial sinusitis into the lids and orbit can occur via several different mechanisms relating to the unique anatomy of the periorbital region. Indirect spread can occur through the rich and complex venous drainage system shared by the cranial and midface structures, including the paranasal sinuses, preseptal soft tissues, and orbit (Figure 3). Phlebotic extension of infection by way of multiple anastomoses in this valveless system is propagated as tissue swelling leads to changes in arterial perfusion, venous drainage, and lymphatic flow (Table 1). Importantly, the primary direction of venous drainage for the ethmoid and superior maxillary sinuses is through the orbit.

Direct extension of ethmoid sinus pathogens can also occur via the thin and fragile lamina papyracea (“paper bone”) through naturally occurring foramina as well as through necrotic bone. This may lead to a relatively contained subperiosteal abscess (see Figure 2c) or may progress further into the orbit. As sinus and orbital edema increases and hemodynamic flow is compromised, the periosteum becomes incompetent and access into the intraorbital space occurs.

Direct extension can also occur from the frontal and maxillary sinuses through the orbital roof or floor respectively. Uncommonly, odontogenic infections may spread to the maxillary sinus, and ultimately the orbit, as the apices of the maxillary molars and premolars are close to the floor of the maxillary sinus. Dental infections can
also extend to the paranasal sinuses through the buccal cortical plate or the infratemporal and pterygopalatine fossae. Intracranial extension through the orbital roof or apex can lead to meningitis, encephalitis, frontal lobe abscess, and even death. Patients with frontal sinusitis are more likely to develop an intracranial infection. These complications are age-dependent since the frontal sinus does not begin to aerate until 5 to 7 years of age.

**Preseptal Cellulitis**

It is imperative that the primary treating physician be able to distinguish between pre- and postseptal infections. Because preseptal infections are contained by the orbital septum, the extraocular muscles are not affected and ocular motility is undisturbed. Ophthalmoplegia and diplopia are worrisome signs and strongly suggest orbital invasion (Figure 4). Likewise, because the optic nerve is unaffected in preseptal infections, visual acuity, color vision, and pupillary function should remain normal. A thorough ophthalmologic exam with particular attention to optic nerve function (visual acuity, color vision, and pupillary reactivity), ocular motility, and the measurement of globe displacement will usually distinguish between pre- and postseptal infections (Table 2).

**Etiology**

Preseptal cellulitis principally occurs by one of three routes: spread of infection from adjacent structures, including the skin and sinuses; direct inoculation following trauma; or nonsuppurative infections due to bacterial spread from upper respiratory or middle ear infections. Hordeola and chalazia, impetigo, erysipelas, blepharitis, conjunctivitis, canaliculitis, and dacryocystitis may cause preseptal inflammation. Viral dermatitis, such as herpes simplex and varicella-zoster, can also lead to a preseptal cellulitis. Look-alike processes such as contact dermatitis, insect stings, thyroid eye disease, and idiopathic eyelid edema (blepharochalasis) can occasionally present a confusing picture. Eyelid swelling both causes and results from impeded venous flow and lymphatic drainage, leading to a self-propagating process.

**Medical Management**

Treatment is guided by the suspected etiology, usually elicited from the patient’s history, physical examination, and radiographic findings. Post-traumatic cellulitis may be accompanied by a draining puncture wound or laceration that permits isolation of the causative organisms. While *Staphylococcus aureus* and *Streptococcus pyogenes* are by far the most frequent pathogens, anaerobic and non-spore-forming bacteria may also be identified, particularly after a human bite. Most patients can be managed on an oral antibiotic on an outpatient basis (Figure 5 and Table 3). An increasing number of preseptal infections are due to antibiotic-resistant organisms creating new challenges in the treatment of infections of the ocular adnexa. (See the section in this module on methicillin-resistant *S. aureus* infections.) Tetanus vaccination should be verified. Most children younger than 2 years of age

![Figure 3 Anatomic illustration demonstrating that the primary direction of venous drainage for the ethmoid and superior maxillary sinuses is through the orbit. Due to this anatomic configuration indirect spread of infection can occur through the venous drainage system, which includes the paranasal sinuses, preseptal soft tissues, and orbit. (Reprinted, with permission, from Harris GJ. Age as a factor in the bacteriology and response to treatment of subperiosteal abscess of the orbit. *Trans Am Ophthalmol Soc.* 1993;91:441–516.)

**Table 1. Sequential Factors in Bacterial Sinusitis**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Viral or allergic inflammation of the sinuses</td>
<td></td>
</tr>
<tr>
<td>Altered mucociliary clearance of normal flora</td>
<td></td>
</tr>
<tr>
<td>Obstruction of sinus ostia ↓ pO₂</td>
<td></td>
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<tr>
<td>Absorption of air by sinus mucosa</td>
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<tr>
<td>Transudation, providing a nutrient medium</td>
<td></td>
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<tr>
<td>Moderate ↓ pO₂, ↑ pCO₂, ↓ pH</td>
<td></td>
</tr>
<tr>
<td>Proliferation of aerobic and facultative organisms</td>
<td></td>
</tr>
<tr>
<td>Accumulation of inflammatory products with increasing sinus pressure</td>
<td></td>
</tr>
<tr>
<td>Decreased mucosal blood flow, ↓ pO₂</td>
<td></td>
</tr>
<tr>
<td>Consumption of remaining O₂ by bacteria</td>
<td></td>
</tr>
<tr>
<td>Proliferation of obligate anaerobes</td>
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</tbody>
</table>

and all children younger than 1 year of age should be hospitalized and begun on intravenous antibiotics. If an abscess develops, it should be incised and drained, and the supplicative material should be cultured.

Treatment of infections of the skin and ocular adnexa is based on the underlying cause of the preseptal inflammation. The majority of cases are most likely treated by primary care physicians and are referred to subspecialists such as ophthalmic or sinus surgeons only when the patient fails outpatient therapy. Typically, impetigo is treated with aggressive skin washing of the affected area, topical antibiotic ointment, and oral antibiotics often guided by cultures of ruptured serous vesicles. Herpes zoster dermatoblepharitis, if identified within 72 hours of onset of skin lesions, is treated with a derivative of oral acyclovir.

In the absence of trauma or skin infection, Haemophilus influenzae type b and Streptococcus pneumoniae are the most frequent causes of preseptal cellulitis in children. Fortunately, potentially life-threatening H influenzae infections have diminished markedly due to the vaccine introduced more than 15 years ago. Fever and leukocytosis are common findings in addition to eyelid edema and erythema. Signs of meningeal irritation should be investigated and a lumbar puncture considered prior to starting antibiotic therapy, particularly in children less than 1 to 2 years of age or in any child with signs of meningitis.

Generally, hospital admission is required if the clinician cannot distinguish between pre- and postseptal cellulitis or if the patient cannot be reliably followed as an outpatient. Inpatient management of this disease varies from hospital to hospital, with the ophthalmic faculty as the primary admitting specialty in some locations and otolaryngology in other communities. Whether pre- or postseptal disease is present, the authors advocate a multidisciplinary approach to achieve the most rapid resolution of infection.
Empiric antibiotic therapy:

- **IV ceftriaxone**
- **IV cefotaxime**

### Acute Periorbital Swelling

- **Abnormal visual acuity, pupillary reactivity, ocular motility, globe position, neurologic examination and/or other signs suggestive of orbital cellulitis: severe chemosis, diminished retropulsion, increased intraocular pressure, fever, leukocytosis**

### Nonsuppurative preseptal cellulitis (less than 6 years old)

- Blood culture +/− conjunctival culture
- Lumbar puncture: <12 months old, meningeal signs, high fever, leukocytosis

#### Typical microbiology:
- *H influenzae*
- *S pneumoniae*

#### Empiric antibiotic therapy:
- **IV ceftriaxone**
- **IV cefotaxime**

#### Empiric antibiotic therapy:
- **Gram positive:**
  - IV nafcillin, vancomycin
  - PO dicloxacillin, cephalaxin, ampicillin/clavulanate
- **Gram negative:**
  - IV ceftazidime
- ****Tetranus prophylaxis**

### Culture-directed antibiotic therapy (MRSA):

- Conventional: PO trimethoprim/sulfamethoxazole—rifampin, doxycycline, clindamycin, fluoroquinolones; IV vancomycin
- Novel: PO linezolid; IV daptomycin

### Investigational antibiotic therapies:

- Carbapenems: meropenem, panipenem, ertapenem
- Dihydrofolate reductase inhibitors: clindamycin
- Streptogramin combo: quinupristin/dalfopristin
- Tetracycline derived: tigecycline
- Cephalosporins: ceftobiprole medocaril
- Glycopeptides: dalbavancin, televancin, oritavancin

### Figure 5
Infectious periorbital cellulitis management algorithm. This treatment algorithm should provide the clinician with a general approach to patient care. Infectious disease protocols change periodically, so it is important to consult a local infectious disease specialist when treating a patient with preseptal cellulitis that is not responsive to conventional antibiotic therapy. Multidisciplinary care is recommended for all patients with orbital cellulitis.
Orbital Cellulitis

Ophthalmic signs most frequently seen with orbital cellulitis are limited ocular motility, proptosis, chemosis, and conjunctival hyperemia (see Figure 4). Fever and leukocytosis are also suggestive of an orbital infection. Vision loss and an afferent pupillary defect may occur due to severe orbital congestion and optic nerve involvement. Exposure keratopathy may also contribute to diminished vision because of disruption of corneal integrity, microbial keratitis, and stromal opacification. Delayed management may result in significant morbidity, including orbital apex syndrome (internal and external ophthalmoplegia, blepharoptosis, diminished corneal sensation, and vision loss) and blindness. Cavernous sinus thrombosis, cranial nerve palsies, meningitis, intracranial abscess formation, and even death can occur without prompt aggressive treatment.

Etiology

As with preseptal cellulitis, infectious orbital cellulitis generally occurs by extension of sinus disease, penetrating trauma, or from infected adjacent structures. Underlying ocular infections—including those associated with aqueous drainage device procedures, scleral buckles, or fulminant endophthalmitis—are less common causes of orbital cellulitis. Orbital infections may have an odontogenic origin, including severe dental caries or a recent dental procedure. Orbital cellulitis secondary to hematogenous dissemination has been reported, particularly in newborns.

In addition to the most common infectious causes of periorbital cellulitis reviewed in this module, a host of unusual infections should be included in the differential diagnosis of patients with periorbital inflammation. Rare infections with clinical involvement of the ocular adnexa include Lyme disease, Rocky Mountain spotted fever, and infectious mononucleosis. Cutaneous palpe-
enal anthrax has drawn attention as fears of biologic warfare and terrorism have become more prevalent.

Noninfectious causes of orbital inflammation and prolapses (eg, thyroid-related ophthalmopathy, orbital pseudotumor, and lymphoma) should be considered in both adults and children (Table 4). In pediatric patients, rhabdomyosarcoma, leukemia, metastatic neuroblastoma, and histiocytic disorders should be included in the differential diagnosis. Advanced necrotic retinoblastoma with anterior segment involvement may also present with clinical findings similar to infectious orbital cellulitis.

**Table 4. Noninfectious Causes of Orbital Inflammatory Disease**

<table>
<thead>
<tr>
<th>Inflammatory/autoimmune:</th>
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<tbody>
<tr>
<td>• Thyroid-related ophthalmopathy</td>
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<tr>
<td>• Orbital inflammatory syndrome (orbital pseudotumor)</td>
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<tr>
<td>• Dermatomyositis-polymyositis</td>
</tr>
<tr>
<td>• Systemic and cutaneous erythematous</td>
</tr>
<tr>
<td>• Wegener granulomatosis</td>
</tr>
<tr>
<td>• TNF-receptor associated periodic syndromes</td>
</tr>
<tr>
<td>• Sjögren syndrome</td>
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<tr>
<td><strong>Trauma of ocular adnexa</strong></td>
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<tr>
<td><strong>Vascular:</strong></td>
</tr>
<tr>
<td>• Orbital venous malformation</td>
</tr>
<tr>
<td>• cavernous sinus thrombosis</td>
</tr>
<tr>
<td>• Arteriovenous fistula (eg, carotid-cavernous fistula)</td>
</tr>
<tr>
<td>• Superior vena cava syndrome</td>
</tr>
<tr>
<td><strong>Neoplasms of orbit and lacrimal gland:</strong></td>
</tr>
<tr>
<td>• Pediatric: rhabdomyosarcoma, leukemia, metastatic neuroblastoma, histiocytic disorders, advanced necrotic retinoblastoma</td>
</tr>
<tr>
<td>• Adult: lymphoma</td>
</tr>
<tr>
<td><strong>Other:</strong></td>
</tr>
<tr>
<td>• Sarcoidosis</td>
</tr>
<tr>
<td>• Melkerson-Rosenthal syndrome</td>
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**Orbital Cellulitis Secondary to Bacterial Sinusitis**

More than 90% of all orbital infections are the result of underlying sinus disease. Although sinusitis occurs more frequently in the adult population, orbital cellulitis secondary to sinus disease is seen more commonly in young adults and children. Orbital complications are the most common type of problem arising from acute ethmoid sinusitis. In some communities, a seasonal incidence can be identified, with up to two-thirds of patients with sinusitis and orbital disease presenting from November to March in the United States.

Bacteria that cause sinus infections are the same organisms typically isolated from orbital infections. In children under 8 or 9 years old, a single organism is usually the cause of acute infections. *S aureus* and *S pneumoniae* are the most commonly encountered causative organisms in young children. Anaerobic infections are less common in the pediatric age group.

The bacteriology of sinus infections in adolescents and adults is more complex, frequently involving 2 to 5 organisms. Aerobic organisms including *Streptococcus* and *Staphylococcus* species as well as *Moraxella catarrhalis* can occur along with anaerobes such as *Peptostreptococcus* (commonly seen in dental infections), *Fusobacterium*, and *Bacteroides* species. The *Streptococcus milleri* group (*S intermedius*, *S constellatus*, and *S anginosus*) is often associated with abscess formation. *H influenzae* type B (Hib) infections have diminished markedly since the early 1990s with widespread use of a capsular polysaccharide vaccine. *Pseudomonas aeruginosa* and fungal organisms (invasive aspergillosis or mucormycosis) occur more commonly in immunocompromised hosts. Group A *Streptococcus* may rarely cause necrotizing infections involving the periorbital region, and as with mucormycosis these infections may demonstrate rapid clinical deterioration. Recent reports have heightened concern regarding potentially aggressive community-associated and hospital-associated methicillin-resistant *S aureus* (MRSA) infections, which may also result in devastating visual consequences (see the section in this module on MRSA infections).

**Laboratory Studies.** The laboratory evaluation of patients with orbital cellulitis should include a white blood cell count, which will usually demonstrate leukocytosis. Blood cultures should be obtained before initiating antibiotic therapy, although they are positive in less than one-third of patients under 4 years old and in less than 5% of adult patients. Intranasal swabs of purulent material from an infected sinus performed under direct visualization may provide useful material. A lumbar puncture is indicated if there is any concern regarding central nervous system involvement (lethargy, neck rigidity, cranial nerve palsy, headache), but it must be performed only when the possibility of elevated intracranial pressure has been excluded.

**Imaging Studies.** An orbital CT scan is critical in the evaluation of any patient suspected of having orbital cellulitis. Thin axial and coronal cuts, without contrast, that include the orbits, paranasal sinuses, and frontal lobes are essential (see Figure 5). Initial CT scanning is
recommended in any patient with proptosis, ophthalmoplegia, deteriorating visual acuity, color vision loss, an afferent pupillary defect, bilateral periorbital edema, or if there is no clinical improvement in an apparent preseptal infection following 36 to 48 hours of antibiotic therapy. Additionally, failure of a confirmed orbital infection to improve on the appropriate antibiotic regimen should prompt consideration of a repeat CT scan. MRI with fat saturation and gadolinium contrast is reserved for patients suspected of having an intracranial complication such as cavernous sinus disease or an aggressive fungal infection. In the setting of neurologic involvement, it is important to request that neuroimaging studies include the head and not just the orbits and sinuses. Similarly, the ordering physician should be aware that head studies (ie, “head CT”) alone typically do not provide adequate detail of the orbits.

**Medical Management.** All children and most adults with orbital cellulitis should be admitted to the hospital for intravenous antibiotics (see Figure 5 and Table 3). A multidisciplinary approach that may involve an ophthalmologist, oculofacial/orbital surgeon, otolaryngologist, pediatrician, infectious disease specialist, and possibly a neurosurgeon is frequently necessary during the course of the patient’s hospital admission.

Empiric drug therapy should be directed against the most frequently occurring sinus pathogens (outlined above). Broad-spectrum cephalosporins such as cefuroxime, cefotaxime, or ceftriaxone along with metronidazole or clindamycin for anaerobic coverage are a frequently used combination therapy. Vancomycin is reserved for patients with MRSA, necrotizing infections, inadequate response of empiric therapy, or if warranted based on culture and sensitivity results (see sections in this module on MRSA infections and future horizons). Nasal decongestant (ephedrine 0.5% or oxymetazoline) nose drops should be administered 3 times daily in the head-back, nostril-up position. After hospital discharge, oral antibiotics (such as amoxicillin-clavulanate) are continued for an additional 1 to 3 weeks.

**Surgical Management.** Although most periorbital infections respond adequately to medical therapy, early surgical drainage of the involved sinus may be indicated if orbital signs progress despite intravenous antibiotic therapy or if an orbital abscess is present. Abscesses usually form in the subperiosteal space of the orbit adjacent to the infected sinus but occasionally occur within the orbital soft tissue or in the preaponeurotic space (see Figures 2 and 6). An abscess may cause ocular dystopia, limited motility, and severe vision loss. CT findings of a medial subperiosteal abscess include a convex mass adjacent to the lamina papyracea with lateral displacement of the medial rectus (Figure 6). In some patients, a serous exudate or granulation tissue (phlegmon) may simulate an abscess.

Children (under age 9) with an isolated medial or inferior subperiosteal abscess generally have a favorable response to antibiotic therapy. In the absence of vision loss or severe proptosis, a trial of medical therapy may be attempted for up to 48 hours. Adolescents, adults, or any patient with decreased visual acuity and an afferent pupillary defect due to optic nerve compromise from orbital inflammation should undergo urgent sinus and orbital drainage. Superior subperiosteal abscesses of the orbital roof, often secondary to frontal sinusitis, are considered more dangerous because of their poten-

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**Figure 6** Medial subperiosteal abscess of the left orbit (axial [a] and coronal [b] CT images). Note opacification of the ethmoid and maxillary sinuses.
tial for intracranial spread and brain abscess formation (Figure 7). Thus, a subperiosteal abscess along the orbital roof typically requires surgical intervention. In addition, accidental and surgical trauma may predispose a patient to orbital cellulitis. Subperiosteal abscesses not secondary to sinus disease may require management that is more aggressive, including early surgical intervention, foreign body removal, long-term intravenous antibiotic therapy, and oral surgery. \textit{S. aureus} is most commonly responsible for orbital cellulitis secondary to trauma. The work-up for this group of patients is similar to that described for nontraumatic orbital cellulitis; however, an open wound or draining fistula may provide an additional culture source. A broad-spectrum cephalosporin is usually appropriate empiric antibiotic therapy. Immunocompromised patients may also benefit from a more intensive, multidisciplinary treatment approach.

Functional endoscopic sinus surgery is considered by many to be the modality of choice for chronic sinusitis. It is generally a safe and effective means of acute surgical drainage of the maxillary and ethmoid sinuses. Since sinus surgery in an acutely infected patient is more technically challenging due to increased vascularity, poor visualization, and the potential increased risk of producing adhesions and stenosis of the frontal recess, the main surgical objective is to drain the sinus and obtain material for culture.

If an orbital abscess requires drainage, an experienced orbital surgeon can generally evacuate the abscess under direct visualization at the time of sinus surgery. A transcaruncular conjunctival incision is the optimal approach to a subperiosteal abscess of the medial orbit. This approach provides visualization of the entire medial orbital wall as well as the medial aspects of the orbital roof and floor. Minimal morbidity is associated with transcaruncular surgery, as a skin incision is avoided and all of the dissection is extraperiosteal. Subperiosteal abscesses of the orbital floor are less common and can be evacuated by a standard transconjunctival approach through the lower eyelid (Figure 8). A superior orbit subperiosteal abscess

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**Figure 7** Multiloculated subperiosteal abscess of the orbital roof (coronal [a] and sagittal [b] CT images). Note the proximity to the frontal sinus and intracranial cavity.

**Figure 8** Orbital floor subperiosteal abscess secondary to an infected orbital implant (coronal [a] and axial [b] CT images).
may require a transcutaneous, eyelid-crease incision and dissection in a suborbicular plane to reach the superior periorbita (see Figure 7). Subperiosteal abscesses along the orbital roof typically require intraoperative placement of a small drain that can be removed 1 to 3 days postoperatively.

**Orbital Cellulitis Secondary to Fungal Sinusitis**

Mucormycosis or phycomycosis is an aggressive fungal infection that typically occurs in diabetics, immunocompromised individuals, or patients on chronic corticosteroid therapy. These invasive sinus infections may extend into the orbit or nasal cavity, causing a thrombosing vasculitis and tissue necrosis. Significant proptosis and/or an orbital apex syndrome are frequently present. Multidisciplinary support is essential. Biopsy of involved tissue in the nasopharynx by an otolaryngologist will demonstrate nonseptate branching hyphae that stain well with hematoxylin-eosin. These fungal organisms belong to the class Phycycomycetes, genus *Mucor* or *Rhizopus*. Resection of involved necrotic tissues with local and systemic administration of amphotericin B is the treatment of choice. Primary exenteration is reserved for patients with fulminant orbital involvement and little chance of globe salvage. The fungus *Aspergillus* can also present in immunocompromised individuals with acute, fulminant sino-orbital disease and clinical findings similar to mucormycosis. Histopathologic evaluation shows septate branching hyphae on Gomori methenamine-silver staining with angioinvasion and tissue necrosis. Management consists of radical surgical excision of involved tissue and administration of amphotericin B, flucytosine, and/or rifampin.

An increasingly recognized sinus disorder, allergic fungal sinusitis (AFS) or allergic aspergillosis sinusitis also occurs in immunocompetent patients with a history of atopic disease, nasal polyposis, and chronic sinusitis. It is estimated that up to 15% of patients with AFS have orbital findings including proptosis, ptosis, and diplopia. The diagnosis of AFS is based on laboratory studies, characteristic neuroimaging findings, and histopathology. Functional endoscopic sinus surgery with evacuation of the allergic mucin and aggressive aeration of the involved sinuses is followed by topical and systemic corticosteroid treatment. The role of immunotherapy has not been definitively established.

**Atypical Mycobacterial Infections**

Nontuberculous organisms (such as *Mycobacterium abscessus*, *M fortuitum*, and *M chelonae*) are an increasingly recognized cause of ocular, periorbital, and orbital infections. Atypical mycobacterial infections of the ocular adnexa typically present with a subacute onset of a chronic, draining minimally purulent wound or abscess. Induration of the involved area is often observed. These infections are associated with a clinical history of surgical (eg, blepharoplasty, dacryocystorhinostomy) or accidental penetrating trauma, prior corticosteroid therapy, and a retained foreign body. A heightened clinical suspicion in patients presenting with the aforementioned clinical characteristics is critical in order to guide initial management. Surgical debridement and foreign body removal is important therapeutically and also provides tissue for histopathologic evaluation. Infected wounds should be cultured on routine media and incubated separately at 30°C and 35°C for up to 2 weeks. Macrolide antibiotics (eg, clarithromycin) are often effective in the empirical treatment of localized soft tissue infections caused by *M chelonae* and *M abscessus* in the immunocompetent patient. Long-term antibiotic therapy should be guided by culture and sensitivity testing.

**Necrotizing Fasciitis**

Necrotizing fasciitis is a rare, severe bacterial infection that may involve the face and periorbital soft tissues. Diabetes, alcoholism, and recent surgical or accidental trauma are predisposing factors. Facial paresthesias including numbness and severe periorbital pain may accompany skin color changes, which typically progress from significant erythema to a dusky, blue-gray color and eventually a bullous dermatitis with signs of tissue necrosis. Management includes immediate initiation of broad-spectrum, intravenous antibiotic therapy. Group A *Streptococcus* is a well-recognized pathogen in this aggressive disease, although aerobic and anaerobic gram-positive and gram-negative organisms have also been identified in cases of necrotizing fasciitis. Prompt surgical debridement is required in most situations; however, well-delineated periorbital cases that respond rapidly to intravenous antibiotics may not necessitate aggressive tissue excision. All patients suspected of having necrotizing fasciitis should also be cared for by an infectious disease specialist and hospitalist or intensivist as rapid
system deterioration may occur, such as hypotension, renal failure, adult respiratory distress syndrome, and toxic-shock syndrome.

Methicillin-Resistant Gram-Positive Infections

Methicillin-resistant Staphylococcus aureus (MRSA) has long been recognized as a cause of severe nosocomial infections. Over the past decade, there has been a marked increase in the incidence of MRSA infections among prison inmates, athletic teams, military personnel, children in day care, intravenous drug users, male homosexuals, homeless persons, and Native Americans. More recently, MRSA infections have appeared on high school and university campuses in students with no history of hospitalization. Crowded living conditions are believed to be a risk factor for developing a community-associated MRSA (CA-MRSA) infection. While hospital-associated MRSA infections occur more commonly in patients 65 years or older, the CA-MRSA infections tend to appear in a much younger patient population, typically in the third and fourth decades.

CA-MRSA skin and soft tissue infections have a propensity to present as a fluctuant abscess with surrounding cellulitis. Pain and erythema are often out of proportion to the appearance of the cutaneous lesion. These infections may initially be mistaken for an insect bite. There are an increasing number of reports in the ophthalmic literature of CA-MRSA infections involving the ocular adnexa, and many oculofacial surgeons in the United States are encountering an increasing incidence of CA-MRSA infections in their practices (authors’ experience and personal communications). Preseptal cellulitis, eyelid abscess formation, and conjunctivitis are the most common ophthalmologic manifestations of CA-MRSA infections. Less common presentations include dacryocystitis, abscesses of the caruncle, orbital infections, endophthalmitis, panophthalmitis, blebitis, scleritis, and septic venous thrombosis. Vision loss from corneal ulceration and bilateral blindness from orbital cellulitis are reported causes of significant ocular morbidity from CA-MRSA. A growing concern is the increasing incidence of postoperative ocular and periorbital MRSA wound infections.

Hospital-associated and CA-MRSA infections are both resistant to methicillin and other β-lactam antibiotics (such as oxacillin and nafcillin). Whereas hospital strains are resistant to all antibiotics except vancomycin (a glycopeptide) and linezolid, CA-MRSA may be sensitive to trimethoprim (TMP)-sulfamethoxazole (SMX) (frequently used with rifampin), doxycycline, and clindamycin. Sulfur antibiotics should be administered with caution due to the incidence (~10%) of allergic reaction to this class of medications. Sulfur-containing medications should also be avoided in pregnancy and in infants. Unfortunately, inducible clindamycin resistance may result in clindamycin treatment failures despite sensitivity on standard susceptibility testing methods. A D-zone disk diffusion test should be requested if clindamycin is to be used.

Current-generation fluoroquinolones, such as levofloxacin, moxifloxacin, and gatifloxacin, have better eradication rates for S aureus and may be useful in some CA-MRSA infections. Concern about joint and cartilage toxicity has limited the use of fluoroquinolones in children. In addition, resistance to fluoroquinolones has risen dramatically due to overuse of these medications in many medical communities. Although resistance is also appearing to fourth-generation quinolones, this class of antibiotics may remain a second-line option in the treatment of serious infections.

Despite their broader antibiotic susceptibility profile, CA-MRSA infections can be quite severe, resulting in large soft tissue abscesses and necrotizing fasciitis. The mainstay of treatment for CA-MRSA soft tissue infections is surgical drainage. Failure to drain an abscess even with appropriate antibiotic therapy can lead to significant morbidity.

CA-MRSA skin and soft tissue infections have a high recurrence rate. Most individuals become colonized or infected from an external source. Skin surface and fomite colonization (eg, wrestling mats, shoulder pads) poses risks to patients, family members, health care providers, and other individuals who come in close physical contact with an infected patient. Frequent and appropriate hand hygiene is an important preventative measure. Alcohol-based hand disinfectants, particularly when paired with an antimicrobial soap that contains 0.3% triclosan, may be the most effective method to address MRSA colonization. Evolving resistance to topical biocides will continue to complicate efforts at prevention. Contact isolation measures are necessary for evaluating patients with known colonization with resistant organisms.

Future Horizons

The rising incidence of serious skin and soft tissue infections caused by multidrug-resistant pathogens poses significant challenges for future antibiotic treatment regimens. S aureus and Group A β-hemolytic streptococci have shown increasing resistance to macrolide antibiotics. The emergence of methicillin-resistant,
vancomycin-resistant, and vancomycin-intermediate susceptible community-associated and nosocomial gram-positive pathogens has created a demand for more effective therapeutic agents. Numerous antibacterial agents are in clinical development for the treatment of these virulent organisms (see Figure 5). Furthermore, available methods of susceptibility testing are evolving and definitions of microbial isolate susceptibility (eg, minimum inhibitory concentrations, MIC) are changing. In order to identify MRSA infections within hours rather than days as with traditional culture techniques, newer detection methods for MRSA have been developed.

Linezolid (Zyvox, Pfizer, New York, New York), a bacteriostatic oxazolidinone derivative, has a similar spectrum of coverage to that of vancomycin but can be administered orally unlike vancomycin, which requires long-term parenteral administration. It may be an appropriate alternative to vancomycin in patients who do not tolerate glycopeptides, have limited venous access, or have impaired renal function.

Daptomycin (Cubicin, Cubist Pharmaceuticals, Lexington, Massachusetts) is a cyclic lipopeptide that is rapidly bactericidal. It has received FDA approval for treatment of severe soft tissue infections (4 mg/kg/day). Daptomycin has shown some in vitro sensitivity to MRSA infections that are resistant to vancomycin. Unfortunately, resistance to daptomycin has been reported and in-disk diffusion testing may not be predictive of clinical outcome.

Antibiotic resistance is an inevitable consequence of antibiotic exposure and will continue to challenge clinicians despite the development of novel antibiotic therapies. Alternative therapies, including proteases and vaccines, are also being explored as options to more traditional antibiotics.

Conclusion

Infectious preseptal cellulitis and orbital cellulitis are relatively common entities. The comprehensive ophthalmologist will often be called upon to treat orbital inflammatory disease and should be able to differentiate between pre- and postseptal infectious disease. Numerous noninfectious causes of periorbital inflammation may mimic an infectious presentation. Both infectious and noninfectious disease processes may pose a serious risk to visual function and if inadequately treated can even lead to death. An understanding of the spectrum of signs and symptoms associated with periorbital infection and inflammation — along with an awareness of the appropriate laboratory work-up, imaging studies, medical management, and surgical intervention — can greatly decrease the morbidity associated with periorbital cellulitis. The increasing incidence of CA-MRSA infections involving the ocular adnexa, the emergence of other multidrug resistant pathogens, the growing number of available antibiotic therapies, and the constantly evolving picture of antibiotic resistance will require ophthalmologists to monitor bacterial susceptibility patterns in their local communities and to follow current antibiotic recommendations regarding treatment of these challenging infectious diseases.

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Clinicians’ Corner

Clinicians’ Corner provides additional viewpoints on the subject covered in this issue of Focal Points. Consultants have been invited by the Editorial Review Board to respond to questions posed by the Academy’s Practicing Ophthalmologists Advisory Committee for Education. While the advisory committee reviews the modules, consultants respond without reading the module or one another’s responses. – Ed.

1. What is your choice for antibiotic coverage in a 35-year-old patient who presents with orbital cellulitis and concomitant cellulitis?

Dr. Allen: I believe treatment of this patient is based on the polymicrobial etiology of the disease in this age group, with S pneumoniae, S aureus, H influenzae (becoming more rare with vaccination), and anaerobes being the main players. Therefore, a broad spectrum, intravenous antibiotic coverage would be appropriate. I continue to use ampicillin/sulbactam primarily. Rarely will I add metronidazole if cultures support its use or an anaerobic infection is suggested. For a patient who is penicillin-allergic, I would go with the mainstay of vancomycin and gentamicin. Also, the sinusitis should be treated with a nasal decongestant.

Dr. Duerksen: With an otherwise healthy patient, my first choice is intravenous Rocephin, 1 g IV q day. If they do not respond quickly—within 24 to 48 hours—I would consider changing to Levaquin, 750 mg IV q day. I usually recommend 5 days of IV therapy, followed by 7 to 10 days of the corresponding antibiotic by mouth. If the patient has only preseptal cellulitis, I would start with Keflex 500 mg qid. I note a trend toward more patients requiring Levaquin. Community-associated MRSA has become much more prevalent and should be suspected when a patient does not respond quickly to antibiotic management, especially pediatric patients. If the improvement is not rapid or the patient is not healthy, I would consult with infectious disease and ENT specialists, and I would think seriously about surgical biopsy.

2. Are there specific physical findings that suggest a fungal orbital cellulitis?

Dr. Allen: Fungal orbital cellulitis is basically due to fungal sinus disease. Fungal sinus disease is usually divided into four categories: chronic indolent (invasive), acute fulminant (invasive), chronic indolent (noninvasive) fungal ball, and allergic fungal sinusitis. Orbital cellulitis is
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associated with the acute fulminant disease, secondary to either mucormycosis or Aspergillus. This is a disease that almost uniformly occurs in immunocompromised patients. Therefore, any patient who is immunocompromised and presents with orbital cellulitis must be considered to have an acute fulminant fungal infection.

The clinical presentation of fungal orbital cellulitis may be very similar to bacterial orbital cellulitis. The clinician must have a heightened suspicion for fungal disease in immunocompromised patients, especially if the disease is developing rapidly. The “black eschar” found on the nasal mucosa is rare, in my experience, and its absence does not rule out mucormycosis. The physical finding that is most predictive in my experience is the virtually bloodless field during biopsy due to the obliteration of the blood vessels. Debridement should proceed to a bloody field.

Dr. Duerksen: Patients with fungal cellulitis are generally not healthy people; they don’t look healthy, often appearing “dusky” or with pallor. Metabolic acidosis is an underlying risk factor. They are patients with significant systemic disease such as diabetes, chronic obstructive pulmonary dysfunction, and autoimmune diseases. They are immune-compromised due to drugs (eg, prednisone, Embril) or disease (eg, HIV). They have significant sinusitis or pansinusitis. Their orbital cellulitis may not appear as “hot” or erythemic, but their extraocular muscle (EOM) palsy tends to be more advanced, with more significant proptosis, vision loss, and pupillary abnormalities upon presentation. They may have a full-blown orbital apex syndrome.

3. What features help differentiate orbital cellulitis from orbital pseudotumor?

Dr. Allen: What this question boils down to is “what is the difference between infectious versus noninfectious, nonspecific orbital inflammation?” I basically consider orbital inflammation to be infectious until proven otherwise, even more so in an immune-compromised patient. The clinical presentation of both types of patients can be very similar with respect to pain and ocular findings; however, infectious causes of orbital inflammation should have a recognizable etiology (eg, sinusitis, penetrating trauma, sepsis), and the physical findings should reflect an infectious cause—fever and elevated white blood cell count.

Imaging is probably most helpful in differentiating between the two. I prefer a CT scan of the orbits. In the absence of trauma or sepsis, orbital cellulitis will most likely be associated with sinusitis. In orbital pseudotumor, the sinuses should be clean, and the sclera, extraocular muscles (including tendons), and lacrimal gland may all or separately be inflamed.

Dr. Duerksen: Orbital cellulitis is usually associated with sinusitis. Orbital cellulitis and orbital pseudotumor patients both have pain and EOM movement restriction, but orbital cellulitis patients may feel sick in general, with symptoms having started with a “cold.” The presence of fever, erythemic chemosis, eyelid erythema and swelling, a history of trauma or dental work, and a left shift in the white count on CBC all suggest cellulitis. Consider checking thyroid studies and ACE level for sarcoid. CT scanning and MRI are essential, especially if an orbital pseudotumor is EOM or lacrimal gland centered. Sinusitis will point towards cellulitis. With evidence of trauma, do not forget about the possibility of a foreign body.

4. What kind of imaging do you request for patients in whom you suspect orbital cellulitis?

Dr. Allen: The primary imaging modality for patients with suspected orbital cellulitis is a CT scan of the sinuses and orbits, with axial and coronal cuts, with and without contrast. CT is less expensive and quicker than MRI. The speed at which the imaging is performed is preferred, especially in patients who may be in more pain in a supine position. Contrast is preferred, but not necessary—I would still prefer a CT scan without contrast over MRI with contrast in suspected orbital cellulitis. The main advantages of the CT are the spatial resolution and the visualization of the bone. This is most helpful if surgery is planned.

Today, plain films of the orbit really have no place, unless the physician is in an area with no CT scanner. In general, the availability of a radiologist or ophthalmologist who is able to reliably read plain films for orbital cellulitis is becoming less and less common.

I would use MRI only after a CT scan has been performed that shows no convincing abnormality. At this
point, orbital cellulitis would be less likely and a non-
infectious inflammatory etiology would be entertained. The one exception would be an organic foreign body. CT scans have been shown to be unreliable in detecting organic foreign bodies, while greater success has been shown with MRI.

I do not believe that orbital ultrasound is useful in patients with suspected orbital cellulitis. Although I am sure there are orbital ultrasonographers who may be able to diagnose orbital cellulitis as well as a CT, I believe it is a user-dependent modality, and one that I rarely use.

**Dr. Duerksen:** I obtain orbital, sinus, and brain CT scans with and without contrast, with both axial and coronal views. If it is not clear whether an abscess is present, then I will also get MRI studies. It is most important to know whether there is an abscess that needs to be drained and cultured. It is also important to know about the presence and extent of sinus disease, the status of the orbital bones, and whether or not brain involvement is present.

## 5. What are your sources for cultures in cases of orbital cellulitis?

**Dr. Allen:** Of course, if an abscess or sinus is surgically drained, that is the best source for a culture. Nasal cultures seem to be useful, but only if there is obtainable purulent discharge. Blood cultures are of a lower yield, but useful and likely required for medico-legal reasons. A lumbar puncture with culture of the cerebrospinal fluid would be performed only in cases of suspected concomitant meningitis. I believe that conjunctival cultures are completely worthless.

**Dr. Duerksen:** Culture sources are nasopharynx, blood, and conjunctiva. If there is any associated or suspected dacryocystitis, then culture the lacrimal drainage system (try irrigation and aspiration or pressure on lacrimal sac). Of course, any sinus or orbital abscess or biopsy should be cultured. Do not try a random needle aspiration of the orbit. If fungus is suspected, a surgical biopsy should be done immediately, probably with the help of ENT and neurosurgery colleagues. Look for an infection elsewhere in the body. For a child not responding as expected, consider a lumbar puncture.

## 6. Has the introduction of *Haemophilus influenzae* (*H flu*) vaccine changed the presentation and management of preseptal or orbital cellulitis in children?

**Dr. Allen:** The short answer is “yes, dramatically.” I think the review of a recent paper by McKinley et al would be a useful exercise for this question. The authors looked at all of the pediatric cases of orbital cellulitis associated with sinusitis that presented to Texas Children’s Hospital from 2001 to 2005. Interestingly, of the 38 cases identified, only one case grew *H influenzae*. The most common organisms isolated were *Staphylococcus* and *Streptococcus*. Of the *S aureus* cultures, 73% were methicillin-resistant (MRSA).

At this time, I continue to use ampicillin/sulbactam primarily in pediatric cases of orbital cellulitis; however, with this recent report, I will be more aware of the possibility of MRSA as the pathogen in these cases and will probably be more apt to obtain specimens for culture and/or change my antibiotic coverage in order to reflect the possibility of MRSA in cases that do not respond as expected.

**Dr. Duerksen:** I think that the vaccine has reduced the incidence of preseptal and orbital cellulitis in normal healthy children under the age of 5, at least judging from my practice. Even considering the vaccine, a young child with preseptal or orbital cellulitis may still have *H flu*; perhaps they never got the vaccine and should be worked-up accordingly, with prompt hospitalization and an infectious disease consultation. Their condition can deteriorate quickly and the risk of meningitis should not be forgotten. A search should be made for a source of an immune-compromised state. Again, a high level of suspicion for community-associated MRSA should be maintained. MRSA infections may be replacing *H flu* as the most common and worrisome infections in children.

## 7. What are your criteria for admitting patients who have preseptal or orbital cellulitis?

**Dr. Allen:** I rarely admit true preseptal cellulitis, which I define as cellulitis secondary to a known event (eg, trauma or stye) with no orbital signs (proptosis, motility deficit, or afferent pupillary defect). The only time I would admit a patient with preseptal cellulitis is if it were atypical (not responding appropriately to antibiotic
therapy or if there were necrotic tissue that might need to be debrided) or if the patient seemed to be unreliable. Necrotizing fasciitis is always in the back of my mind whenever I see a “bad” preseptal cellulitis. Also, preseptal cellulitis secondary to MRSA is becoming more and more common.

I always admit a patient with orbital cellulitis (defined as cellulitis with orbital signs) due to the need for intravenous antibiotic therapy. I am aware of reports of successful treatment of patients with orbital cellulitis with oral antibiotics and close follow-up. I personally do not think this is appropriate therapy.

**Dr. Duerksen:** I would admit children with preseptal and orbital cellulitis, for intravenous therapy and for proper continuous care by a pediatrician and for appropriate consultations (eg, pediatric infectious diseases, ENT, and possibly neurosurgery). I would also admit patients who are significantly immune-compromised. The immediate need for surgery because of an abscess or sinus disease is also a reason to admit. A patient with any hint of fungal disease would be admitted, in order to expedite consultations and surgery if the patient’s progress dictates. I would admit a patient if he or she were unable to have IV treatment as an outpatient, whether due to logistics or reliability.

8. How often is antecedent trauma or a bug bite, as described by many patients, the actual cause of preseptal cellulitis?

**Dr. Allen:** I always try to tease out an etiology for preseptal cellulitis. The difficulty in this is that every patient seems to be able to pinpoint an antecedent event. If I am unable to find a point of entry or convincing etiology, then I entertain the thought of an orbital mechanism. Usually that would necessitate imaging, preferably a CT scan.

**Dr. Duerksen:** Although in Arizona we do have a number if suspects—kissing bugs, scorpions, and spiders to name a few—I think that the majority of preseptal cellulitis is related to sinus disease or nasolacrimal duct obstruction. Of course, it is still very important to ask about trauma or bites. A complete history is important for appropriate care. In my practice, the “red herring” of a history of a bug bite or trauma more commonly occurs when evaluating a person with a noninfectious orbital inflammatory process.

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