STRATEGIES FOR THE INITIAL MANAGEMENT OF ACUTE PRESEPTAL AND ORBITAL CELLULITIS*

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INTRODUCTION

PRESEPTAL CELLULITIS AND ORBITAL CELLULITIS ARE POTENTIALLY SEVERE, life threatening infections of the ocular adnexa and orbital tissue. Preseptal cellulitis is infection of the soft tissue of the eyelids and periocular region anterior to the orbital septum. Orbital cellulitis is infection of the soft tissue within the orbit posterior to the orbital septum. We present an algorithm for the management of these entities based on our clinical experiences and a review of more than 300 cases of preseptal and orbital cellulitis at the Cullen Eye Institute, Texas Children's Hospital, and Ben Taub General Hospital.

RESULTS

The distinctive features of preseptal cellulitis are hyperemia of the skin and distention of the eyelids *without* signs of orbital congestion. The principal entites are posttraumatic suppurative cellulitis and cellulitis secondary to skin infections, both caused predominantly by *Staphylococcus aureus* and *Streptococcus pyogenes*; and nonsuppurative preseptal cellulitis in children caused by *Haemophilus influenzae* type B and *Streptococus pneumoniae*. The principal risk factors are trauma, skin infection, and age less than 6 years.

The distinctive features of orbital cellulitis are hyperemia of the skin, distention of the eyelids, conjunctival inflammation, orbital pain, proptosis and limitation of ocular motility. The principal entities are posttraumatic and postsurgical orbital cellulitis, caused predominantly by *S aureus*; orbital cellulitis secondary to sinusitis, caused by *S pneumoniae*, other

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streptococci, *S aureus*, *H influenzae*, and non-sporeforming anaerobes; orbital cellulitis secondary to other infections of the face and adnexa; and mucormycosis. The principal risk factors are trauma, surgery, sinusitis, diabetes mellitus, and immunosuppression.

The initial management of unilateral, acutely swollen and inflamed eyelids is based on the conventional steps in problem solving for ocular infectious diseases: (1) assimilate the clinical findings, (2) select the most distinctive signs, (3) generate a differential diagnosis based on the distinctive signs, (4) consider the other findings, (5) perform the proper laboratory studies, and (6) initiate therapy. The first objective is to distinguish preseptal cellulitis from orbital cellulitis (Fig 1). If inflammation and distention of the eyelids are present *without* proptosis and orbital congestion, the presumed diagnosis is preseptal cellulitis. If the conjunctival inflammation, orbital pain, proptosis, and limitation of ocular motility are additional findings, acute microbial orbital cellulitis should be suspected and a computed tomography (CT) scan obtained (Fig 1).

PRESEPTAL CELLULITIS

If the clinical signs suggest preseptal cellulitis, the next step is to search for two principal risk factors: (1) trauma and (2) infection of the skin of the eyelids or face (Fig 2).

Posttraumatic Preseptal Cellulitis

Infection follows lacerations and puncture wounds but may occur following blunt trauma without an apparent entry site. Subcutaneous edema and

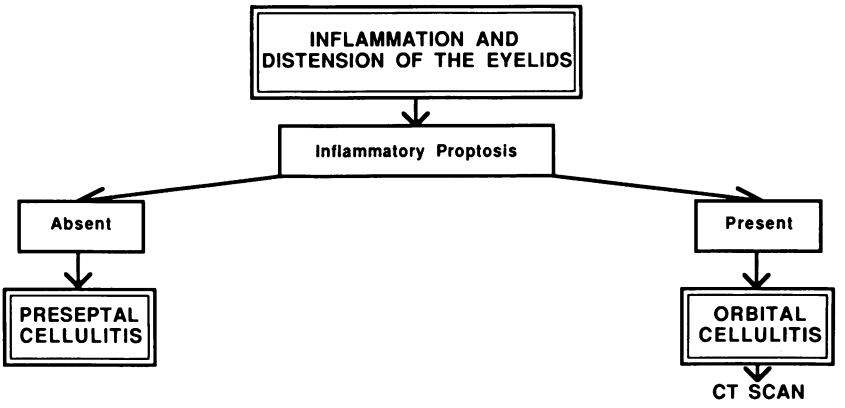

FIGURE 1
Scheme for initial distinction and management of acute preseptal and orbital cellulitis.

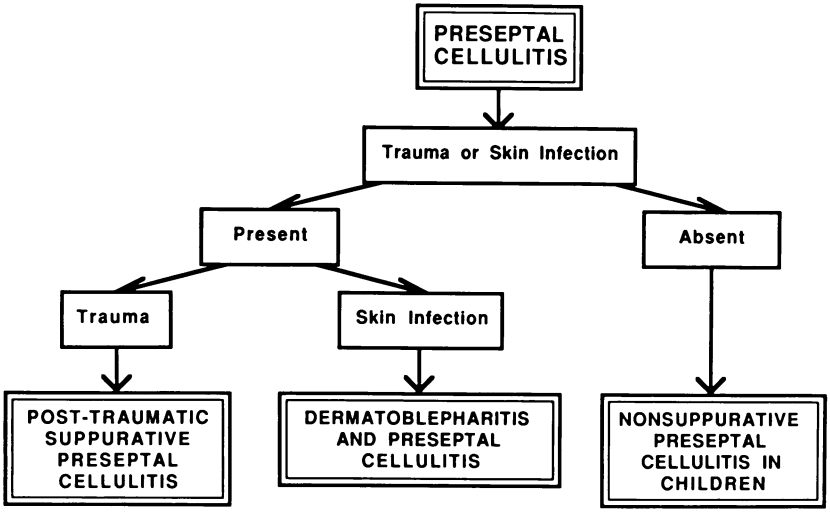

FIGURE 2
Scheme for recognition of the principal entities in acute preseptal cellulitis. Importance of trauma and skin infection as risk factors.

Purulent material should be collected with a sterile syringe and needle and inoculated directly to blood and chocolate agar and to an anaerobic orbital rim. There is edema of the upper lid which may extend into the thick subcutaneous and submuscular layers of the eyebrow and forehead. The skin is taut and inflamed, although some degree of fluctuation can usually be detected. Lymphedema may produce swelling of the contralateral upper and lower lids. In severe cases, the upper lid cannot be opened to examine the globe. Pus may drain spontaneously from the wound or conjunctiva. Despite the severity of the adnexal signs, the globe is not displaced and ocular motility is normal.

The principal causes of posttraumatic cellulitis are *S aureus* and *S pyogenes*. Anaerobic, non-sporeforming bacteria, such as *Peptococcus*, *Peptostreptococcus* and *Bacteroides*, are associated with infections following human or animal bites. Anaerobic infection is suggested by foul-smelling discharge, necrotic tissue, gas in the tissue, or severe toxemia.

Treatment is incision of the skin, drainage of the suppurative material, and initiation of intravenous antibiotics based on the gram stain of the material. A CT scan should be obtained if the globe cannot be adequately examined or there is likelihood of injury to the globe or penetration of the orbital septum. Tetanus anaphylaxis should be administered according to current guidelines.

hematoma within the preseptal space predispose to abscess formation. The clinical signs are more pronounced following injury along the superior medium, ideally brucella agar to be incubated in a GasPak bag system. Thin smears should be prepared for gram stain by spreading a drop of the material over the surface of a glass slide and fixing the slide in 95% methyl alcohol for 5 minutes.

Unless otherwise directed by the gram stain, the preferred initial therapy is intravenous nafcillin. We prefer nafcillin because it has more intrinsic activity against both staphylococci and streptococci than methicillin. Some pediatricians prefer to use oxacillin in neonates because nafcillin is excreted primarily by the liver. A first generation cephalosporin antibiotic, such as cefazolin, may be used for patients with a history of penicillin allergy other than severe anaphylaxis, for which vancomycin is the drug of choice. Penicillin G, or an alternate agent such as chloramphenicol or cefuroxime, should be added for infections following human or animal bites, or suspected anaerobic infections. Oral cloxacillin or cephalexin is the preferred initial antibiotic in mild posttraumatic preseptal cellulitis.

Dermatoblepharitis and Preseptal Cellulitis

Profound inflammation and edema of the preseptal space may accompany infections of the skin of the face and eyelids. The etiology can generally be recognized by the type and distribution of the skin lesions.

Impetigo is pyoderma due to *S aureus* or group A *S pyogenes*. Infection is most common in children under age 6 years and in conditions of poor hygiene. Impetigo may complicate preexisting skin lesions in varicella, herpes simplex, or eczema.

The exposed areas of the face and extremities are most commonly involved. Small, red macules initially develop and rapidly progress to thin-walled, serous vesicles surrounded by a narrow areola of erythema. Involvement of the ocular adnexa produces marked erythema of the lids and edema of the preseptal spaces. The vesicles rupture to release serous, purulent material which dries over the denuded areas to form a characteristic thick, golden yellow crust. Satellite lesions may develop by autoinoculation. Regional lymphadenopathy is common. There may be mild temperature elevation and leukocytosis. Although marked erythema is more typical of streptococcal infection, there is no clinical feature which reliably distinguishes staphylococcal from streptococcal impetigo.

Laboratory investigation should include a smear of vesicle fluid or the surface of denuded skin for gram stain and for inoculation onto a blood and a chocolate agar plate. Moistening the swab with a nutrient medium such as trypticase soy broth may enhance the recovery of organisms.

Treatment consists of systemic antibiotics, thorough scrubbing of the involved areas with soap and water two or three times daily, and a topical antibiotic ointment applied to the skin lesions. Intravenous nafcillin should be administered in severe cases. The preferred antibiotic in mild infections is oral cloxacillin or cephalexin. Systemic therapy should be continued for at least 10 days.

An exception to the algorithm is erysipelas, a rare form of preseptal cellulitis caused by *S pyogenes* group A. Infection presumably occurs by invasion of the organism to the subcutaneous tissue through an abrasion or inflammatory ulceration of the skin. The process begins as an elevated, erythematous plaque which gradually evolves to sharply demarcated, bright red or crimson erythema and marked edema of the eyelids accompanied by pain and tenderness. In distinction to other forms of preseptal cellulitis, inflammation typically involves the orbit, presumably by diffusion or toxins, to produce chemosis, mild proptosis, and limitation of motion. Vision usually remains normal. High temperature (103° to 104°F), leukocytosis, chills, and malaise are common.

Diagnosis of erysipelas is aided by the typical skin lesions and signs of preseptal cellulitis combined with mild orbital congestion. A CT scan should be obtained. Cultures of material swabbed from the skin of the lids and conjunctiva rarely yield streptococci. Needle aspiration from the lids or orbit is contraindicated because of the possibility of spread of the infection and injury to other structures. Blood cultures should be obtained. The preferred initial treatment is intravenous penicillin G for 48 to 72 hours or until there are definite signs of improvement, followed by oral penicillin for 5 to 7 days.

Nonsuppurative Preseptal Cellulitis in Children

In the absence of trauma or skin infection, the determinant of management is the age of the patient. Preseptal cellulitis without injury or dermatoblepharitis in children under age 6 years is caused almost exclusively by *H influenzae* type B and *S pneumoniae*.[1] Although the exact pathogenesis has not been defined, cellulitis presumably develops by spread of *H influenzae* or *S pneumoniae* from the upper respiratory tract, sinuses, or middle ear to the preseptal space via the vascular or lymphatic systems.

Serious *H influenzae* type B infections occur most commonly between ages 6 months and 2 years. Before 6 months, infants are partially protected by passively acquired maternal antibody.[2] Natural antibodies to the capsular polysaccharide of *H influenzae* type B develop between ages 18 and 24 months, presumably by colonization with cross-reactive strains of other bacteria.[3]

H influenzae preseptal cellulitis typically begins with mild upper respi-

ratory infection, fever, leukocytosis, and unilateral hyperemia and edema of the soft tissue of the eyelids. Sharply demarcated, dark purple discoloration of the skin of the eyelids and adnexal region is characteristic and similar to *H influenzae* buccal cellulitis. Mild conjunctival hyperemia and chemosis may be present. Vision is normal and signs of orbital congestion are typically absent.

Approximately one-half of the children with *H influenzae* and *S pneumoniae* preseptal cellulitis have antecedent or concurrent upper respiratory infection.[1,4,5] Plain films may suggest sinusitis, however, these studies are difficult to interpret in this age group. Bacteremia is common.

Children should be hospitalized because of the potential rapid progression of the infection and the risk of consecutive meningitis. Swab cultures should be obtained from the ipsilateral and contralateral conjunctiva and inoculated to blood and chocolate agar plates. Nasopharyngeal cultures are difficult to interpret because of the normal indigenous flora. Blood cultures should be obtained. Irrigation and aspiration of the subcutaneous tissue or sinuses are not indicated. Lumbar puncture should be performed in young children with irritability, high fever, and extreme leukocytosis.

The selection of initial antibiotics is based on the likelihood of *H influenzae* infection and the increasingly high incidence of beta lactamase-producing type B strains. Although intravenous ampicillin and chloramphenicol are effective, we prefer cefuroxime, a second generation cephalosporin.[1,6,7] Cefuroxime is highly active in vitro against *H influenzae*, including beta-lactamase-producing strains, *S pneumoniae*, other streptococci, and *S aureus*. In addition, cefuroxime is the only second generation cephalosporin with consistent penetration into the cerebrospinal fluid. Mild infections in older children may be treated initially with oral cefuroxime axetil, trimethoprim-sulfamethoxasole, or amoxicillin-clavulanate.

Preseptal cellulitis in older children and adults is extremely rare without trauma or skin infections. The presumed mechanism is spread of organisms from the sinuses, upper respiratory tract, or middle ear by the venous channels, principally *S pneumoniae*, other streptococci, and *S aureus*. The typical findings of *H influenzae* preseptal cellulitis as noted in children has not been documented in adults.

ORBITAL CELLULITIS

Acutely swollen, inflamed eyelids accompanied by inflammatory proptosis and limitation of motion should be managed as microbial orbital cellulitis pending other evaluation (Fig 1). The first step is to distinguish exogenous infection, caused by accidental trauma or surgery, from endogenous infections, caused primarily by bacterial sinusitis (Fig 3).

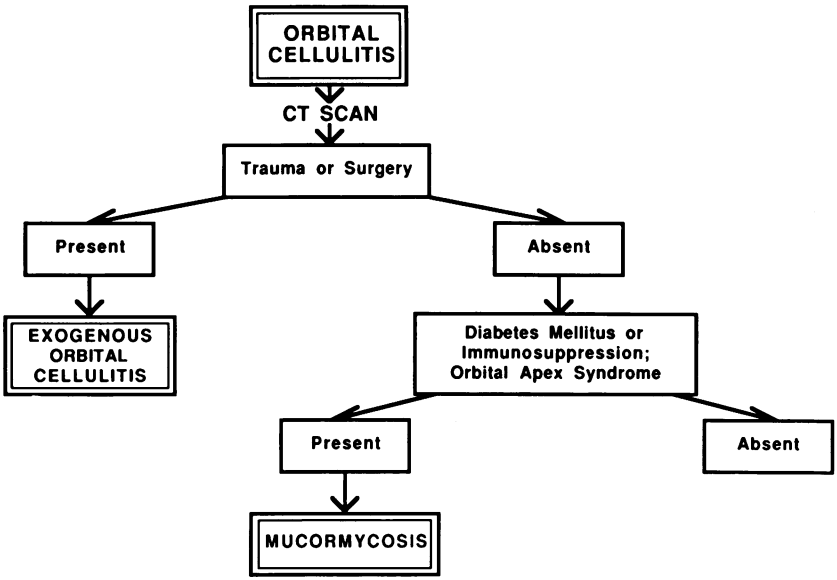

FIGURE 3
Scheme for initial distinction of principal entities in acute orbital cellulitis. Importance of trauma, surgery, and diabetes mellitus or immunosuppression as risk factors.

High resolution CT scans are essential in the initial assessment and management of all forms of suspected orbital cellulitis. CT scans should include axial and coronal views, although the latter require hyperextension or hyperflexion of the head which are difficult to maintain in acutely ill and uncomfortable children. Axial scans should include low narrow cuts of the frontal lobes to rule out abscess formation. Coronal cuts are more likely to identify subperiosteal abscesses of the orbital roof and floor and intraorbital abscesses. Intravenous contrast medium is generally not required. The value of magnetic resonance imaging (MRI) in orbital cellulitis has not been fully established. Plain films of the orbit and sinuses generally do not provide additional important information, particularly in children. Orbital echography is not as specific and accurate as CT scan in defining the severity of cellulitis and sinusitis or identifying a subperiosteal or orbital abscess, particularly in the posterior orbit.[5]

Posttraumatic Orbital Cellulitis

Posttraumatic orbital cellulitis may follow any injury that penetrates the orbital septum. Typical signs usually appear within 48 hours to 72 hours but may be delayed for several months if there is a retained foreign body. The

injury may be judged trivial by the patient, and edema of the skin or conjunctiva may hide the wound. Hematoma of the lids or orbit may prevent early recognition of signs of infection. Severe stab or gunshot may also mask infection by extensive hemorrhage and edema of the orbit. Orbital cellulitis following orbital roof fracture and frontal sinusitis is rare.[8] Micro-organisms may be inoculated by the injurious material or enter the open wound from the indigenous microflora of the skin or adjacent structures. The most common cause is *S aureus*. Mixed and anaerobic infections may occur.

Patients should be hospitalized. Echography may be helpful in locating an orbital foreign body. Drainage material from the wound should be smeared for gram stain and inoculated to aerobic and anaerobic media. Transcutaneous aspiration of material from the orbit is contraindicated. Concurrent suppuration of the preseptal space should be incised, drained, and the material smeared and cultured. Blood cultures should be obtained.

Unless otherwise directed by the gram stain, the preferred initial treatment is intravenous nafcillin and tobramycin. Penicillin G or chloramphenicol should be added if clinical signs or microbiological studies suggest anaerobic infection. Although large, protruding foreign objects should be removed promptly, exploration for foreign material embedded deeply within the orbit should be deferred for 5 to 7 days of intravenous antibiotics. In the absence of a retained foreign body, surgical exploration and drainage of the orbit are reserved for patients who fail to improve following 48 to 72 hours of antibiotic therapy, worsen after a period of initial improvement, or develop a discrete intraorbital abscess.

Postsurgical Orbital Cellulitis

Orbital cellulitis is a rare complication of intraorbital surgery. Infection may also occur by direct extension of micro-organisms in postoperative endophthalmitis. The most common cause is *S aureus*. Mixed and anaerobic infections occur.

Signs of infection may not appear until the second or third postoperative day and may be difficult to distinguish from orbital congestion caused by the surgical procedure, hematoma, or reaction to foreign material. Fever, orbital pain, and pronounced leukocytosis may develop.

Microbiologic investigation is difficult because of the frequent absence of external drainage. Blind aspiration from the orbit is contraindicated. Purulent discharge should be smeared for gram stain and inoculated to aerobic and anaerobic media. Blood cultures should be obtained.

Intravenous nafcillin and tobramycin are the preferred agents unless otherwise directed by the gram stain or if purulent material cannot be

obtained. Penicillin G or chloramphenicol should be added if there is clinical or microbiologic suggestion of anaerobic infection. Other guidelines for management are similar to posttraumatic orbital cellulitis.

Mucormycosis

In suspected orbital cellulitis without antecedent trauma or surgery, the first objective is to eliminate the possibility of mucormycosis (Fig 3). The most common risk factors are diabetic ketoacidosis, other forms of metabolic acidosis, and immunosuppression secondary to disease or therapy. Mucormycosis has also occurred in mild or unrecognized diabetes.

The initial symptoms are unilateral headache, orbital pain, fever, and rhinorrhea. Blurred vision may precede other nerve involvement. Lid edema, proptosis, internal and external ophthalmoplegia, corneal anesthesia, and anesthesia of the ophthalmic and maxillary division of the trigeminal nerve develop within 1 to 7 days following the initial symptoms. Progressive loss of consciousness is typical and may be unrelated to the degree of metabolic acidosis or other predisposing factors. Ipsilateral facial weakness due to intracranial involvement of nerve VII distinguishes the disease from other forms of cellulitis and inflammatory proptosis. Other cranial nerve palsies and contralateral hemiparesis follow. Ecchymosis and necrosis of the ocular adnexal tissue results from the diffuse ischemic necrosis. Infection of the nasal mucosa produces dark, gangrenous lesions frequently accompanied by perforation of the nasal septum and necrosis of the turbinates. There may also be ulceration of the hard and soft palate. Inflammation and perforation of the ipsilateral eardrum have been noted. Ipsilateral maxillary and ethmoidal sinusitis typically develop. There is profound leukocytosis, usually above 20,000/mm.

Inflammatory proptosis, accompanied by the orbital apex syndrome (II, III, IV, V-1, V-2, and VI palsy), altered consciousness, and tissue necrosis requires immediate investigation and treatment for presumed mucormycosis. Otorhinolaryngological consultation should be obtained. A biopsy or smear should be obtained from any necrotic area of the skin, nasal mucous, or palate. If visible lesions are not present, biopsy of the nasopharynx and middle meatus and irrigation of the maxillary sinus should be performed. Material should be smeared for gram, calcoflour white, and other special stains; inoculated to blood agar, Sabouraud's agar, brain heart infusion broth and an anaerobic medium; and fixed in 10% formalin for histologic sections. Calcoflour white is a new, rapid, chemofluorescent stain which has an affinity for the chitin in the cell wall of fungi.[9] The stain can be used for either direct smears of clinical material or fixed sections. Genera of *Phycomycetes* grow well between 25° and 37°C and generally appear on solid media within 2 to 5 days.

In serious infections with typical clinical features, intravenous amphotericin B should be initiated prior to laboratory confirmation of infection. Other treatment includes control of metabolic acidosis, elimination of other predisposing factors, and debridement of necrotic tissue.

Orbital Cellulitis Secondary to Sinusitis

If risk factors and clinical features do not suggest mucormycosis, the next consideration in the algorithm is orbital cellulitis secondary to sinusitis (Fig 4). Onset is characterized by headache, fever, lid edema, and rhinorrhea. Orbital pain and tenderness of the lids develop rapidly. Purulent nasal discharge is not a consistent feature. Progression of infection is rapid and produces dark, red coloration of the eyelids and signs of orbital congestion. Fever (102° to 104°F) and leukocytosis (> 15,000 white blood cells [WBC]/mm) follow. Vision is usually normal during the early stages but may be difficult to assess in the presence of lid edema, proptosis, and prostration.

The principal causes are the major sinus pathogens: *S pneumoniae*, other streptococci, *S aureus*, *H influenzae*, and non-sporeforming anaerobes.[10,11] Anaerobes implicated in sinusitis and orbital cellulitis include *Peptostrep-*

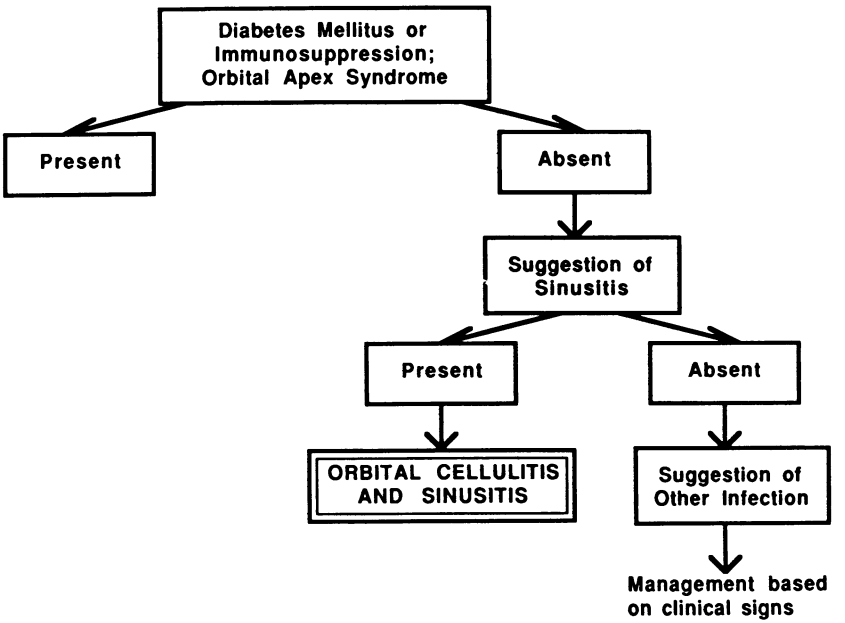

FIGURE 4
Scheme for distinction of orbital cellulitis and sinusitis.

tococcus, *Veillonella*, *Bacteroides*, *Fusobacterium*, and *Eubacterium*. Polymicrobial infections may occur. There is no clinical feature to distinguish the responsible organism within the various age groups or type of sinusitis. *S pneumoniae* and *H influenzae* are the most common pathogens in young children.

Subperiosteal abscesses develop by spread of organisms to the subperiosteal space by natural foramina, dehiscenses, or veins or by extension of purulent material directly through the thin, bony wall. The most common site is the medial wall of the orbit, presumably due to the direct passage from the ethmoidal sinus through the lamina papyracea. Abscesses may also develop in the superior and inferior orbital walls from the extension of infection from the maxillary or frontal sinus or dissection of purulent material from the initial site along the medial wall. Subperiosteal abscesses cause increased intraorbital pressure, thereby increasing the degree of proptosis and limitation of motion and enhancing the likelihood of loss of vision by direct pressure on the optic nerve. Risk factors for development of periosteal abscess have not been identified. Staphylococci and streptococci are isolated most often from subperiosteal material.[12,13]

Intraorbital abscesses presumably develop from organization of purulent material within the orbit or rupture of a subperiosteal abscess into the orbit. Orbital abscesses also cause increased intraorbital pressure which enhances the likelihood of damage to the optic nerve and other intraorbital structures.

Blood cultures should be obtained prior to administration of antibiotics but are usually negative. Random cultures of the conjunctiva and nasopharynx are not helpful. Purulent material from the nose should be collected by calcium alginate or cotton swab, smeared for gram stain, and inoculated to aerobic and anaerobic media. In maxillary sinusitis, many otolaryngologists prefer to aspirate material by direct puncture through the medial wall of the antrum from below the inferior turbinate. Needle aspiration of the orbit is contraindicated.

The preferred initial antibiotics are intravenous nafcillin and chloramphenicol. Cefazolin should be substituted for nafcillin in patients with a history of mild penicillin allergy. Vancomycin is preferred in individuals with a history of penicillin anaphylaxis. Although some pediatricians recommend initial management by only a second or third generation cephalosporin, such as intravenous cefuroxime or ceftriaxone, the efficacy of these agents in orbital cellulitis in all age groups has not been fully established. Infection by aerobic gram-negative bacilli other than *H influenzae* is rare and the addition of an aminoglycoside antibiotic, such as tobramycin or gentamicin, is unnecessary prior to obtaining the results of

laboratory investigations and assessing the clinical response to clinical therapy. Although limited studies have compared the ability of certain antibiotics to concentrate in infected sinus tissue, the pharmacokinetics of antimicrobial agents in sinusitis and orbital cellulitis have not been adequately defined.

Orbital periosteal elevation detected by CT scanning suggests the possibility of a subperiosteal abscess. As a subperiosteal abscess cannot be distinguished from sterile effusion or granulation tissue by CT scan or echography,[14,15] the decision for surgical drainage should be based on the severity of the clinical signs and the response to initial therapy. Several authors have noted periosteal elevation or "subperiosteal abscess" to resolve on medical therapy without surgery[8,14-17] and drainage of periosteal elevation to yield only sterile fluid or granulation tissue.[8,14,15] Subperiosteal hematoma may also simulate abscess formation.[18] The value of MRI in distinguishing suppurative from nonsuppurative or noninfectious periosteal elevation has not been determined.

If periosteal elevation is detected initially and the infection is severe, particularly with reduction in visual acuity, afferent pupillary defect, or loss of ocular motility, immediate surgical drainage of the subperiosteal material is indicated. The anatomical location of the periosteal elevation and the involved sinuses determine the surgical approach and the requirement for concurrent drainage of the sinuses. Purulent material from the subperiosteal space and sinuses should be aspirated into a sterile syringe for inoculation to aerobic and anaerobic media. Thin films of material should be prepared for gram stain, although these are often difficult to interpret and may not demonstrate the responsible organism(s).

If subperiosteal elevation is detected and the initial infection is mild, with normal visual acuity, minimal orbital congestion, and alert mental status, surgical exploration may be deferred and the clinical signs followed carefully. If the condition fails to improve following 48 to 72 hours of intravenous antibiotic therapy or worsens at any time, CT scans should be repeated and surgical drainage of the involved area and sinuses should be performed promptly.

Development of a discrete intraorbital abscess is rare. The specificity and validity of CT scanning, MRI, and orbital echography for detection of intraorbital abscess have not been fully defined. If studies suggest accumulation of purulent material within the orbit, surgical drainage should be performed unless the clinical signs are mild or the patient is improving rapidly. Guidelines for additional management are similar to subperiosteal abscess.

In the absence of orbital periosteal elevation or density within the orbit,

the decision to explore and drain the infected sinuses should be made by the otorhinolaryngologist. Surgery is based on the age of the patient, severity of the ocular signs, and extent of sinusitis as judged by CT scans. The sinuses should be drained in any patient who fails to improve after 48 to 72 hours of antibiotic therapy or worsens during the course of treatment. Drainage material should be obtained for aerobic and anaerobic cultures.

Orbital Cellulitis Secondary to Other Infections

Consecutive orbital cellulitis is a rare complication of other infections of the face and adnexa, including acute dacryocystitis,[19] osteomyelitis of the orbital bones, phlebitis of facial veins,[8] and dental infections. Acute dacryocystitis is caused primarily by *S aureus*, *S pneumoniae*, *S pyogenes*, and *H influenzae*. Maxillary sinusitis secondary to dental infections is caused by a variety of micro-organisms comprising the indigenous microflora of the mouth, including anaerobes. *S aureus* and *S pyogenes* are the principal causes of soft tissue infections of the eyelids and skin of the face. Microbiological investigation and treatment are generally directed by the type and severity of the primary infection. Blood cultures should be obtained. Selection of antibiotics and principles of management follow guidelines for other types of orbital cellulitis. Nafcillin is the preferred initial treatment for infection secondary to dacryocystitis. Intravenous nafcillin and chloramphenicol should be initiated in suspected odontogenic infections or osteomyelitis of the orbital bones.

DISCUSSION

We have constructed an algorithm for the management of acute preseptal and orbital cellulitis based on the distinctive signs, risk factors, and likely responsible organisms. Of note, the principal entities in both preseptal and orbital cellulitis can be distinguished by two routes of inoculation: exogenous and endogenous (Tables I and II). Exogenous infections are caused predominantly by indigenous microflora of the skin and adnexa, *S aureus* and *S pyogenes*. Although other aerobic and anaerobic bacteria may occasionally be involved, the strategy for initial management of exogenous preseptal and orbital cellulitis is to use a beta-lactam antibiotic resistant to beta-lactamase activity. We prefer intravenous nafcillin for serious infections and oral cloxacillin for mild posttraumatic preseptal cellulitis and dermatoblepharitis and preseptal cellulitis. In exogenous orbital cellulitis, the preferred initial therapy is intravenous nafcillin and tobramycin unless otherwise directed by the gram stain. A first generation cephalosporin, such as cefazolin, should be substituted in patients with mild allergy to penicillin. Vancomycin remains the alternate drug of choice in patients

TABLE I: PRINCIPAL ENTITIES IN PRESEPTAL CELLULITIS

ROUTE	ENTITY	ETIOLOGY	INITIAL THERAPY
Exogenous	Posttraumatic Secondary to dermato-blepharitis	*Staphylococcus aureus* *Staphylococcus pyogenes*	Nafcillin
Endogenous	Nonsuppurative in children	*Haemophilus influenzae* *Streptococcus pneumoniae*	Cefuroxime or ampicillin and chloramphenicol

TABLE II: PRINCIPAL ENTITIES IN ORBITAL CELLULITIS

ROUTE	ENTITY	ETIOLOGY	INITIAL THERAPY
Exogenous	Posttraumatic Postsurgical	*Staphylococcus aureus*	Nafcillin and tobramycin
Endogenous	Secondary to sinusitis	*Streptococcus pneumoniae* Other streptococci *Staphylococcus aureus* *Haemophilus influenzae* Non-sporeforming anaerobes	Nafcillin and chloramphenicol

with history of penicillin anaphylaxis.

In the two principal forms of endogenous preseptal and orbital cellulitis, nonsuppurative preseptal cellulitis in children and orbital cellulitis secondary to sinusitis, the presumed pathogenesis is spread of micro-organisms from the nasopharynx or sinus to the tissues by either vascular or lymphatic channels. The predominant responsible organisms are the indigenous microflora of the nasopharynx and sinuses, *H influenzae* and S *pneumoniae*. Treatment must consider the frequency and probability of beta-lactamase-producing strains of *H influenzae*. Although others have suggested the use of a third generation cephalosporin, such as cefotaxime or ceftriaxone, for initial therapy of orbital cellulitis secondary to sinusitis, we prefer intravenous nafcillin and chloramphenicol. The role of the newer beta-lactam and fluoroquinolone antibiotics has not been adequately defined.

We propose that the initial management of acute preseptal and orbital cellulitis is simplified by recognition of the distinctive signs, principal risk factors, and most likely responsible organisms. Proper management of these entities should prevent loss of vision and life-threatening intracranial complications and sepsis.

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DISCUSSION

DR ROBERT P. BURNS. Doctor Jones has given us a road map and a recipe. The road map is in the form of an algorithm for stratified problem solving in cases of preseptal and orbital cellulitis, and the recipe is the text of the entire article, proceeding critically from point to point in various clinical settings. I appreciate his sending his text in time for review, and so do our residents.

Doctor Jones has an outstanding ability to logically clarify complicated cases, and the present report is further evidence of his skill. His modern microbiologic and pharmacologic competence are evident.

It must never be forgotten that preseptal and orbital cellulitis are potentially lethal diseases. Casey Wood's *American Encyclopedia of Ophthalmology*, published in 1919, lists many cases of orbital cellulitis that ended fatally from septicemia

or meningitis. I investigated this myself as a resident 30 years ago when I became dissatisfied with the often negative cultures and slow response to therapy in these cases, so I reviewed the chart with these diagnoses from the early 1930s at the Columbia-Presbyterian Eye Institute. In those pre-sulfa days, Casey Wood was right—this disease could kill.

However, we must progress to another era, and in these modern days, we have to remember the cost of therapy. I have collected the usual charges, according to the 1987 contract for the University of Missouri Hospital, for what the hospital pays for drugs in 1-day dosage. This does not include the mark-up fee for dispensing the drug, or giving it intravenously to the patient, or monitoring the blood level. The price of antibiotic drugs may vary from the wholesale price of $81.00 per day for intravenous vancomycin, down to a rather modest charge of $5.40 per day for oral erythromycin.

Sometimes, physicians who are not in constant use of modern antibiotics, may be somewhat bewildered by the names of all these drugs. Therefore, I have included a quotation from "Drug Intelligence and Clinical Pharmacology," as a poem entitled, "Cephawonderful." This is authored by Maurice A. Kibel, of Cape Town, South Africa and John P. Jameson of Big Rapids, Michigan.

Fools Guide to Cephalosporins

Do not speak to us of gent or ampicillin
Of Bactrim or the paltry macrolides.
At the risk of being borin'
We give praise to ceph'losporin.
Just listen—we shall be your willing guides.

There are Velosef and Keflex, yes, and Kefzol,
Cephalexin, cephalothin, cephradine.
They're the oldest generation
Very food for inflammation
  Of the orbit, bladder, bowel, and the spleen.

They all work against the golden Staph'lococcus,
  Cephalothin, Cephradine, and all the rest.
But the dreaded Kelbsiella
Is a much more awkward fella
So a different generation would be best.

The second generation ceph'losporins—
Cefuroxime, cefamandole, cefaclor—
Hemo-file-us influenzee
Won't put them in a frenzy.
Beta-lactamase has got to lose the war.

Cefuroxime, cefamandole, cefotan,
As broad a spectrum as you'll ever see—

But when micro lab has phoned us
"Bout a slimy Pseudomonas,"
It is time for generation number three.

Ceph, ceph, ceph, ceph,
Let the voices sing!
Ceph, ceph, ceph, ceph
Will cure most anthing!

I recommend Doctor Jones' road map and recipe to you for keeping conveniently at hand when these severe, vision and life-threatening, uncommon but not rare, cases are seen.

DR FRANK W. NEWELL. We should be grateful to Doctor Jones for pointing out a logical system of managing these difficult infections.

Some years ago at the University of Chicago we reviewed our experience with preseptal and orbital cellulitis. The preseptal cellulitis usually responds rapidly to antibiotics. Orbital cellulitis is a serious problem and we found that the most serious complications arose with patients between the ages of 11 and 19 years. They delayed treatment and oftentimes developed an orbital abscess or even a brain abscess. Many of these patients required surgical drainage of the sinuses. We did not find that culture of the spinal fluid was of value at any time. Blood culture is rarely helpful. The culture of the nasal pharynx is of questionable value because of all of the normal flora. Doctor Jones has outlined a most useful method of management of these patients.

DR LEONARD APT. I would appreciate having Doctor Jones' response to comments I have relating to several areas in his presentation. My remarks are restricted to orbital cellulitis in the pediatric age group.

First, I am interested to know why nafcillin was chosen over oxacillin, a similar semi-synthetic antistaphylococcal penicillin. I ask this question because nafcillin is particularly irritating to veins; it can cause thrombophlebitis or tisue ulceration if extravasation occurs. Probably for this reason the Physician's Desk Reference (PDR) advised against intravenous use of the drug for more than 24 to 48 hours. Since veins of infants and children are smaller and thinner than those of adults, and antibiotic therapy usually is required for at least 5 to 7 days, nafcillin seems less desirable than oxacillin in pediatric patients.

Recall also that nafcillin is a rather unique penicillin in that it is primarily metabolized and excreted by the liver. Hence its use in neonates and young infants is not advisable because immaturity of liver function in this age group may lead to erratic blood levels.

Doctor Jones recommends the use of cefuroxime as one primary antibiotic regimen for treatment of orbital cellulitis that could be caused by *Haemophilus influenzae* type b bacteria. Although cefuroxime at present is effective against most strains of *H influenzae*, it still is considered an alternate drug to chloramphenicol or

to the combination of ampicillin and chloramphenicol for treatment of serious *H influenzae* infections in pediatric patients (Report of the Committee on Infectious Diseases, 12th edition; Elk Grove, IL: American Academy of Pediatrics, 1986, pp 171). Not enough experience with cefuroxime in serious *H influenzae* infection has yet been gathered to alter this position. Furthermore, we are not certain how quickly this organism will become resistant to cefuroxime. Drug resistance certainly has occurred to some extent with ampicillin (12% to 40% of strains depending on locality). Over 90% of the strains, however, are still sensitive to chloramphenicol.

Another major attribute of chloramphenicol is its ability to penetrate tissue areas (including the eye) so well. This ability to penetrate is particularly important in orbital cellulitis secondary to sinusitis because the subperiosteal site is relatively avascular. The rare complication of aplastic anemia from the use of chloramphenicol does not seem to concern pediatricians as much as ophthalmologists.

Doctor Jones' antibiotic recommendations for the treatment of orbital cellulitis assumes special importance because of the recent trend by some ophthalmologists to conservative (that is, medical rather than surgical) management in the later stages of the infection associated with sinusitis. The classic teaching in the past has been to promptly incise and drain the area when there is radiologic evidence of subperiosteal absces. Recent experience has challenged this dictum. We have learned that (1) a subperiosteal abscess may not be found on exploration even though it is supposedly seen in radiographs or CT scans, and (2) early subperiosteal abscess may respond well to the proper use of antibiotics given before there is impairment of vision and when limitation of globe movement is minimal.

Dr Arthur H. Keeney. Mr President, ladies and gentlemen. Not only have I learned much from Doctor Jones in regard to inflammatory disease in the orbit, but also from a patient who gave me an irrefutable lesson on the urgent significance of pulsating visual loss. I recall her warning that her intraorbital pressure from orbital cellulitis was exceeding the systolic pressure in her ophthalmic artery when she said, "My vision is coming and going." This was synchronous with her pulse. I didn't realize at the moment, she was announcing a short time interval in which orbital decompression must be done or permanent blindness would occur from a secondary or compression glaucoma precluding arterial access to the globe. Intraocular pressure would soon exceed systolic pressure in the ophthalmic artery. In addition to anti-inflammatory drug therapy, emergency surgical decompression of the orbit is indicated by pulsating visual obscuration.

Dr Dan B. Jones. I would like to thank the discussants for emphasizing several additional important factors in the management of preseptal and orbital cellulitis. I agree with Doctor Burns that the cost of these various antibiotics, particularly the new cephalosporins, should be considered and that lesser expensive agents should always be used if equally effective and appropriate. In a recent consensus report on antimicrobial therapy for bacterial meningitis in infants and children, pediatricians emphasized the high cost of administering two different antibiotics four times daily,

including pharmacy charges for preparation of the intravenous drugs and costs for the materials to deliver each dose. Although many infectious disease pediatricians still prefer the combined administration of chloramphenicol and ampicillin for meningitis in this age group, there is increasing evidence of the efficacy of a third generation cephalosporin, such as cefotaxime, alone or in combination with ampicillin. Our preference for cefuroxime in the management of suspected *H influenzae* type b preseptal cellulitis is based on in vitro susceptibility of the organism, clinical efficacy, and the fact that this is one of only a few agents that penetrates the cerebrospinal fluid which may be an important feature in the early management of these children with potentially life-threatening *H influenzae* infection.

Doctor Apt made an important point with regard to the pathogenesis and management of subperiosteal elevation. I attempted to emphasize this in the presentation, namely that we are unable to distinguish subperiosteal abscess from accumulation of sterile, nonsuppurative material. Doctor Gerald Harris and others have emphasized this in the literature. Although many authors previously recommended immediate surgical exploration and drainage of presumed subperiosteal abscess, this decision should be based on the severity of infection and response to antimicrobial therapy. Perhaps new technology in MRI will assist us in these decisions. The advantages of exploration and drainage of subperiosteal elevation are to confirm the process, obtain proper materials for laboratory investigations, and perhaps enhance the likelihood of antibiotics reaching these spaces. Very little work has been done with regard to the pharmacokinetics of antibiotics within the nasal sinuses, and certainly not the subperiosteal space.

Doctor Apt has also added caution in the use of nafcillin in young children because of the potential problems related to its excretion by the liver. We prefer nafcillin because it has good activity against non-penicillinase-producing staphylococci and streptococci as well as penicillin-resistant strains of staphylococci and, with the possible exception of premature infants and neonates, have not excluded nafcillin because of these other potential risks.

I appreciate Doctor Newell's comments. Indeed, prompt recognition of these entities, proper laboratory methodology, and the introduction of new, highly effective antibiotics have reduced the morbidity of these potentially blinding and life-threatening infections.

I am grateful to Doctor Burns for his discussion, the additional remarks from the other discussants, and the opportunity to present this paper to the members and guests.