

AGE AS A FACTOR IN THE BACTERIOLOGY AND RESPONSE TO TREATMENT OF SUBPERIOSTEAL ABSCESS OF THE ORBIT*

BY *Gerald J. Harris*, MD

INTRODUCTION

BACTERIAL INFECTIONS OF THE ORBIT, WHICH CAN THREATEN BOTH VISION and life, are caused by paranasal sinusitis in about 75% of affected patients.¹⁻³ While these infections are still discussed generically as "orbital cellulitis" in some quarters, anatomic subgroups were distinguished by physical and surgical findings many years ago.⁴⁻⁶ Among these variants, subperiosteal abscess (SPA) prompts specific concerns about vision and control of the infection.⁷ An SPA results from the accumulation of purulent material between the periorbita and the orbital bones. Expansion of the potential subperiosteal space may be rapid, and optic nerve function can be compromised by mechanical distortion and elevated orbital pressure. In addition, the infection is sequestered within a relatively avascular zone, raising doubts about antibiotic penetration and suppression of bacterial growth.

The recognition of SPA as a specific entity within the general clinical setting of orbital cellulitis has increased dramatically since the introduction of computed tomography (CT). With that recognition, SPA has been the object of many studies, and its management has been the source of some controversy. Citing reports of rapidly progressive visual and intracranial complications of SPA, some investigators have forcefully argued for prompt surgical drainage of the abscess and paranasal sinuses when an SPA is first diagnosed by CT scanning.^{2,7-16} Others, citing many patients who recovered with antibiotic treatment alone, have recommended medical therapy for those without visual compromise, reserving surgical drainage for patients who fail to respond after several days.^{1,17-24} In some reported cases, prompt drainage shortened the course of hospitalization,²⁵ while surgery prolonged

*From the Section of Orbital and Ophthalmic Plastic Surgery, the Department of Ophthalmology, Medical College of Wisconsin, Milwaukee. Supported in part by Core grant EY01931-15 from the Department of Health and Human Services, National Institutes of Health, National Eye Institute, and by an unrestricted grant from Research to Prevent Blindness, Inc, New York.

the hospital stay in others.^{1,22,23} Arguments that early drainage might prevent extraorbital complications²⁵ have been countered by suggestions that surgery may have seeded intracranial abscesses.^{1,22}

Strongly-held opinions about the management of SPA seem to derive from individual experiences with what, in fact, may be a heterogeneous condition. In a bacteriologic analysis of 17 cases, 3 patients recovered completely with medical therapy alone, and 3 others had negative cultures at the time of surgical intervention.²⁶ In that same study, however, eight patients had persistently positive subperiosteal cultures despite more than 3 days of antibiotics that were effective *in vitro* against the recovered pathogens. The findings demonstrated a marked variation in *in vivo* antibiotic efficacy, even within a single series of patients. In some of the refractory cases, even prompt surgical drainage did not lead to rapid sterilization of the subperiosteal space or prevent visual or intracranial complications. The same study also showed a broad range of pathogens isolated from the SPAs, with single aerobes at one extreme and multiple, mixed aerobes and anaerobes at the other.

Taken as a whole, the studies of SPA to date have raised questions about the necessity of surgical drainage in some cases; they have supported an aggressive surgical approach in other cases; and they have stimulated interest in the lack of response to even this treatment in still others. SPA would seem to involve a spectrum of complexity, which calls for a systematic approach to management based on guidelines that might be derived from its analysis.

Although the microbiology of acute sinusitis varies little with patient age,²⁷⁻³⁷ the complexity of bacteria isolated in a small number of culture-positive SPAs secondary to acute sinusitis appeared to be greater in older patients in the series.²⁶ This observation prompted an interest in patient age as a potential factor in management decisions. In the present study, 37 consecutive cases of SPA secondary to bacterial sinusitis were analyzed with respect to the influence of patient age on the bacteriology and response to treatment. These associations have not been specifically addressed by other investigators, but age and outcome data could be extracted from published reports, permitting additional investigation for linkage. The CT features in all cases were carefully reviewed with regard to the subperiosteal material encountered at surgery, the culture results and the clinical course. Efforts were made to explain the observed findings. Finally, a management protocol was developed, which considers patient age in the election and timing of surgical drainage.

BACKGROUND

PATHOGENESIS OF SPA OF THE ORBIT

Suppuration within the subperiosteal space has occasionally resulted from causes other than sinusitis. Gamble³⁸ reported three patients with distant infection that metastasized to an orbital rim or wall, producing osteomyelitis, periostitis, and SPA. Harris⁷ described a 1-week-old infant with a superior orbital SPA that developed from phlebitis of a scalp vein. In almost all reported cases, however, SPA of the orbit has been a complication of bacterial infection of the paranasal sinuses.^{1,2,4,7-24,26,39-41}

The bony walls that are shared with the sinuses account for approximately half of the orbital surface area. Neurovascular foramina, congenital dehiscences, and the osteitis and necrosis that can complicate sinusitis all permit the direct extension of bacteria and inflammatory products into the orbit.^{4,39,42,43} In addition, anastomosing valveless venous channels allow the phlebitic and periphlebitic propagation of organisms (Fig 1).^{4,7,39,42,44}

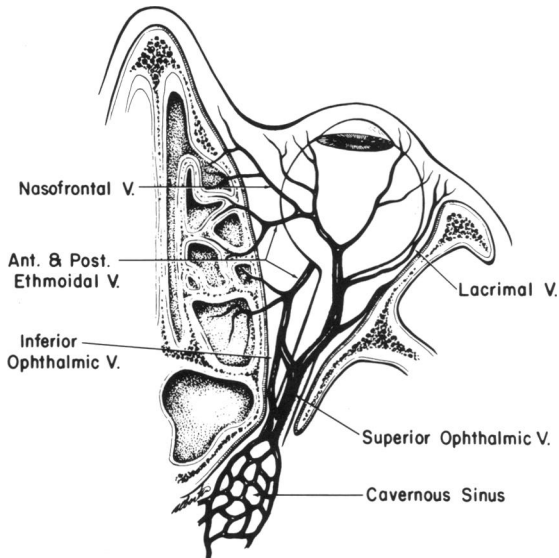


FIGURE I

Anatomic relationships between orbit and paranasal sinuses include continuity of extensive valveless venous system.

The orbital complications of sinusitis occur more frequently in children than adults.^{2,4,16,45,46} Children are more susceptible to upper respiratory infections in general, and the anatomic barriers between their orbits and

sinuses are less substantial.¹² The bony septa of sinus walls are thinner, vascular foramina are larger, bones are more porous, and suture lines may be open.

The orbital complications of sinus infections often are grouped indiscriminately under the rubric of "orbital cellulitis." Appropriate management requires finer distinctions, however, and Chandler and colleagues,⁴ modifying the earlier classifications of Hubert⁶ and Smith and Spencer,⁵ proposed the following categories: (1) inflammatory edema, (2) orbital cellulitis, (3) subperiosteal abscess, (4) orbital abscess, (5) cavernous sinus thrombosis. In that schema, simple inflammatory edema without infection was explained by impedance of orbital venous drainage into obstructed sinus vessels.⁴ While venous drainage from the orbit into the paranasal sinuses is minimal compared with drainage into the cavernous sinus, pterygoid plexus, and facial venous system, the absence of valves does permit the elevated venous pressure in the sinuses to be transmitted to the vascular bed of the orbit and eyelids, with resultant transudation and local edema.⁷

The same venous continuity allows bacterial migration and true infection. Because their visual implications differ, it is useful to distinguish the diffuse infections that occur anterior to the orbital septum from those that occur posterior to this fibrous barrier. Therefore, the terms "preseptal cellulitis" and "orbital cellulitis" should have precise anatomic denotations. These terms are preferable to "periorbital cellulitis," which has been applied at times to both preseptal and orbital cellulitis, and at other times to only the former.⁴⁷⁻⁵⁰

Continued posterior propagation of phlebitis, either from the orbit or directly from the sinuses, may produce a septic cavernous sinus thrombosis.

Anastomotic veins traverse the subperiosteal space and may play a pathogenetic role in a subperiosteal abscess.⁷ However, direct extension of bacteria and inflammatory products through the meager sino-orbital partitions is probably the predominant mechanism.

An orbital abscess, within the confines of the periorbita, may follow the intraorbital extension of an SPA, but it rarely occurs as an independent complication of bacterial sinusitis.⁷ It is more likely to follow metastatic infection or orbital trauma with retained foreign material.⁵¹

Trauma may play an indirect role in the pathogenesis of SPA. Fractures through the orbital plates of previously noninfected sinuses were responsible for SPAs in two reported cases.^{7,52} Bone fragments, edema or hemorrhage may have obstructed sinus drainage and led to acute infection, which was then continuous with the subperiosteal space through the fracture sites.

The staging of orbital involvement secondary to sinusitis does not imply a rigid chronology.⁷ Unlike orbital abscesses, SPAs do not require several days

for the liquefaction of solid tissue. Rather, the direct spread of purulent material through insubstantial bony walls allows an SPA to develop early in the course of acute sinusitis.

Extension of inflammatory exudate into the subperiosteal space can have serious visual consequences.⁷ Because the periorbita is loosely applied to the orbital bones, there is a potential space that can be rapidly expanded by a fulminant pyogenic sinusitis. An overall elevation of orbital pressure embarrasses the blood supply to the optic nerve and retina. In addition, extreme globe displacement may cause a conical deformation of the back of the eye, as documented by CT,^{7,53} and the traction at the posterior pole can further compromise neuroretinal perfusion. The visual impairment caused by an SPA may or may not be responsive to surgical drainage.^{1,7,15,54} The degree and/or duration of ischemia prior to drainage are probably factors in the reversibility of such vision loss. Other mechanisms of vision impairment also have been invoked, including septic optic neuritis and embolic or thrombotic lesions in vessels supplying the optic nerve, retina or chorioid.^{38,40,45,55,56}

The venous continuity shared by the sinuses and orbits extends to the intracranial cavity. Meningitis, epidural and subdural abscesses, parenchymal brain abscesses and osteomyelitis of the frontal bone may all complicate bacterial infection of the orbit.^{18,26,39,46,57-59}

RELATIVE FREQUENCY

The relative frequency of SPA among the orbital complications of sinusitis is difficult to determine with accuracy. The populations encompassed by reviews of "orbital" and "periorbital" cellulitis differ with the orientation of the investigators. Series compiled by ophthalmologists and otolaryngologists may be weighted toward more complicated cases, which eventuated in referral and surgical intervention.^{39,40,57} Pediatric series include cases of preseptal and orbital inflammation secondary to causes other than sinusitis, such as facial cellulitis resulting from *Hemophilus influenzae* bacteremia.^{48,49}

Reports compiled in the CT era are more meaningful than earlier ones for determining the relative frequency of SPA, but none have involved scanning of every patient. Because some SPAs may have responded rapidly to medical therapy without a radiologic diagnosis, many reports may underestimate their occurrence. With this qualification, the following two pediatric series can be considered.

Eustis and colleagues²⁵ reviewed the records of 257 children with a hospital discharge diagnosis of periorbital or orbital cellulitis secondary to sinusitis. Twenty-two patients were found to have orbital involvement on the

basis of CT scans in 19 cases and operative or other records in 3 cases. Ten of the 22 patients had inflammatory edema, 10 had SPAs, 1 had a suspected intraorbital abscess, and 1 had unconfirmed cavernous sinus thrombosis. Souliere and co-workers²² reviewed records of 120 children with an admission diagnosis of periorbital or orbital cellulitis. Ten cases of SPA were documented by CT scans.

Perhaps the most significant study for current purposes was that of Patt and Manning,¹⁵ who reviewed the records of 220 patients admitted to a general hospital with a diagnosis of acute sinusitis from 1978 to 1988. Among the 159 patients with orbital or periorbital complications, 89 (56%) had preseptal cellulitis, 38 (24%) had orbital cellulitis, 30 (19%) had SPA, and 2 (1%) had orbital abscess. Among the 70 patients with a final diagnosis of true orbital involvement, 60 had undergone CT scanning.

DIAGNOSIS

The typical patient with an SPA of the orbit gives a history of recent upper respiratory symptoms and rapidly developing eyelid edema, proptosis, and pain. Fever, generalized toxicity, and leukocytosis should be present, but prior antibiotic therapy may have mitigated these findings.^{40,47} Depending on the completeness of the clinical profile, the differential diagnosis might include other causes of rapidly progressive proptosis. In children, consideration would be given to rhabdomyosarcoma, metastatic neuroblastoma, hemorrhagic cyst, orbital myositis, and other conditions.^{60,61}

The distinction of SPA from diffuse orbital cellulitis may be difficult on the basis of the physical findings alone. The degree of proptosis, pupillary and ophthalmoscopic signs that reflect the orbital pressure, and generalized motility impairment will not differentiate these stages of inflammation. Features that do suggest a localized collection of pus include selectively limited ductions and displacement of the globe in a direction away from the infected sinus.

Clearly, the advent and evolution of orbital imaging techniques in the past two decades have facilitated the diagnosis of SPA.^{7,41,52,62} CT depicts a localized elevation of the periorbita adjacent to an opacified paranasal sinus. Medial SPAs that result from ethmoiditis are best imaged in the axial plane. Coronal views are preferable for superior SPAs that have extended from the frontal or ethmoid sinuses below the orbital roof and for inferior SPAs that have spread from ethmoid or maxillary sinuses above the floor.^{7,26,63} CT also permits evaluation of the cavernous sinuses and the intracranial cavity, which may harbor epidural, subdural or parenchymal brain abscesses in these cases.

Orbital echography reveals an acoustically low-reflective space between the high spikes of the dense periorbita and the bony orbital walls. The study can be used as a screening office procedure for patients suspected of having SPAs, but CT is still necessary to assess the sinuses. Thus far, magnetic resonance imaging has offered no particular advantage over CT in depicting SPA, and the former has disadvantages in evaluating the shared bony walls.

In some reported cases, these CT or echographic features have been present, but surgical exploration yielded clear or hemorrhagic fluid, edema or granulation tissue rather than frank purulence.^{18,19,23,26,64,65} Considering these findings, the CT and echographic depiction of periorbital elevation was designated subperiosteal inflammation to include SPAs in a large proportion of cases.²⁶ These distinctions may not be of overriding importance, however, since the absence of purulent material did not guarantee sterility.

Eustis and colleagues²⁵ described the CT finding of inflammatory edema between the medial rectus muscle and the periorbita. The muscle was laterally displaced and variably widened, and the medial extraconal fat had increased radiodensity. While this localized form of orbital cellulitis can usually be distinguished from SPA by intravenous contrast enhancement, which shows displacement of the inflamed periorbita in the latter condition, some investigators have found differentiation difficult.²³

BACTERIOLOGY OF SPA OF THE ORBIT

The bacteriologic profile of sinus-related orbital infection has been slow to unfold. Attempts to identify the pathogens by culturing readily accessible sites such as the conjunctiva, nose, and throat have been unrewarding, with cultures yielding local flora not representative of the offending organisms.^{2,29,35,47,49,66} Blood cultures are more reliable indicators of the pathogens, but they are often negative, particularly after antibiotics have been initiated.^{23,48,49}

It might be assumed that the pathogens in orbital cellulitis and its variants can be predicted from classic studies of sinusitis. The microbiology of sinus infection has usually been dichotomized along temporal lines. Acute and subacute sinusitis, with symptom duration of less than 3 to 4 months, has been generally attributed to single aerobes.²⁷⁻³⁷ The predominant organisms in all age-groups were *Streptococcus pneumoniae*, *Hemophilus influenzae*, and *Moraxella (Branhamella) catarrhalis*. Less frequently isolated bacteria included group A and group C streptococci, *Streptococcus viridans*, other *Moraxella* species, and *Eikenella corrodens*.^{34,35} Staphylococci and anaerobes were rarely recovered in these studies, except in odontogenic infections.²⁸ In reports of chronic sinusitis, in which the duration of symptoms varied from more than 3 months to at least 1 year, polymicrobial

infections were the rule.^{37,67-73} The predominant aerobic isolates were staphylococci and alpha-streptococci. Anaerobes were recovered in high proportions in several series.^{37,67,70,71}

Because orbital infections usually result from acute sinusitis, a simple bacterial constituency would be anticipated from these reports. However, cultures taken directly from the subperiosteal space of many patients have shown bacteriologic profiles that have been classically associated with chronic sinusitis.^{2,3,7,14,26} Staphylococci accounted for 11 of 12 organisms isolated from the orbit by Jackson and Baker.¹⁴ Schramm and associates² and Goodwin³ found staphylococci and beta-streptococci, or the two in combination, as the predominant organisms. Anaerobes were identified in a minority of cases in early series, but their role has been more widely recognized in recent studies.^{26,74-76} In general, as the techniques of anaerobic isolation have been refined, the role of anaerobes has been confirmed in a variety of diseases, particularly in body sites with complex normal flora where physiologic derangements can lead to polymicrobial infection.^{77,78}

In a bacteriologic analysis of SPA, a surprisingly wide range of pathogens was recovered from the subperiosteal space in 11 culture-positive cases.²⁶ The organisms varied from single aerobes to multiple, mixed aerobes and anaerobes. The predominant aerobes were alpha- and beta-streptococci and staphylococcal species. Gram-negative isolates included *E. corrodens* in two cases and *Klebsiella pneumoniae* in one case. In accord with other studies,^{2,3,14} *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* were surprisingly underrepresented in the subperiosteal cultures. It was suggested that those organisms might have been involved in the patients who had responded rapidly to presumptive antibiotic therapy prior to surgical drainage. In one patient, for example, cultures from the subperiosteal space after 3 days of treatment were negative, but a pretreatment blood culture had yielded *S. pneumoniae*. Anaerobes were recovered from 7 of 11 culture-positive patients, almost always in combination with multiple aerobic bacteria. *Bacteroides* species and anaerobic gram-positive cocci were most commonly isolated. Four of the seven cases with anaerobic pathogens included species that elaborated beta-lactamase. As noted by Bartlett,⁷⁸ anaerobes above the diaphragm may be penicillin-resistant, despite earlier assurances to the contrary.

Although the bacteria isolated in 7 of 11 culture-positive SPAs were those classically associated with chronic sinusitis, none of the seven patients had had respiratory symptoms for more than a few days, and none had a history of sinus disease.²⁶ In addition to these SPAs with a mixed constituency despite very brief symptoms, the series included one patient with prolonged disease from whom a single aerobe was isolated. It was postulated that the

agents responsible for the SPA and underlying sinusitis may be less closely related to a fixed time element than to the degree of alteration of local physical conditions.²⁶

The microbiology of sinusitis is inextricably linked to the pathophysiology of the condition (Table I).^{26,27,30,69,79-83} Initially, viral or allergic inflammation impairs the mucociliary clearance of nasal flora from the sinuses and often narrows or completely obstructs the sinus ostia. Absorption of intrasinus air by the mucosa then creates negative pressure, which increases transudation and provides a nutrient medium for bacteria. Absorption of air moderately reduces the oxygen tension within the sinus, enhancing the growth of aerobic and facultative organisms. These include *S pneumoniae* and *H influenzae*. As inflammation continues and inflammatory products accumulate, pressure within the sinus rises. Mucosal blood flow decreases, and the ischemia further reduces the oxygen tension. The flourishing aerobic and facultative bacteria consume much of the remaining intrasinus oxygen. Conditions then favor the growth of microaerophilic organisms and, ultimately, obligate anaerobes.

TABLE I: SEQUENTIAL FACTORS IN BACTERIAL SINUSITIS^{27,30,69,79-83}

1. Viral or allergic inflammation
 2. Altered mucociliary clearance of normal flora
 3. Obstruction of sinus ostia
 4. Absorption of air by sinus mucosa
 5. Transudation, providing a nutrient medium
 6. Moderate ↓PO₂, ↑PCO₂, ↓pH,
 7. Proliferation of aerobic and facultative organisms
 8. Accumulation of inflammatory products, increasing sinus pressure
 9. Decreased mucosal blood flow, ↓PO₂
 10. Consumption of remaining O₂ by bacteria
 11. Proliferation of obligate anaerobes
-

Although time undoubtedly plays a role in the biphasic transition of sinus pathogens from those classically associated with acute sinusitis to those commonly recovered in chronic sinusitis, it has been suggested that extreme alterations in the physical environment could reduce these intervals from months to days.²⁶ In support of this proposal was the earlier demonstration by Carenfeldt and Lundberg⁸⁴ that *S pneumoniae* was unable to grow exponentially in vitro as long as ventilation of the nutrient medium maintained the gas tensions that occur in nonpurulent sinus secretions. When

ventilation was stopped for only 2 hours, growth was dramatically enhanced; when ventilation was restarted, the increased population maintained the reduced oxygen tension of the medium.

The bacteriology of SPA appears to involve a spectrum of complexity—with single aerobes at one extreme and multiple, mixed aerobes and anaerobes at the other. The pathogenic constituency may be less related to the duration of the underlying sinusitis than to its severity.

TREATMENT

The management of SPA has been both medical and surgical. Specific antibiotic recommendations have changed with the introduction of new drugs and with the revelation of an increasingly broad range of pathogens.^{7,26} The general desiderata of antibiotic therapy have included high intravenous dosage and prolonged administration to compensate for presumably poor penetration into the relatively avascular subperiosteal space. Passage through the blood-brain barrier has been desirable for all cases, but essential for infections that have already spread into the intracranial cavity.

Because of the wide range of potential pathogens, appropriate presumptive therapy has included broad coverage, although no single drug or combination has satisfied every demand of spectrum and penetration. The combination of a semisynthetic penicillin, such as nafcillin sodium, with chloramphenicol sodium succinate was popular for many years. Newer-generation cephalosporins, such as ceftriaxone sodium, have generally replaced the former combination, avoiding the potential bone marrow toxicity of chloramphenicol.^{23,85} Vancomycin hydrochloride has been used as an alternative to penicillins and cephalosporins in cases of known allergy. Additional drugs or alternative single antibiotics have been employed as the role of both beta-lactam sensitive and resistant anaerobes has been recognized. Clindamycin phosphate has been used in combination with cephalosporins for this purpose. Alternatively, single drugs that involve the conjugation of beta-lactam antibiotics with agents that block beta-lactamase activity have been utilized. These include ampicillin sodium/sulbactam sodium and ticarcillin disodium/clavulanate potassium. In individual cases, the broad presumptive therapy has been narrowed in response to drainage cultures and *in vitro* sensitivity testing.

The optimum duration of intravenous therapy and subsequent oral treatment has not been determined. As a general guideline, Harris⁷ recommended that intravenous antibiotics be continued for at least 1 week after surgical drainage. Goodwin³ proposed a 2-week course of oral antibiotics following hospital discharge. In individual cases, the clinical course has usually dictated these intervals. The choice of oral agents has generally been

based on the culture results. With negative cultures or recovery without surgery, amoxicillin/clavulanate potassium has been used frequently.²³

Early surgical drainage of SPA has been strongly advocated.^{2,7-16,25} If the subperiosteal space has expanded to the point of visual impairment, evacuation has been clearly indicated. Reasons for draining *all* SPAs have been offered, including the difficulty in assessing vision in acutely ill children, problems in drug selection without identification of the specific pathogens, questionable antibiotic delivery into the poorly perfused subperiosteal space, and the need to restore aerobic conditions to discourage microbial proliferation.^{7,26} Prompt drainage has been recommended to prevent extraorbital extension and to shorten hospital stay.²⁵

Because an SPA usually results from adjacent sinusitis, surgical evacuation of the SPA is unlikely to be effective without eradication of the underlying sinusitis. Therapy for bacterial sinusitis is primarily medical, but an orbital SPA has been usually considered by otolaryngologists to be an indication for surgical drainage of the affected sinuses.^{4,39,44,57,86}

The anatomic localization of the SPA on CT scans and the specific sinuses involved have determined the surgical approach.⁷ Medial SPAs associated with ethmoiditis have been successfully managed by external ethmoidectomy.^{4,12,44,57,87} If an intranasal ethmoidectomy is preferred by the otolaryngologist,^{39,57} an orbital rim approach has been used to assure adequate subperiosteal exploration and drainage.⁷ The skin incision extends from a point medial to but level with the trochlea, to just above the medial canthal tendon. The wound is deepened to the periosteum, which is then incised. The medial canthal tendon is retracted inferiorly and anteriorly and the periosteal incision is carried to the anterior lacrimal crest. Periosteal elevation is continued posteriorly until the abscess is encountered. The recovered material is smeared for Gram's stain and is cultured, directly into both aerobic and anaerobic media, if possible. All dissection is performed extra-periosteally, unless there is CT evidence for a secondary intraorbital abscess, which is then accessed through the periorbita at the appropriate site. A drain is placed and maintained until all postoperative drainage subsides. A superior SPA is approached through an incision over the superior orbital rim that avoids the supraorbital neurovascular bundle and the trochlea. Inferior SPAs can be accessed with the same lower eyelid approach used for repair of orbital floor fractures.

Additional sinus surgery, including open or endoscopic evacuation of the maxillary, frontal, and sphenoid sinuses, is performed at the discretion of the otolaryngologist.

Despite the rationale for draining all SPAs, reasonable arguments have been advanced for limiting surgery. These include the precedent for suc-

cessful treatment of some lung and brain abscesses without surgical drainage,^{18,88,89} the implication that surgical drainage of SPAs may have caused intracranial seeding,^{1,22} the demonstration of longer hospitalization for patients treated surgically,^{1,22,23} and the recovery with antibiotic therapy alone of at least 44 patients with CT evidence for SPAs.^{1,17-24,26,64,65}

BACTERIAL RESPONSE TO TREATMENT

No study of SPA of the orbit that detailed the bacteriologic findings has involved a uniform therapeutic protocol. In general, prior treatment by primary care physicians and the point of referral relative to the time course of the illness have varied considerably. The visual status, which influences the timing and election of surgical drainage, also has differed. However, a sense of the responsiveness of SPA can be gained by evaluating the culture results and the clinical course in individual cases—in the context of prior treatment of each patient. Having analyzed 17 patients in this manner, Harris²⁶ found a wide range of responses to treatment.

In 3 of the 17 patients, clinical improvement was rapid, and drainage was not performed. Two of the three were treated with chloramphenicol and nafcillin. The third received cefuroxime.

Among the 14 patients in whom the drainage was performed, cultures were negative in 3. All three had been treated with intravenous antibiotics for 3 days before drainage using the following combinations: ampicillin and cefazolin; penicillin and ceftriaxone; and ampicillin and nafcillin.

Cultures were positive in the other 11 patients in whom drainage was performed. In three of those cases, the cultures were obtained within the first 24 hours of treatment, and positive cultures were expected. The culture results did not dictate a change in the antibiotic regimen, and follow-up cultures from indwelling drains were negative.

Of great interest were the remaining eight patients in the series who had persistently viable bacteria in the subperiosteal space for 3 or more days after the initiation of antibiotic therapy. In six of the eight cases, the initial or follow-up cultures were positive for at least 6 days after the treatment had begun. In seven of the eight cases, some or all of the species recovered were sensitive *in vitro* to the previously administered drugs. In the eighth case, sensitivity of the cultured anaerobe was not tested but was probable on the basis of published studies of the organism. An interplay of multiple factors that can influence the infection outcome—in addition to antibiotic susceptibility—was invoked to explain these refractory cases (Table II).²⁶

 TABLE II: FEATURES OF SPA/SINUSITIS THAT NEGATIVELY INFLUENCE
 HOST-BACTERIA-DRUG INTERPLAY

Restricted access ^{79,90}
Antibiotics; cellular, humoral immune factors
Anaerobic conditions ⁹¹
Enhance bacterial growth
Compromise oxidative transport-dependent antibiotics, oxidative metabolism-dependent natural defenses
Bacterial virulence ^{92,93}
Beta-lactamase, superoxide dismutase
Bacterial synergy ^{77,94}
Aerobes consume O ₂ for anaerobes; anaerobes can deactivate drugs otherwise effective against aerobes

**PRESENT STUDY: AGE AS A FACTOR IN THE BACTERIOLOGY AND RESPONSE
TO TREATMENT**

PURPOSE

As noted, prior studies of SPA secondary to sinusitis showed considerable variation in the bacteriology and response to treatment. In some cases, recovery with antibiotics alone or negative cultures at the time of drainage implied adequate drug penetration into the subperiosteal space and a relatively submissive pathogenic constituency. In other cases, the use of antibiotics with in vitro efficacy did not guarantee the rapid sterilization of the subperiosteal space or an early clinical resolution. Even the combination of appropriate antibiotics with prompt and/or repeated surgical drainage did not produce a rapid cure in every case.

Subperiosteal abscess of the orbit secondary to bacterial sinusitis is not a homogeneous condition, and identification of factors that might direct therapy would be advantageous.

This study of 37 cases was undertaken to explore the influence of age on bacteriology and clinical course—and, perhaps, on management decisions. A secondary objective was the analysis of the CT features of SPA, with respect to the nature of the subperiosteal material and the clinical course.

STUDY DESIGN

The primary source data consisted of individual SPA, sinus, and other culture results; the date and time each culture was acquired; in vitro antibiotic sensitivities; and the antibiotic regimen in each case, including the

specific time intervals for each drug. The time course of each patient's illness was diagrammed, and the culture results were evaluated with respect to the treatment administered up to the point of culture acquisition. An internal evaluation of the pathogens' response to the treatment schedule was used because of variations in the drugs administered before referral, in the point of referral relative to the time course of the illness, and in the visual status (which was a factor in the timing of surgical drainage).

The 37 cases were then ordered according to patient age. For analytical purposes, three groups were defined: under 9 years of age; 9 through 14 years; and 15 years or older. The species recovered from the subperiosteal space in each age group were then tabulated as aggregates, and compared among the three groups. Each age group was also analyzed with respect to the response to treatment, based on the following classification: (1) resolution without drainage, (2) drainage cultures negative, (3) drainage cultures (≤ 3 days of therapy) positive, with follow-up cultures negative, and (4) drainage cultures (> 3 days of therapy) positive. The persistence of viable organisms in the subperiosteal space after more than 3 days of intravenous antibiotic therapy was considered a "refractory" infection. The distribution of patients among these four categories of treatment response was compared among the three age groups.

The nature of the material recovered from the subperiosteal space (eg, pus, granulation tissue, hemorrhagic fluid) and its relationship to the culture results were also analyzed. The appearance of SPAs in imaging studies was reviewed with respect to the material recovered and the clinical course.

Attempts were made to explain the observed findings by viewing SPA and the underlying sinusitis as a complex infectious disease whose outcome is influenced by multiple factors. Finally, a therapeutic approach was formulated which considers patient age as a factor in the election and timing of surgical drainage.

MATERIALS AND METHODS

The records of 37 patients with a CT diagnosis of SPA secondary to bacterial sinusitis were reviewed. Patients were treated at affiliated hospitals of the Medical College of Wisconsin from 1977 to 1992. All patients were immunocompetent. In each case, the time course of the clinical infection was diagrammed. The time line was numbered in days, with day 1 representing the onset of orbital symptoms. Because resolution of the clinical infection was never a well-defined end point, each time line was carried through at least 30 days for uniformity. The routes, dosages, and periods of administration of all antibiotics were recorded. In some instances, the dosage of oral antibiotics administered before referral could not be determined from the

retrievable data. Also noted were the points at which initial and follow-up cultures were obtained from the subperiosteal space and other sites, including the paranasal sinuses, dental or brain abscesses, and blood. The results of conjunctival, nasal, and throat cultures were excluded because they lack predictive value.^{2,29,35,47,49,66} Subperiosteal cultures included those derived from surgical procedures and from indwelling drains postoperatively. Positive cultures were those with growth in one or more media within 5 days.

Bacterial isolates were identified as specifically as possible, consistent with the general policies of the microbiology laboratories of the affiliated hospitals of the Medical College of Wisconsin. For example, speciation of alpha-hemolytic *Streptococcus* was limited to pneumococcus and enterococci. The remaining organisms were designated " α -*Streptococcus* (*viridans*).” If beta-hemolytic streptococci were isolated, efforts were made to identify groups A, B, and D. The remaining organisms were designated " β -*Streptococcus* (not group A, B, or D).”

Antibiotic sensitivity testing of some identified aerobes was not performed, either because they were not viable for testing or were considered universally sensitive to standard drugs. For example, group A and B beta-streptococci were not tested because susceptibility to penicillin was assumed. Beta-lactamase activity was noted in those cases of anaerobic infection in which it had been tested.

Because of the variable metabolic demands and tolerances of some organisms, the same species may have been recovered from aerobic, anaerobic, or both media in individual cases. *Streptococcus constellatus* was one such example.

Although there were minor variations in microbiologic technique during the period spanned, the methods employed were generally as follows. In most of the cases, material was inoculated immediately after drainage onto culture media. In other cases, specimens were transported on rayon swabs in tubes (both Culturette and Anaerobic Culturette tubes, Marion Laboratories Inc, Kansas City, MO). For primary aerobic culturing, specimens were inoculated on Columbia agar with 5% sheep blood, chocolate agar, MacConkey agar, and thioglycolate or brain-heart infusion broth (BD Microbiology Systems [BBL], Hunt Valley, MD). The cultures were incubated at 35°C in 5% to 10% carbon dioxide and 70% to 80% humidity. For primary anaerobic culturing, specimens were inoculated on CDC Anaerobic Sheep blood with Vitamin K and Hemin blood agar and chopped-meat glucose broth (BD Microbiology Systems [BBL], Hunt Valley, MD). The cultures were incubated at 35°C (using the anaerobic chamber, Forma Scientific, Marietta, OH). Aerobic organisms were identified using standard laboratory methods. Anaerobic bacteria were identified with a combination

of Gram's stain and the API ANIDENT System (Analytab Products, Plainview, NY). Antibiotic sensitivity testing was performed with Vitek MIC method for aerobic gram-negative bacilli and the Kirby-Bauer⁹⁵ disk diffusion technique. Testing for beta-lactamase production by anaerobes was performed with the Ceffinase Disc method.⁹⁶

RESULTS

Culture Results and Antibiotic Regimen: Bacteriologic Case Histories

The time course of the clinical infection in each of the 37 cases is depicted in the diagrams. A sampling of representative clinical photographs, CT scans, and echograms is provided with some of the bacteriologic case histories. The majority of pertinent CT scans are grouped in subsequent sections to facilitate their analysis and comparison.

On the time lines, day 1 represents the onset of orbital symptoms. The routes of administration were intravenous, unless otherwise indicated (po, oral; im, intramuscular). The symbols used to designate different sites of culture acquisition were as follows: ●, blood; ■, SPA; ◆, sinus; △, brain abscess; ▲, dental abscess; ●, orbital drain; □, preseptal abscess; ∇, preseptal wound. Patients 2, 4, 10, 21, and 22 recovered without surgical drainage, and no SPA cultures are indicated in those diagrams.

The organisms recovered from aerobic and anaerobic cultures are listed in each diagram. All specimens were cultured in aerobic and anaerobic media. No growth is indicated by a "-." For aerobes, in vitro sensitivity to one or more of the administered antibiotics is indicated by an "S." If cultured organisms were not viable for testing, or if susceptibility to standard antibiotics was assumed, sensitivities were not tested (NT). In the diagrams, sensitivities refer to the drugs given prior to the acquisition of SPA and sinus cultures. Since blood cultures were usually obtained prior to initiation of antibiotics, sensitivities of pathogens recovered from blood usually apply to drugs administered after the acquisition of blood cultures (eg, cases 1, 2, 11).

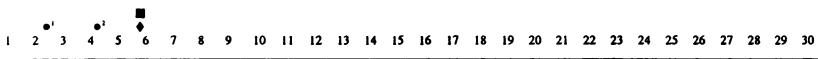
For anaerobes, beta-lactamase activity is indicated as "β-L+" for organisms producing the enzyme; "β-L-" for nonproducers; and "NT" for organisms that were not tested.

Every organism recovered from every pertinent culture is indicated in each diagram, with one exception. Patient 37 had a particularly protracted and complex infection with multiple species recovered from many cultures for several weeks. For simplicity, the results of the follow-up cultures in case 37 are abbreviated in the following manner. Recovery of one or more of the organisms that had been found in the initial cultures is indicated by a "+". In

the aerobic media, that organism was *Streptococcus intermedius*, which maintained its sensitivity to one or more of the administered antibiotics throughout the illness. The anaerobic organisms recovered in follow-up cultures varied, and some cultures yielded additional organisms not isolated in the initial cultures. The latter are named in that diagram as they were identified.

The 37 diagrams are ordered according to the ages of the patients.

Case 1 (3 mo)



AMPICILLIN

250 mg

CLEFAXIME

250 mg/6h

NALIDIXIC ACID

250 mg/6h

VANCOMYCIN

100 mg/6h

DICLOXACILLIN

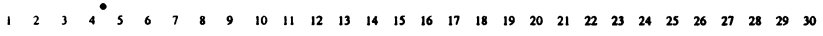
31.25 mg/6h po

Aerobic

Anaerobic

● ¹ Blood	<i>Staphylococcus aureus</i> (S)	-
● ² Blood	-	-
■ SPA	<i>S aureus</i> (S)	-
◆ Sinus	<i>S aureus</i> (S)	-

Case 2 (18 mo)



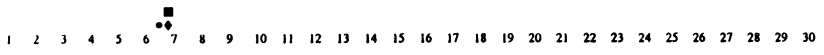
NAFCLLIN
200 mg/6h

CHLORAMPHENICOL
200 mg/6h

CEFACLOR
125 mg/6h po

	Aerobic	Anaerobic
● Blood	<i>Staphylococcus coag - (S)</i>	-

Case 3 (2 y)



CLINDAMYCINE
im

AMOXICILLIN/CLAVULANATE
po

CEFOTAXIME
550 mg/8h

NAFCLLIN
400 mg/6h

AMOXICILLIN/CLAVULANATE
250 mg/8h po

	Aerobic	Anaerobic
● Blood	-	-
■ SPA	-	-
♣ Sinuses	-	-

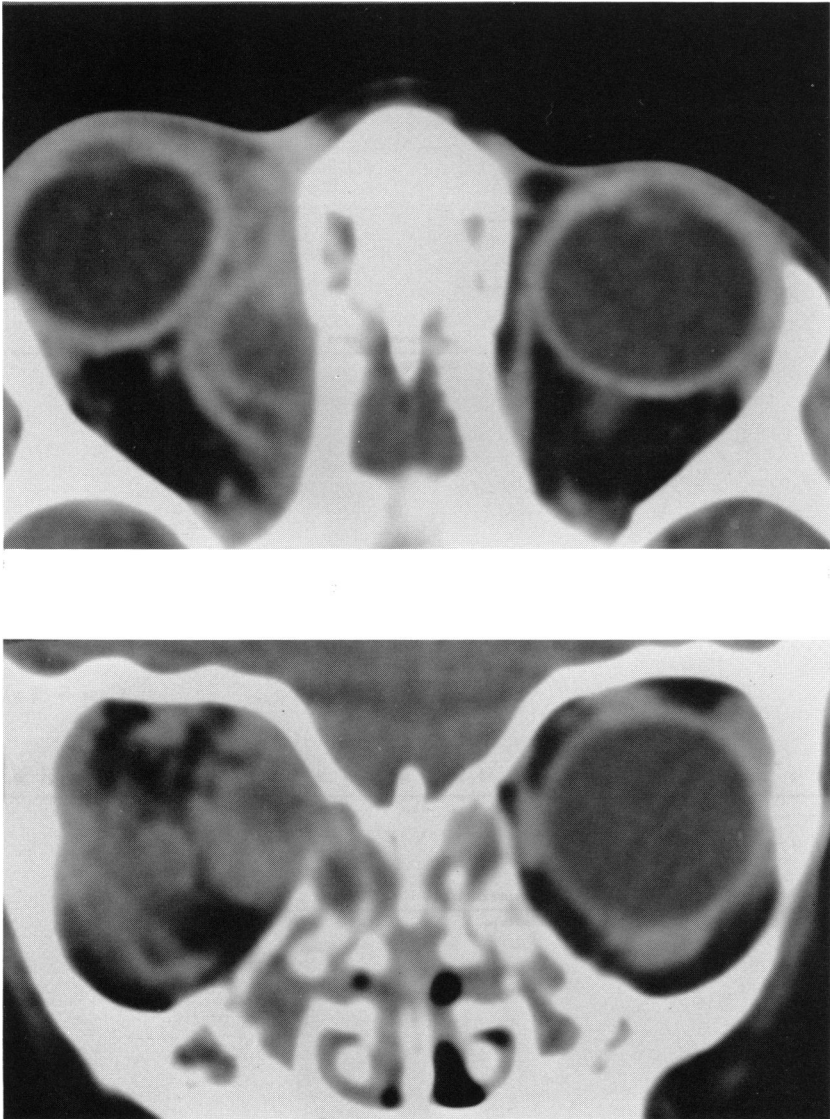
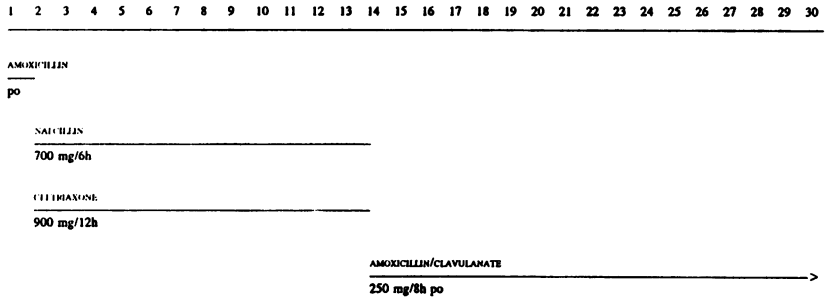


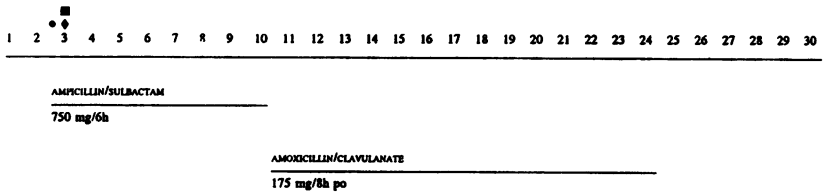
FIGURE 2

Case 3. Axial (top) and coronal (bottom) CT scans demonstrate medial SPA associated with bilateral ethmoid and maxillary sinusitis.

Case 4 (2 y)

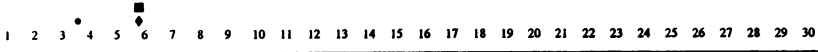


Case 5 (2 y)



	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-
■ SPA	<i>Streptococcus pneumoniae</i> (NT)	-
◆ Sinus	<i>S pneumoniae</i> (NT)	-

Case 6 (4 y)



NAICILLIN

425 mg/4h

CEFTAZIDIME

600 mg/8h

CHEMORONE

800 mg/12h

CEFUROXIME

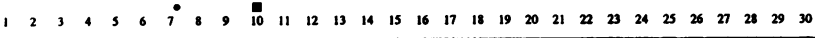
830 mg/8h

AMOXICILLIN/CLAVULANATE

250 mg/8h po

	Aerobic	Anaerobic
• Blood	-	-
■ SPA	-	-
◆ Sinuses	-	-

Case 7 (6 y)



AMPCILLIN

im

1 g/6h

1.5 g/6h

CEFAZOLIN

750 mg/8h

400 mg/6h

ERYTHROMYCIN

250 mg/6h po

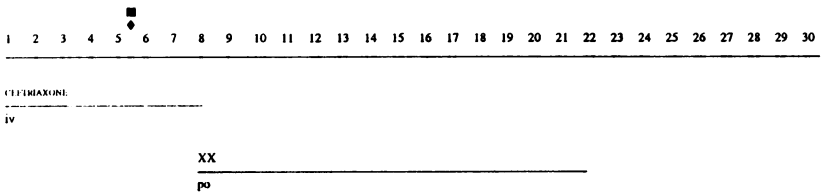
	Aerobic	Anaerobic
• Blood	-	-
■ SPA	-	-



FIGURE 3

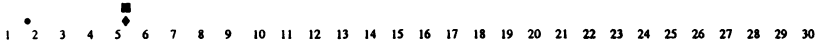
Case 7. While there is marked preseptal cellulitis, proptosis of globe and limited abduction suggest true orbital involvement. Large medial SPA prevented complete extension of medial rectus muscle.

Case 8 (6 y)



	<u>Aerobic</u>	<u>Anaerobic</u>
■ SPA	-	-
◆ Sinus	-	-

Case 9 (6 y)

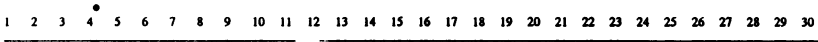


CINDAMYCIN
220 mg/6h

CEFTAXIME
1 g/6h

	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-
■ SPA	-	-
◆ Sinus	-	-

Case 10 (8 y)

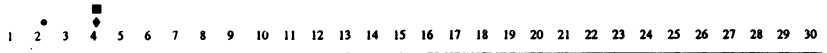


CEFUROXIME
1 g/8h

AMOXICILLIN/CLAVULANATE
250 mg/8h po

	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-

Case 11 (8 y)



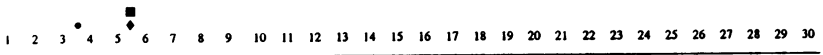
CEFTRIAXONE
1.5 g/12h

PENICILLIN G
1.25 million u
1.5 million u

PENICILLIN VK
500 mg/6h po

	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	<i>Streptococcus pyogenes</i> (S)	-
■ SPA	-	-
◆ Sinuses	-	-

Case 12 (8 y)



CERACLON
po

CEFOTAZIDIME
1.8 g/8h
1.4 g/8h

NAICILIN
1.4 g

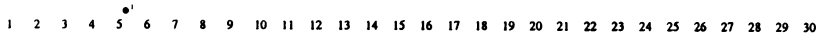
CLINDAMYCIN
350 mg/6h

CEFTRIAXONE
2 g/24h

AMOXICILLIN/CLAVULANATE
250 mg/8h po →

	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-
■ SPA	-	-
◆ Sinuses	-	-

Case 13 (9 y)



AMOXICILLIN

250 mg/8h po

NAFCILLIN

1300 mg/6h

AMPCILLIN

900 mg/6h

DICLOXACILLIN

500 mg/6h po

Aerobic

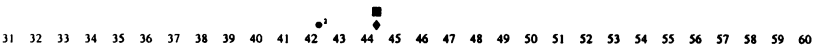
Anaerobic

●¹ Blood

-

-

Case 13 (9 y) , continued



DICLOXACILLIN

500 mg/6h po

CERPHALOTHIN

1 g/6h

AMOXICILLIN

500 mg/8h po

Aerobic

Anaerobic

●¹ Blood

-

-

■ SPA

Haemophilus influenzae (S)

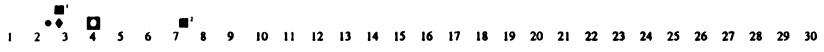
-

◆ Sinus

H. influenzae (S)

-

Case 14 (9 y)



CLEFACILOR
250 mg/8h po

CLEFAXIME
1500 mg/6h

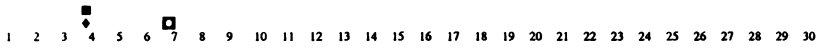
CHLORAMPHENICOL
750 mg/6h

NARICILIN
1 g/4h

DICLOXACILLIN
250 mg/6h po

	Aerobic	Anaerobic
◆ Blood	-	-
■ SPA	<i>Staphylococcus coag</i> + (S)	-
◆ Sinus	<i>Staphylococcus coag</i> + (S)	-
□ Orbital drain	<i>Staphylococcus coag</i> + (S)	-
■ SPA	-	-

Case 15 (9 y)



NARICILIN
500 mg/4h

CHLORAMPHENICOL
400 mg/6h
750 mg

CERAMANDOLE
1 g/8h

CLEFACILOR
250 mg/8h po

	Aerobic	Anaerobic
■ SPA	<i>Staphylococcus coag</i> - (S)	-
◆ Sinuses	<i>Hemophilus influenzae</i> (S) <i>Staphylococcus coag</i> - (S) <i>Streptococcus faecalis</i> (S) <i>Streptococcus faecium</i> (S) <i>Streptococcus avium</i> (S)	-
□ Orbital drain	-	-

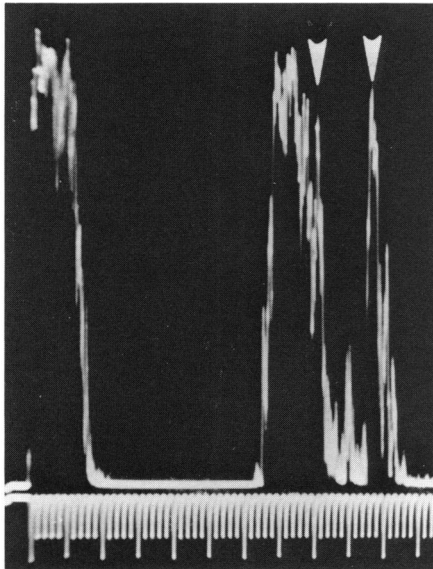


FIGURE 4

Case 14, Top: Marked preseptal cellulitis masks underlying proptosis caused by medial SPA. Bottom: Quantitative A-scan shows high spikes of periorbita and bony orbital wall (*arrowheads*) circumscribing low reflective SPA.



FIGURE 5

Case 14. Site of initial anterior orbitotomy for drainage of medial SPA. Dissection extended to, but did not include, trochlea above and medial canthal tendon below.

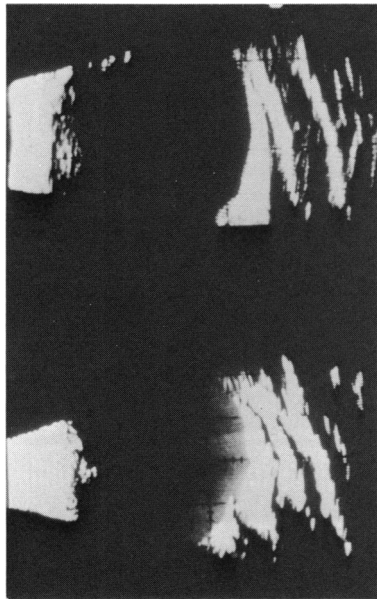
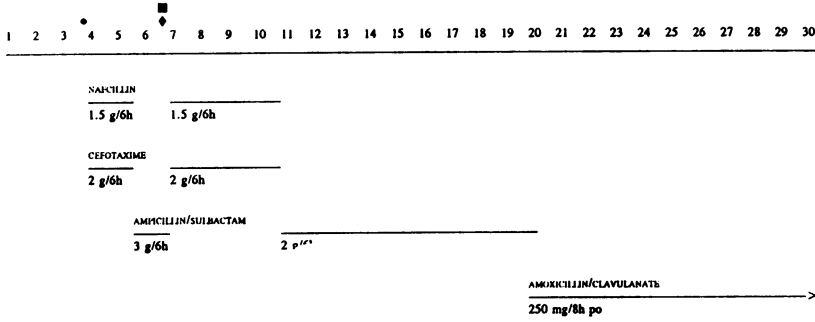


FIGURE 6

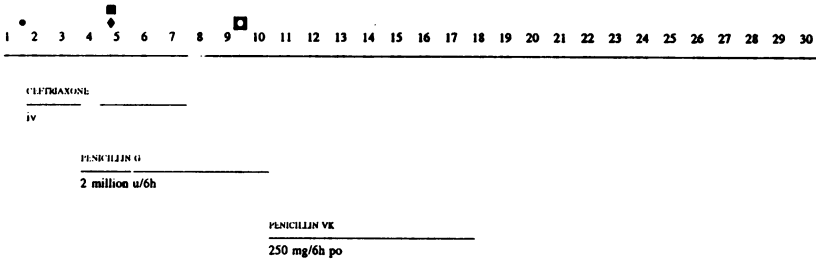
Case 15. Serial B-scans before (top) and after (bottom) drainage of medial SPA. From left to right can be seen globe, medial rectus muscle, and SPA. Abscess cavity has contracted in interval between scans.

Case 16 (9 y)



	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-
■ SPA	<i>β-Streptococcus (gp C) (NT)</i>	<i>Bacteroides intermedius (NT)</i>
◆ Sinus	<i>α-Streptococcus (NT)</i>	-

Case 17 (9 y)



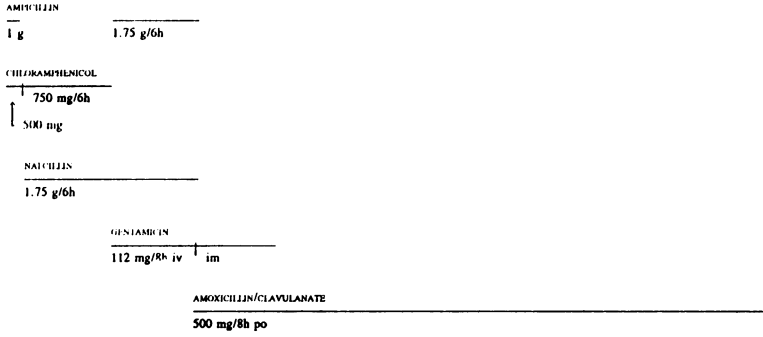
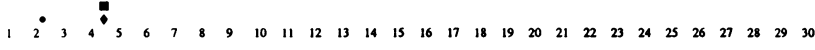
	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	<i>Streptococcus pneumoniae (NT)</i>	-
■ SPA	-	-
◆ Sinus	-	-
□ Orbital drain	-	-



FIGURE 7

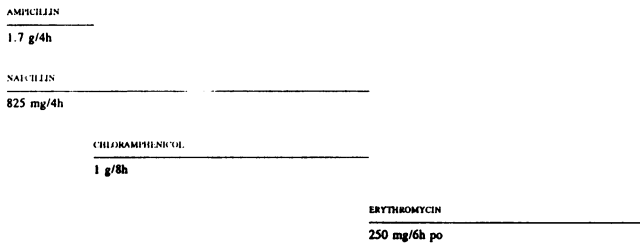
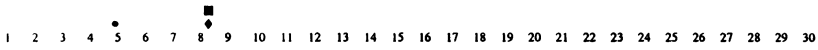
Case 17, Top: Marked proptosis and inferior displacement caused by massive superior SPA.
Bottom: 3 months after surgical evacuation of SPA and sinuses.

Case 18 (10 y)



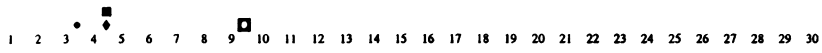
	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-
■ SPA	-	-
◆ Sinuses	<i>α-Streptococcus</i> (gp D enterococcus) (S) <i>Streptococcus MG-intermedius</i> (NT)	-

Case 19 (10 y)



	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-
■ SPA	-	-
◆ Sinus	-	-

Case 20 (10 y)



NAFCILLIN
500 mg/6h

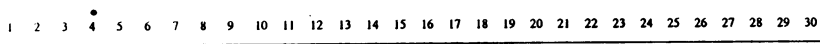
CHLORAMPHENICOL
500 mg/6h

INCLIXACILLIN
250 mg/6h po

METRONIDAZOLE
250 mg/12 h po

	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-
■ SPA	<i>α-Streptococcus (viridans)</i> (NT)	-
◆ Sinuses	<i>α-Streptococcus</i> (NT) <i>Staphylococcus coag +</i> (S)	<i>Bacteroides</i> sp (β-L +) <i>††-Bifidobacterium parvula</i> (β-L -)
■ Orbital drain	<i>α-Streptococcus (viridans)</i> (NT)	-

Case 21 (10 y)



NAFCILLIN
400 mg/6h

CHLORAMPHENICOL
160 mg/6h

PENICILLIN G
680,000 u/6h

CEFAZOLIN
150 mg/8h po

	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	-	-

Case 22 (12 y)

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

CETIRIZINE
1 g/12 h

CHLORAMPHENICOL
1 g/6h
750 mg/6h po

SALICILIN
1.5 g/6h

TICARCILLIN/CLAVULANATE
3 g/6h

AMOXICILLIN/CLAVULANATE
250 mg/8h po

Aerobic

Anaerobic

● Blood

-

-

Case 23 (13 y)

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

CLPTAZIDIME
1.5 g /8h

SALICILIN
1.25 g/4h
1.5 g

CLINDAMYCIN
600 mg/6h

AMOXICILLIN/CLAVULANATE
500 mg/8h po

Aerobic

Anaerobic

● Blood

-

-

■ SPA

Streptococcus intermedius (S)

-

◆ Sinus

S intermedius (S)

-

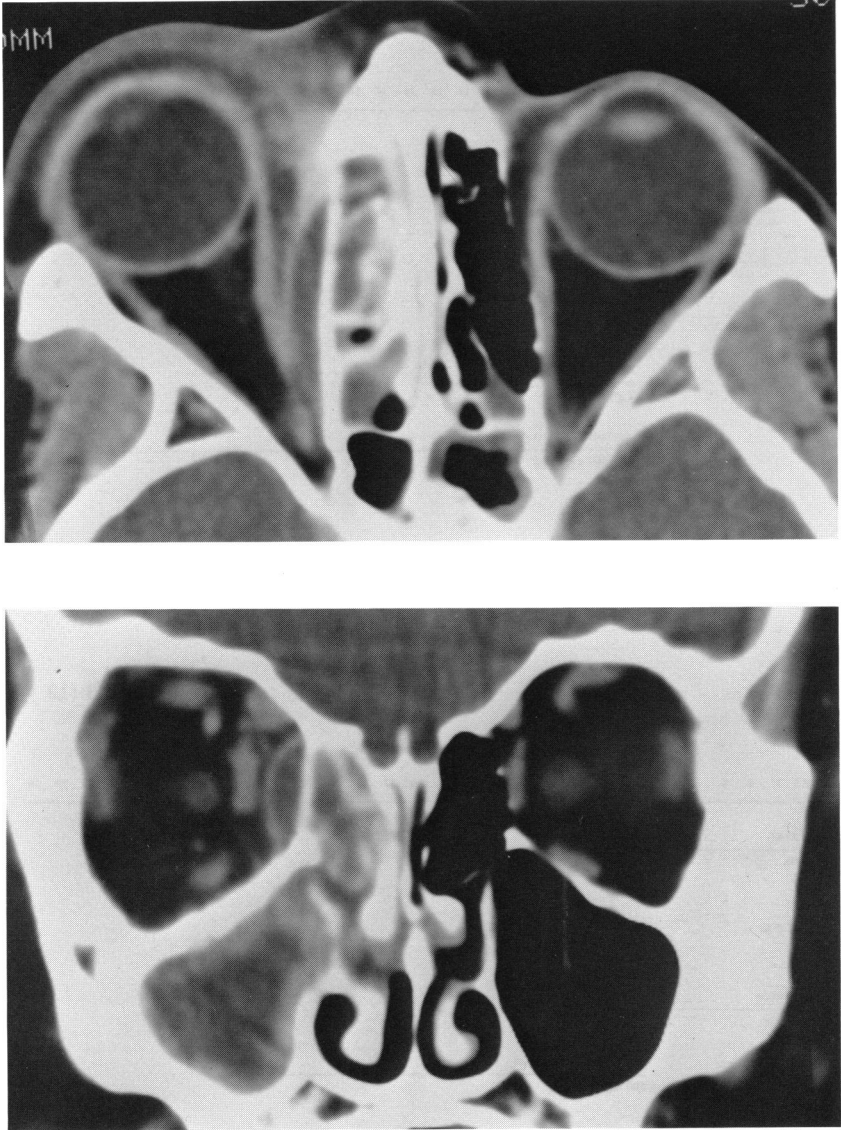


FIGURE 8

Case 23. Axial (top) and coronal (bottom) CT scans show medial SPA associated with right ethmoid and maxillary sinusitis. SPA is shallow, but extensive, and has caused significant proptosis. Intravenous contrast enhancement of displaced periorbita helps to define SPA.



FIGURE 9

Case 24. Top: Mild preseptal swelling with disproportionate ptosis, suggesting superior orbital involvement. Bottom: Globe is inferiorly displaced and elevation is markedly limited. Large superior SPA was present.

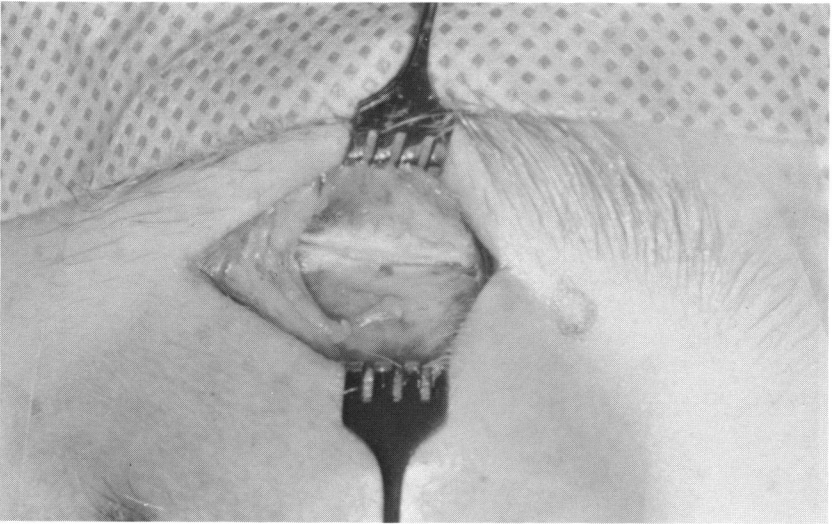
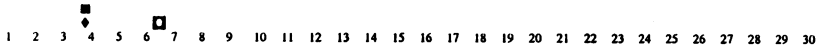


FIGURE 10

Case 24. Top: Surgical approach to superior SPA involved incision directly over superior orbital rim, which respected supraorbital neurovascular pedicle (*circle*). Bottom: Dissection continued to periosteum, which was then incised and elevated into superior subperiosteal space for drainage of SPA. While this area can be accessed with eyelid crease incision for less visible scarring, direct approach was used to avoid disseminating infection.

Case 24 (13 y)



CHLORAMPHENICOL

1 g/6h
1 g po

CIFAZIMIN

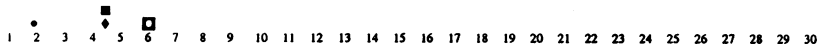
1 g/6h

CEFTALEXIN

250 mg/6h po

	<u>Aerobic</u>	<u>Anaerobic</u>
■ SPA	<i>Staphylococcus</i> <i>coag</i> - (S) <i>α-Streptococcus</i> (<i>viridans</i>) (NT)	-
◆ Sinuses	<i>α-Streptococcus</i> (<i>viridans</i>) (NT) <i>Moraxella catarrhalis</i> (NT)	-
□ Drain	-	-

Case 25 (13 y)



CEFTOXIME

1 g

FUSIDILIN G

3 million u/4h

NAICILIN

1 g/6h

CHLORAMPHENICOL

875 mg/6h | 1.1 g/6h

AMOXICILIN/CLAVULANATE

500 mg/8h po

	<u>Aerobic</u>	<u>Anaerobic</u>
● Blood	Streptococci (NT)	-
■ SPA	<i>β-Streptococcus</i> (<i>sp A</i>) (NT)	-
◆ Sinus	<i>Streptococcus faecium</i> (S) <i>Staphylococcus coag</i> - (NT)	-
□ Orbital drain	-	-

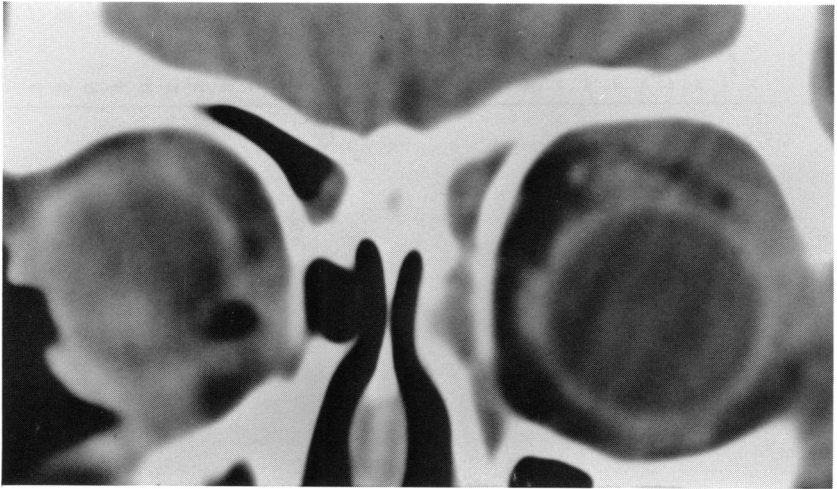
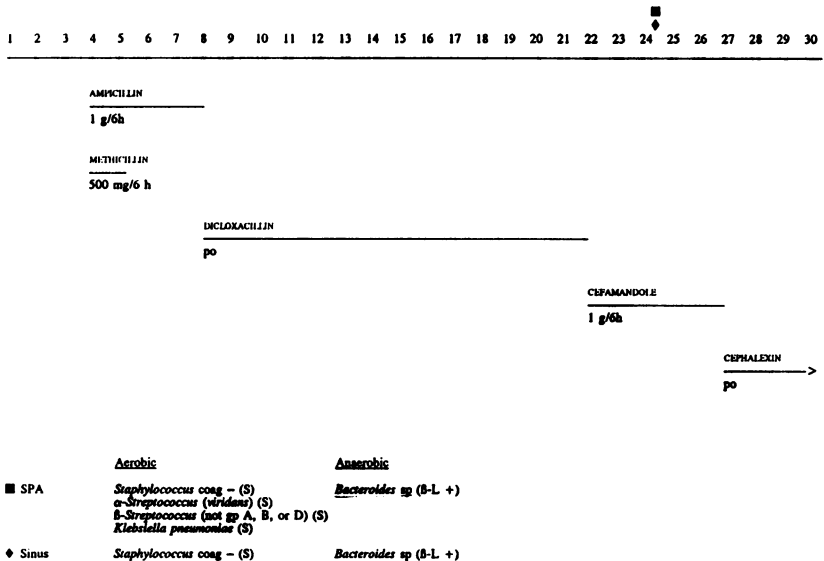


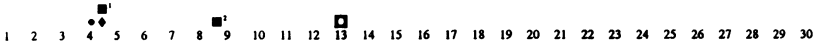
FIGURE 11

Case 25. Coronal CT scans can demonstrate shallow SPAs along roof of orbit. Here, superior SPA related to left frontal and ethmoid sinusitis has produced inferior globe displacement.

Case 26 (13 y)



Case 27 (14 y)



AMPCILLIN/SULBACTAM

1.5 g

CEFTAXIME

2 g/6h

CLINDAMYCIN

500 mg/8h

500 mg/6h

NAPCHLIN

1 g/4h

1 g/6h

AMPCILLIN

1.5 g/4h

PENICILLIN

2.1 million u/4h

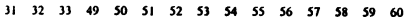
CHLORAMPHENICOL

750 mg/6h

900 mg/6h

900 mg/8h

Case 27 (14 y), continued



PENICILLIN

2.1 million u/4h

AMOXICILLIN

250 mg/8h po

• Blood

■ SPA

◆ Sinuses

■ SPA

■ Orbital drain

Aerobic

-

β-Streptococcus (gp C) (S)
Eikenella corrodens (S)

β-Streptococcus (gp C) (S)
E. corrodens (S)

β-Streptococcus (gp C) (S)
E. corrodens (S)

-

Anaerobic

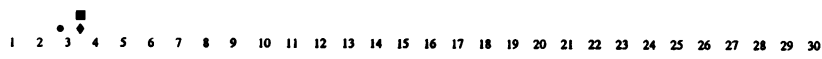
-

-

-

-

-



CEFURIXIME
1.5 g

NAFCLIXIN
500 mg

CLINDAMYCIN
650 mg/6h

CEFTIAXONE
1 g/12h

AMOXICILLIN/CLAVULANATE
250 mg/6h po

	Aerobic	Anaerobic
● Blood	-	-
■ SPA	<i>Streptococcus intermedius</i> (NT)	-
◆ Sinus	-	-

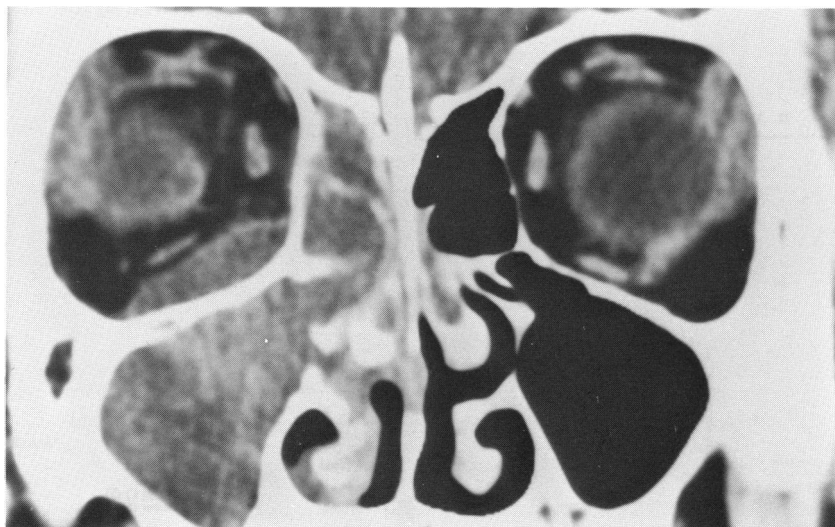
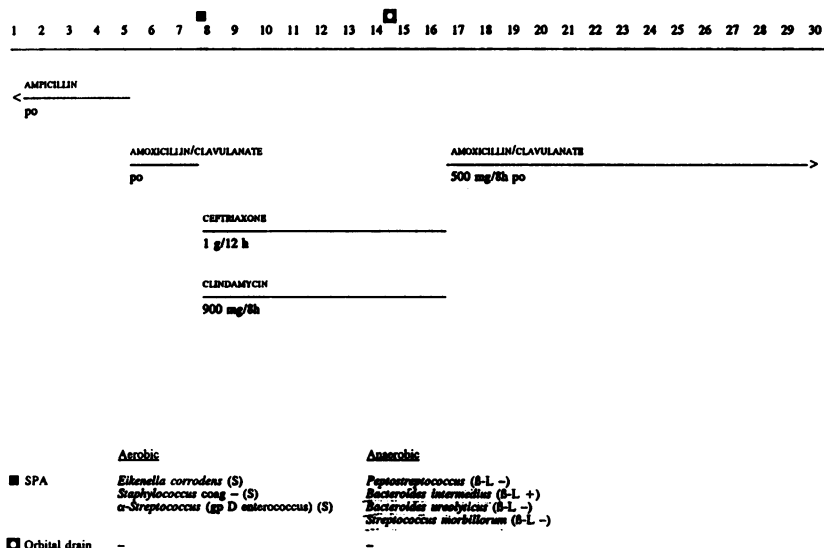


FIGURE 12
Case 28. Coronal CT scan shows inferior SPA related to right ethmoid and maxillary sinusitis.

Case 29 (15 y)



Response to Antibiotics and Organisms Isolated, By Age Group

The response to antibiotic treatment and the pathogenic constituency were evaluated with respect to three age groups: (a) under 9 years; (b) 9 through 14 years; and (c) 15 years or older (Tables III and IV). The specific age ranges and patient numbers within each group were as follows: (a) 3 months to 8 years 10 months (12 patients); (b) 9 years 3 months to 14 years 8 months (16 patients); and (c) 15 years 6 months to 30 years 5 months (9 patients).

Four classes of treatment response were considered. Infections that (1) "cleared without drainage" showed a complete clinical response to antibiotic therapy without either orbital or sinus surgery. The patients remained asymptomatic after antibiotics were discontinued through the follow-up, which ranged for this cohort from 2 months to several years. Patient 2 did undergo an elective ethmoidectomy during the month following resolution of the SPA and acute sinusitis: the surgical findings were unremarkable and the cultures were negative. Among the patients with (2) "drainage cultures negative," the timing of surgical intervention varied widely, and the earliest point at which pathogens had been eradicated from the subperiosteal space was indeterminant. These two classes of treatment response implied adequate antibiotic penetration into the subperiosteal space and susceptibility of the pathogens to the treatment regimen.

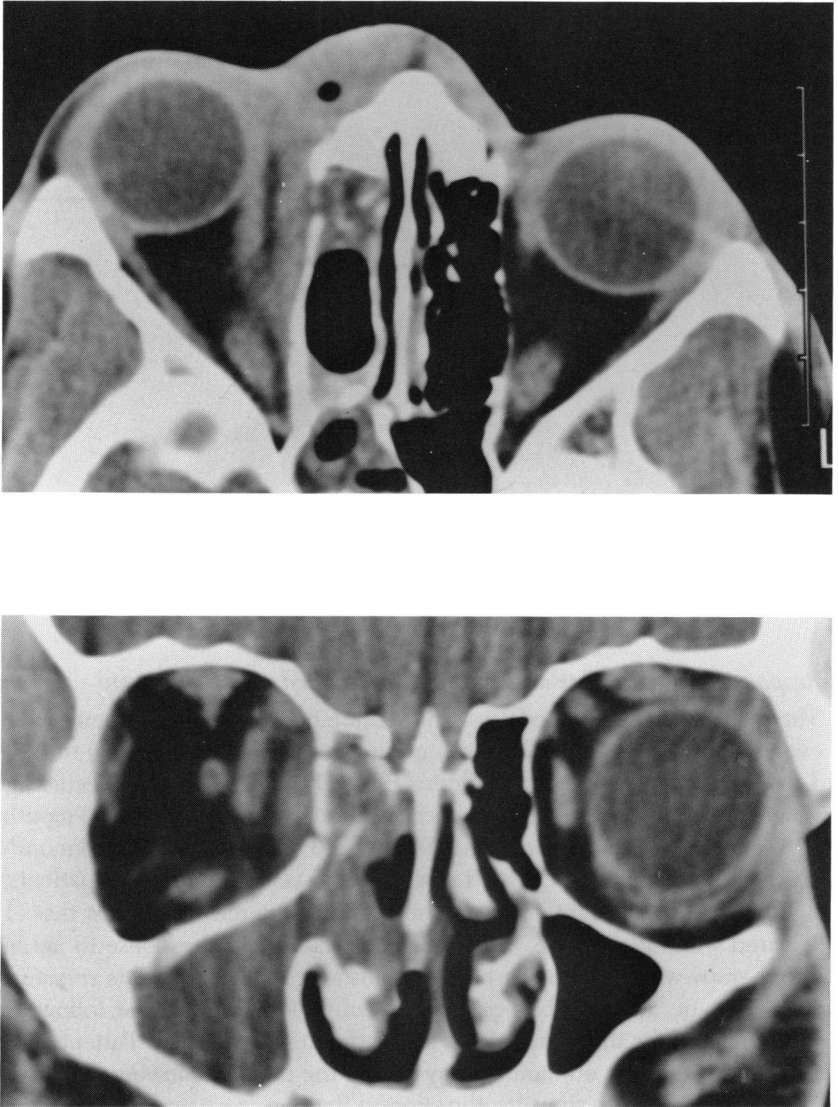


FIGURE 13

Case 29. Axial (top) and coronal (bottom) CT scans show medial SPA of moderate radiodensity. Frankly purulent material yielded mixed pathogens on culture. Cultures taken from indwelling drain 1 week later were sterile.

In the third class of treatment response (3), drainage cultures that were obtained within the first 3 days of antibiotic treatment were positive, but the infections then cleared rapidly. If any follow-up cultures were acquired, they proved negative. Allowing for the time-dependent pharmacokinetics involved (achieving therapeutic drug levels in the local environment; incorporation of the antibiotics into the microbial growth cycles), this course was considered acceptable for a "responsive" infection. It is unknown whether drainage cultures would have been negative if obtained after more than 3 days of treatment, or whether the infections would have resolved completely without surgical intervention.

TABLE III: RESPONSE TO ANTIBIOTIC TREATMENT, BY AGE GROUP

SUBPERIOSTEAL CULTURE RESULTS	NO. (%) OF PATIENTS		
	< 9 YR (n=12)	9-14 YR (n=16)	≥ 15 YR (n=9)
Cleared without drainage	3 (25.0)	2 (12.5)	0 (0.0)
Drainage cultures negative	7 (58.3)	2 (12.5)	0 (0.0)
Drainage cultures (≤ 3 days of therapy) positive, fol- low-up cultures negative	1 (8.3)	8 (50.0)	0 (0.0)
Drainage cultures (> 3 days of therapy) positive	1 (8.3)	4 (25.0)	9 (100)

In the final class (4), initial or follow-up cultures from the subperiosteal space were positive despite more than 3 days of antibiotic therapy that was generally effective in laboratory testing. Persistence of viable organisms for these intervals, in the face of qualitatively appropriate antibiotic therapy, was viewed as a "refractory" infection. While these classifications are admittedly artificial, they serve to identify the range of treatment response in this condition.

Among the 12 patients under 9 years of age, 10 patients (83%) either cleared without drainage or had negative cultures at the time of intervention (Table III). In one of the remaining two cases, the drainage cultures were positive when obtained within the first 3 days of antibiotic treatment, but the infection then cleared rapidly. In the other case, SPA and sinus cultures were positive after more than 3 days of antibiotics that were effective in vitro against the recovered pathogen. In the two patients in this age group with positive SPA cultures, single aerobes were isolated from each, and

TABLE IV: ORGANISMS ISOLATED FROM SUBPERIOSTEAL ABSCESES IN CULTURE-POSITIVE CASES, BY AGE GROUP

AGE GROUP	AEROBIC	ANAEROBIC
< 9 yr (n=2)	<i>α-Streptococcus (pneumoniae)</i> <i>Staphylococci</i> (coag +)	
9-14 yr (n=12)	<i>α-Streptococci (viridans</i> [°] ; <i>intermedius</i> [°] ; gp D†) <i>β-Streptococci</i> (gp A; gp C‡; gp D‡‡; not gp A, B, D) <i>Staphylococci</i> (coag +‡; coag - [°]) <i>Hemophilus influenzae</i> ‡ <i>Moraxella catarrhalis</i> ‡ <i>Eikenella corrodens</i> <i>Klebsiella pneumoniae</i>	<i>Bacteroides (intermedius; sp)‡</i> <i>Veillonella parvula</i> ‡
≥ 15 yr (n=9)	<i>α-Streptococci (viridans</i> ‡; <i>intermedius</i> ‡; gp D) <i>β-Streptococci</i> (gp B; anginosis- <i>constellatus</i> ; not gp A,B,D‡) <i>γ-Streptococcus</i> <i>Staphylococci</i> (coag +; coag - [°]) <i>E corrodens</i> [°]	<i>Bacteroides (bivius; oralis; mel- aninogenicus; capillosus; ureo- lyticus</i> ‡; <i>intermedius</i> ‡; <i>fragilis</i> ‡; sp) <i>V parvula</i> [°] <i>Peptostreptococci (micros</i> [°] ; <i>magnus</i> ; <i>anaerobius</i> ‡‡; sp) <i>Eubacterium (lentum; sp)</i> <i>Fusobacterium (nucleatum</i> ‡; <i>necrophorum)</i> <i>Propionibacterium sp</i> <i>Streptococcus (morbillorum</i> [°] ; <i>constellatus</i> ‡)

[°]Isolated from three to five cases in each age group.

†Isolated from sinuses only.

‡Isolated from two cases in each age group.

anaerobes were not found (Table IV).

In the age group from 9 to 14 years, a transition toward more complex infections was seen (Table III). Only 4 of 16 patients (25%) cleared without drainage or had negative cultures. Another 4 (25%) had refractory infections. Multiple organisms were recovered in individual cases, including some unexpected gram-negative species (Table IV). Among the 12 patients with positive cultures, anaerobes were isolated from three. Patient 16, at age 9 years 10 months, was the youngest in the series from whom anaerobes were recovered.

In the final age group, 15 years or older, all nine patients had refractory infections (Table III). Polymicrobial infections were the rule, with an average of five different species isolated from each abscess—including anaerobes in every case (Table IV). Pathogens were recovered from the drainage sites of 30-year-old patient 37 for almost 4 weeks. They included a *S intermedius* that was sensitive to drugs given throughout the period. De-

Case 30 (16 y)

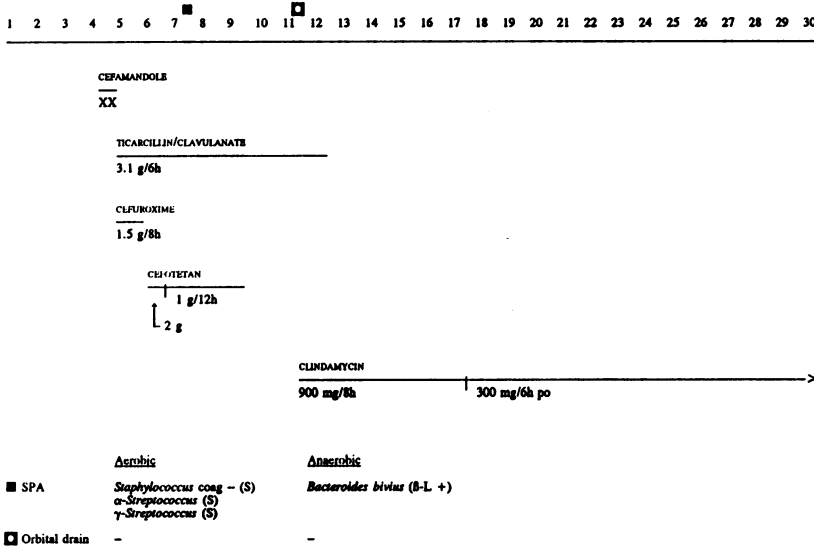
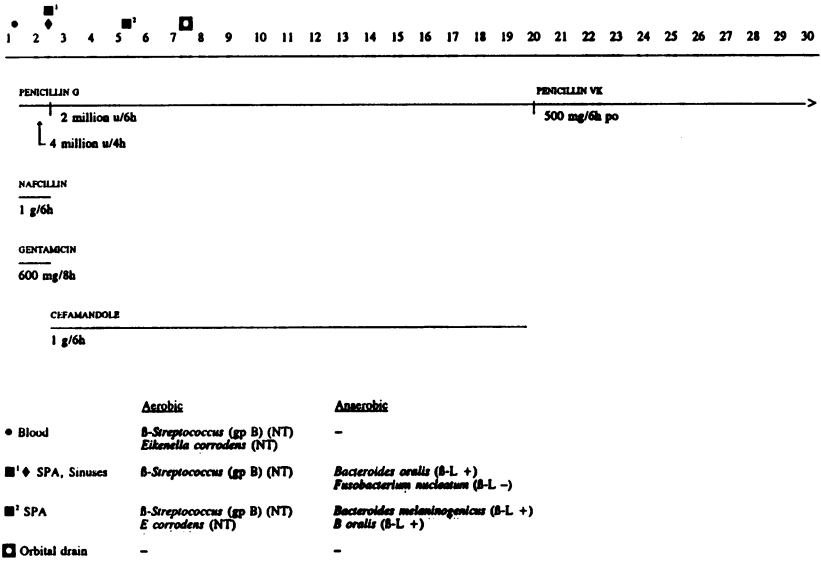


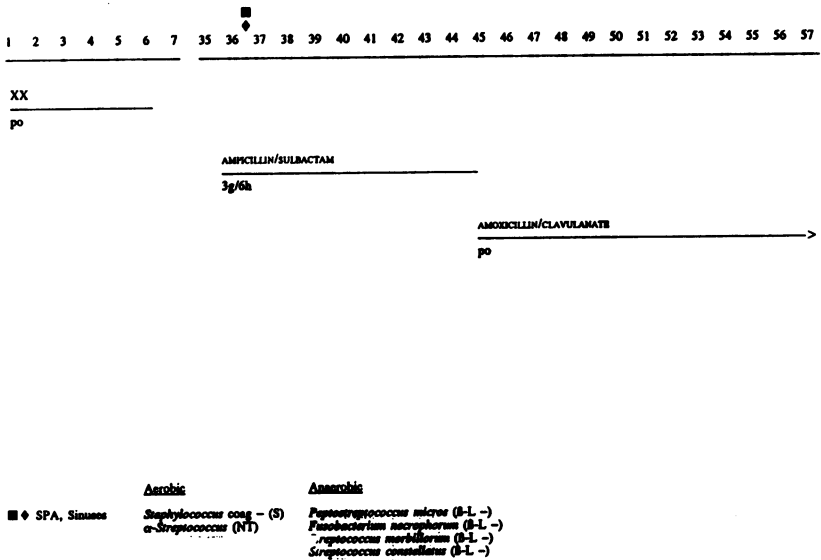
FIGURE 14

Case 30. Marked inferior globe displacement was caused by a large superior SPA. Visual acuity on left was correctable to 20/70; there was mild afferent pupillary defect; and intraocular pressure was elevated. Vision returned to normal following drainage of SPA.

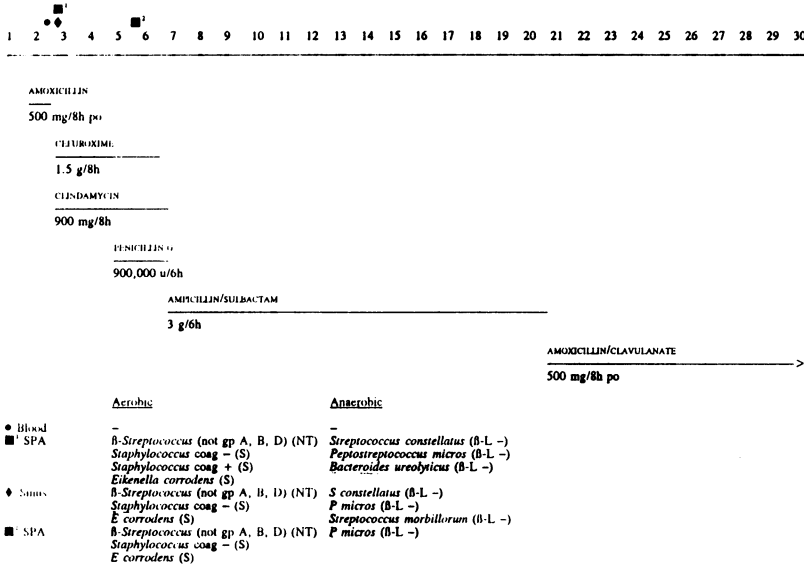
Case 31 (17 y)



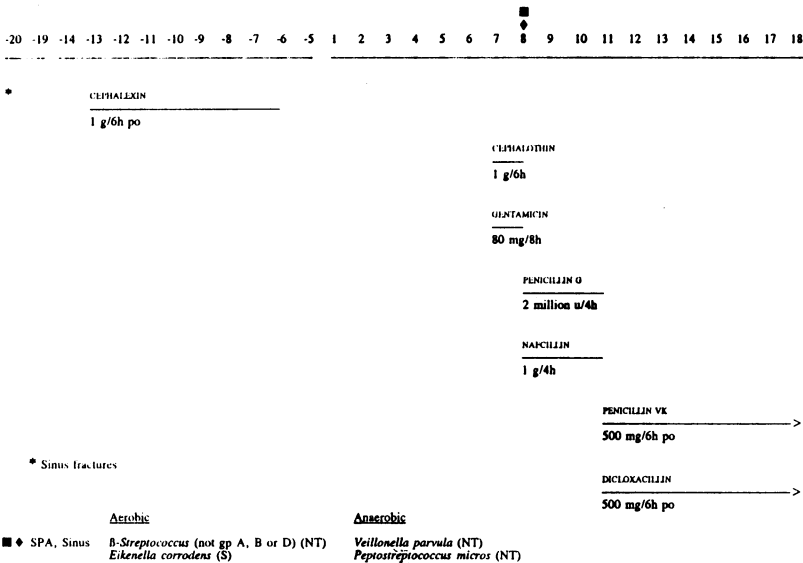
Case 32 (21 y)

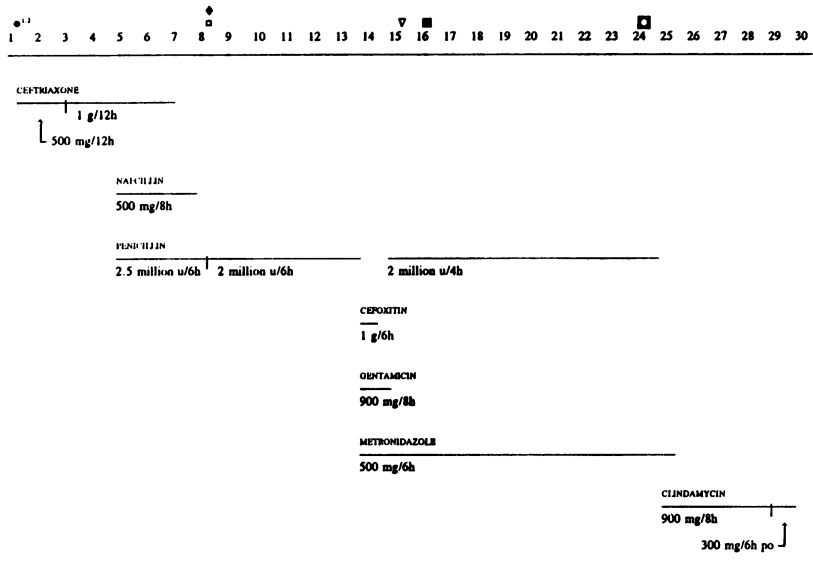


Case 33 (24 y)

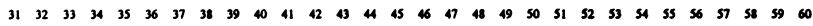


Case 34 (26 y)





Case 35 (26 y), continued



	<u>Aerobic</u>	<u>Anaerobic</u>
● ¹ Blood	<i>α-Streptococcus (viridans)</i> (S)	-
● ² Blood	<i>α-S viridans</i> (S)	-
◆ Sinus	<i>α-S viridans</i> (S)	<i>Peptostreptococcus anaerobius</i> (B-L -) <i>Bacteroides fragilis</i> (B-L +)
□ Preseptal abscess	<i>α-S viridans</i> (NT)	<i>P. anaerobius</i> (B-L -) <i>B. fragilis</i> (B-L +)
▽ Preseptal wound	<i>Streptococcus intermedius</i> (NT)	<i>Bacteroides</i> sp (B-L +) <i>Bacteroides</i> sp (B-L -)
■ SPA	<i>S MG-intermedius</i> <i>Streptococcus anginosus-constellatus</i>	<i>Bacteroides intermedius</i> (B-L +) <i>Bacteroides</i> sp (B-L +) <i>Bacteroides</i> sp (B-L -) <i>Veillonella parvula</i> (B-L -)
□ Orbital drain	-	-

CLINDAMYCIN
300 mg/6h po

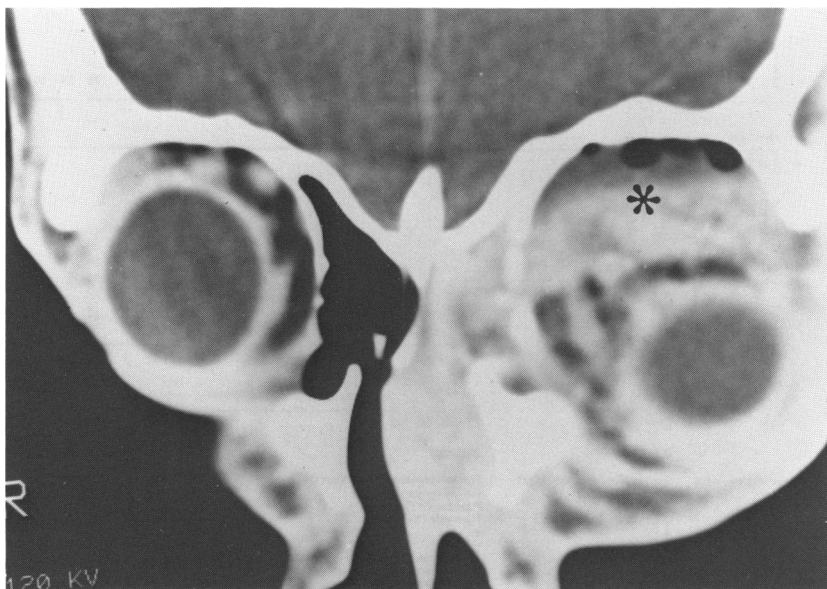
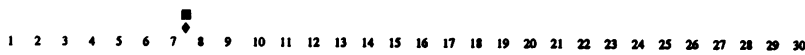


FIGURE 15

Case 35. Large superior SPA (asterisk) and sinusitis in 26-year-old with dental abscess, after 2 weeks of intravenous antibiotic treatment elsewhere. Bacterial synergy may have supported viability of mixed pathogens.

Case 36 (30 y)



AMPCILLIN
po

CEPHALOXIN
1 g/6h po

NAPICILLIN
2 g/6h

GENTAMICIN
60 mg/8h im

PENICILLIN G
1 million u/4h

CEPHALOTHIN
1 g/6h

Aerobic

Anaerobic

■ SPA

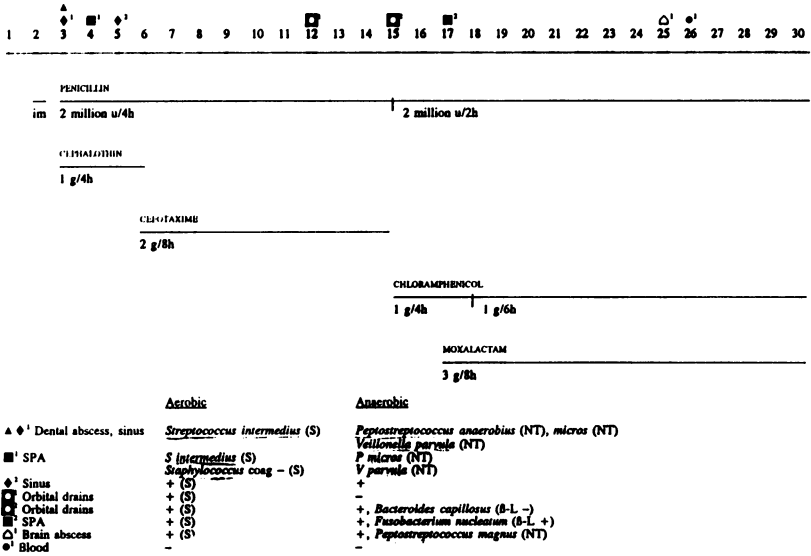
-

Eubacterium sp (NT)

◆ Sinus

-

Eubacterium sp (NT)



Case 37 (30 y), continued

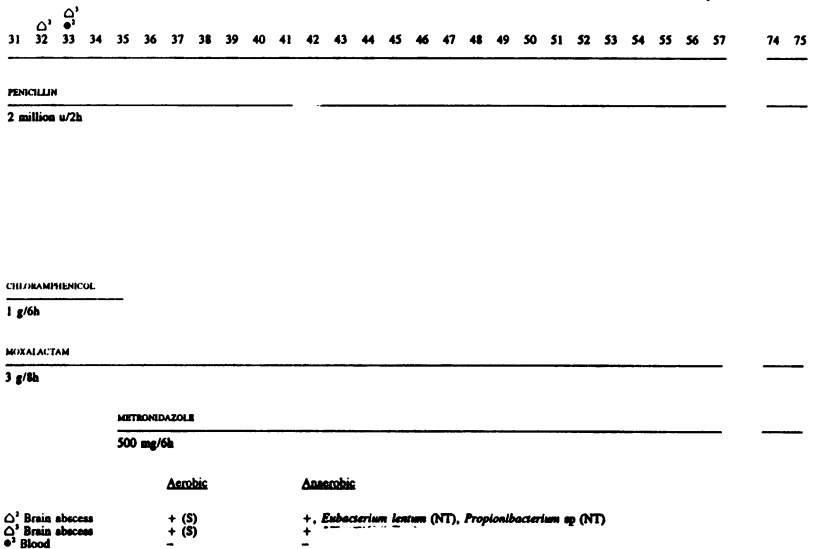




FIGURE 16

Case 37. Persistent globe displacement and proptosis 2 weeks after initial drainage of superior and medial SPAs. Purulent drainage continued to be culture-positive, yielding organisms sensitive *in vitro* to antibiotic regimen.

spite early and repeated drainage and appropriate drugs, a brain abscess developed and was slow to clear (Fig 17). Patient 35, a 26-year-old woman, had fulminant pansinusitis and an SPA that began with a periapical dental abscess (Fig 15). She was referred after a 2-week course of intravenous penicillin and a cephalosporin. Drainage of the SPA yielded two aerobic streptococcal species that were each sensitive to the drugs given. However, cultures also yielded two beta-lactamase producing anaerobes, which may have blocked the effect of the antibiotics against the streptococci.

Although every anaerobic isolate was not tested for beta-lactamase activity, the enzyme was confirmed in species recovered from six patients in the series.

Table V lists the specific SPA culture results in each case. The cases are ordered by age, and the trend toward more complex constituencies in older children and adults can be seen.



FIGURE 17

Case 37. Right frontal lobe abscess (*asterisk*) developed despite appropriate antibiotics and repeated drainage of SPA and sinuses

TABLE V: SUBPERIOSTEAL CULTURE RESULTS

PATIENT/SEX/AGE	CULTURE	
	AEROBIC	ANAEROBIC
1/M/3 mo	<i>Staphylococcus aureus</i>	—
2/M/18 mo°	...	—
3/M/2 y	—	—
4/F/2 y°	...	—
5/M/2 y	<i>Streptococcus pneumoniae</i>	—
6/M/4 y	—	—
7/F/6 y	—	—
8/F/6 y	—	—
9/F/6 y	—	—
10/M/8 y°	...	—
11/M/8 y	—	—
12/M/8 y	—	—
13/M/9 y	<i>Hemophilus influenzae</i>	—
14/M/9 y	<i>Staphylococcus coag +</i>	—
15/M/9 y	<i>Staphylococcus coag -</i> <i>H influenzae</i> † <i>Streptococcus faecalis</i> † <i>Streptococcus faecium</i> † <i>Streptococcus avium</i> †	—
16/F/9 y	β - <i>Streptococcus</i> (gp C) α - <i>Streptococcus</i> †	<i>Bacteroides intermedius</i>
17/M/9 y	—	—
18/F/10 y	α - <i>Streptococcus</i> (gp D enterococcus)† <i>Streptococcus MG-inter-</i> <i>medius</i> †	—
19/M/10 y	—	—
20/F/10 y	α - <i>Streptococcus (viridans)</i> <i>Staphylococcus coag +</i> †	<i>Bacteroides sp</i> † <i>Veillonella parvula</i> †
21/F/10 y°	...	—
22/M/12 y°	...	—
23/M/13 y	<i>Streptococcus intermedius</i>	—
24/M/13 y	<i>Staphylococcus coag -</i> α - <i>Streptococcus (viridans)</i> <i>Moraxella catarrhalis</i> †	—
25/M/13 y	β - <i>Streptococcus</i> (gp A) <i>S faecium</i> † <i>Staphylococcus coag -</i> †	—
26/M/13 y	<i>Staphylococcus coag -</i> α - <i>Streptococcus (viridans)</i> β - <i>Streptococcus</i> (not gp A, B, or D) <i>Klebsiella pneumoniae</i>	<i>Bacteroides sp</i>
27/F/14 y	β - <i>Streptococcus</i> (gp C) <i>Eikenella corrodens</i>	—
28/M/14 y	<i>S intermedius</i>	—

29/M/15 y	<i>E. corrodens</i> <i>Staphylococcus</i> coag - α - <i>Streptococcus</i> (gp D enterococcus)	<i>Peptostreptococcus</i> <i>B. intermedius</i> <i>Bacteroides ureolyticus</i> <i>Streptococcus morbillorum</i>
30/F/16 y	<i>Staphylococcus</i> coag - α - <i>Streptococcus</i> γ - <i>Streptococcus</i>	<i>Bacteroides bivius</i>
31/M/17 y	β - <i>Streptococcus</i> (gp B) <i>E. corrodens</i>	<i>Bacteroides oralis</i> <i>Fusobacterium nucleatum</i> <i>Bacteroides melaninogenicus</i>
32/M/21 y	<i>Staphylococcus</i> coag - α - <i>Streptococcus</i>	<i>Peptostreptococcus micros</i> <i>Fusobacterium necrophorum</i> <i>S. morbillorum</i> <i>Streptococcus constellatus</i>
33/M/24 y	β - <i>Streptococcus</i> (not gp A, B, D) <i>Staphylococcus</i> coag - <i>Staphylococcus</i> coag + <i>E. corrodens</i>	<i>S. constellatus</i> <i>P. micros</i> <i>B. ureolyticus</i> <i>S. morbillorum</i> †
34/M/26 y	β - <i>Streptococcus</i> (not gp A, B or D) <i>E. corrodens</i>	<i>V. parvula</i> <i>P. micros</i>
35/F/26 y	<i>S. MG-intermedius</i> <i>Streptococcus anginosus-</i> <i>constellatus</i>	<i>Peptostreptococcus</i> <i>anaerobius</i> † <i>Bacteroides fragilis</i> † <i>B. intermedius</i> <i>Bacteroides</i> sp <i>V. parvula</i>
36/F/30 y	—	<i>Eubacterium</i> sp
37/M/30 y	<i>S. intermedius</i> <i>Staphylococcus</i> coag -	<i>P. anaerobius</i> <i>P. micros</i> <i>Peptostreptococcus magnus</i> <i>V. parvula</i> <i>Bacteroides capillosus</i> <i>F. nucleatum</i> <i>Eubacterium lentum</i> <i>Propionibacterium</i> sp

*Drainage was not performed in patients 2, 4, 10, 21, and 22.

†Recovered from sinus only.

Subperiosteal Material and CT

Among the 32 patients who underwent surgical drainage, 25 (78%) had frankly purulent material in the subperiosteal space. Seven patients (22%) had granulation tissue and/or hemorrhagic fluid, without frank pus (cases 1, 6, 12, 15, 17, 24, and 36). The absence of pus could not be equated with sterility, however, since cultures in four of seven patients with nonpurulent material were positive—indicating active infection (cases 1, 15, 24, and 36). The subperiosteal material was not related to the timing of drainage, or to the size or appearance of the collections on imaging studies.

The following cases with granulation tissue and/or hemorrhagic fluid (Figs 18 through 20) can be compared with others in the series in which frank pus was present (Figs 2, 8, 11 to 13, 15, 24 to 27). Each of these subperiosteal materials may have a radiodensity that varies from low to medium. In judging densities, the subperiosteal space can be compared with the vitreous cavity to compensate for variable windows of exposure. The juxtaposition of a contrast-enhanced periorbita with a very low density subperiosteal collection may be fairly reliable for fluid, but even this picture will not differentiate hemorrhage from purulence (Figs 19 and 24).

CT and Clinical Course

Among the five patients who recovered completely without drainage (cases 2, 4, 10, 21, and 22), the imaging features were not particularly distinctive (Figs 21 through 23). While the nature of the subperiosteal material was indeterminant in those cases, a subperiosteal collection could usually be differentiated from simple inflammatory edema of the medial orbit by a layer with the radiodensity of normal fat between the periorbita and the medial rectus muscle.

Analysis of serial scans in individual cases revealed several interesting findings. The size of the subperiosteal collections often increased during the first few days of intravenous antibiotic therapy regardless of the ultimate response to treatment (Figs 20 and 22 through 26). In some refractory cases, the CT findings worsened despite surgical evacuation of the SPA and sinuses (Fig 27). In most of the cases in the series with follow-up scans, contraction of the subperiosteal space lagged behind clinical improvement by several days to a few weeks.

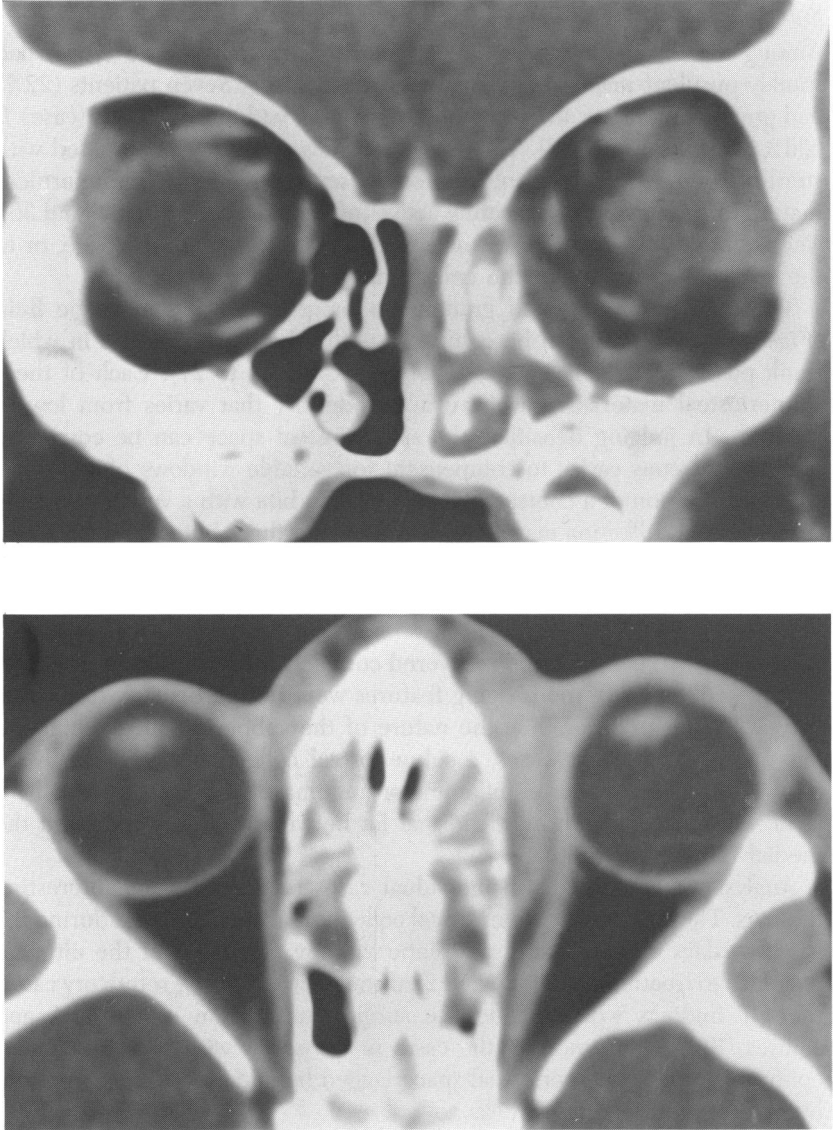


FIGURE 18

Case 1 (top) and case 6 (bottom): Subperiosteal space in both patients contained mainly granulation tissue, with negligible fluid. Case 1 was culture-positive; case 6 was culture-negative.

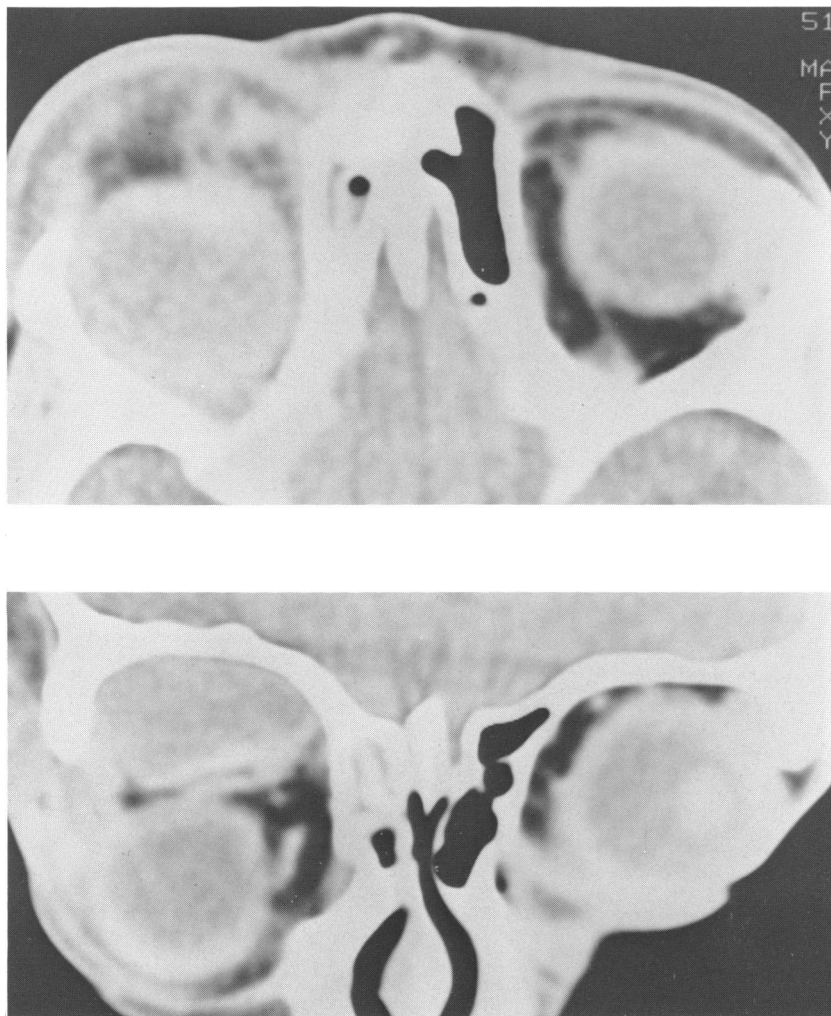


FIGURE 19

Case 17. Axial (top) and coronal (bottom) CT scans show large superior subperiosteal collection secondary to acute ethmoiditis. Despite size, no purulent material was found, and hemorrhagic fluid accounted for most of contents.

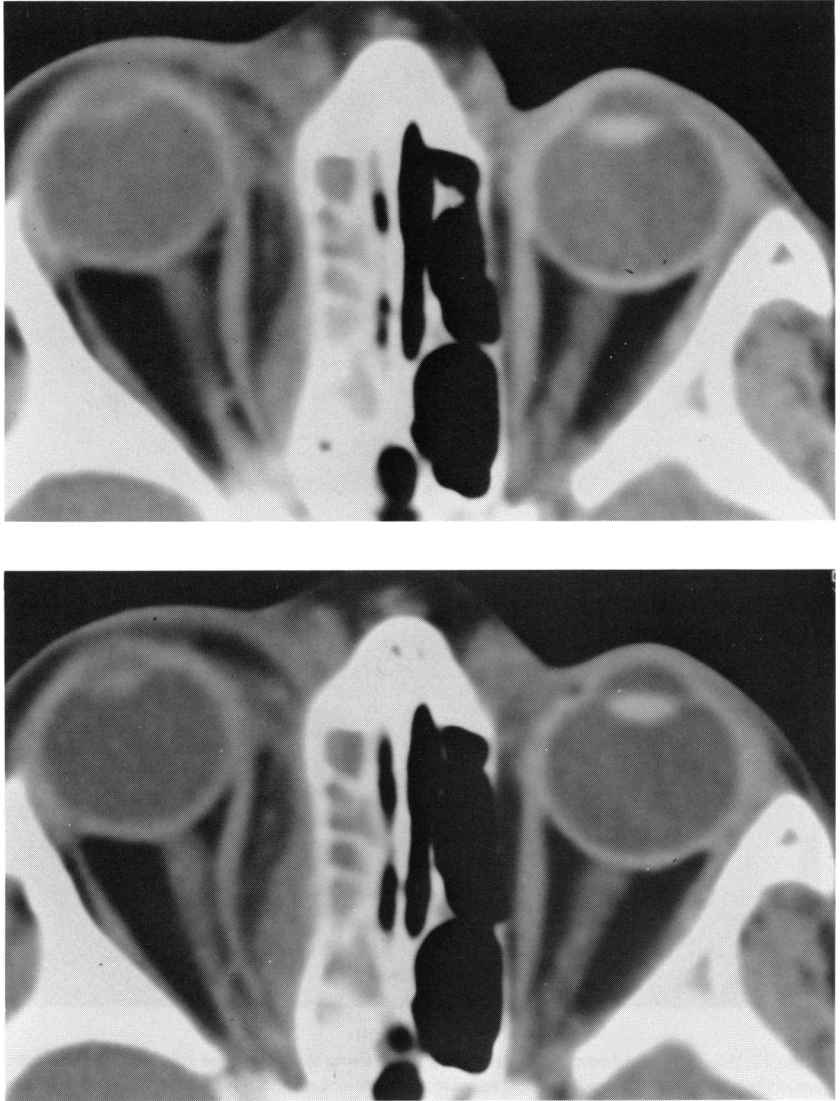


FIGURE 20

Case 12. Posterior medial subperiosteal collection of hemorrhagic fluid and edematous tissue. Collection enlarged in interval between admission CT scan (top) and scan obtained 2 days later (bottom). Drainage cultures were negative.

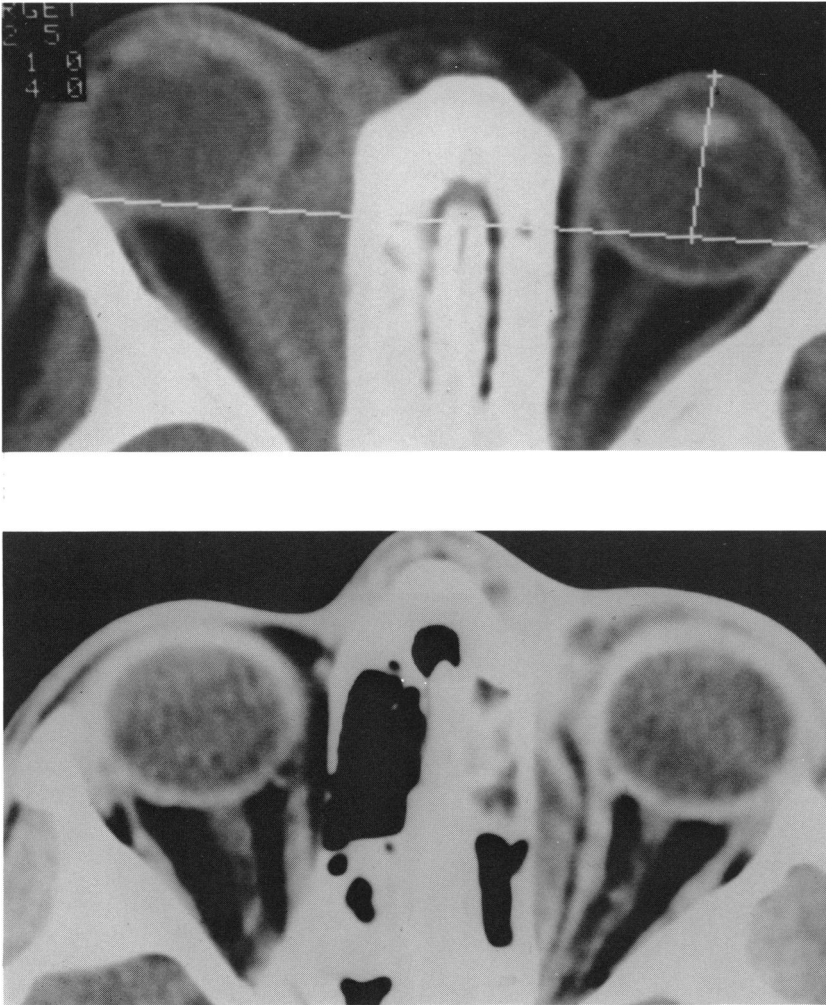


FIGURE 21

Subperiosteal collections that cleared without surgical drainage (class 1 response to treatment). Top (case 2): Although periorbita cannot be seen distinctly, anterior contour of mass suggests periosteal elevation. Bottom (case 22): Distinct fat density nasal to medial rectus muscle distinguishes subperiosteal collection from simple inflammatory edema of orbital fat.

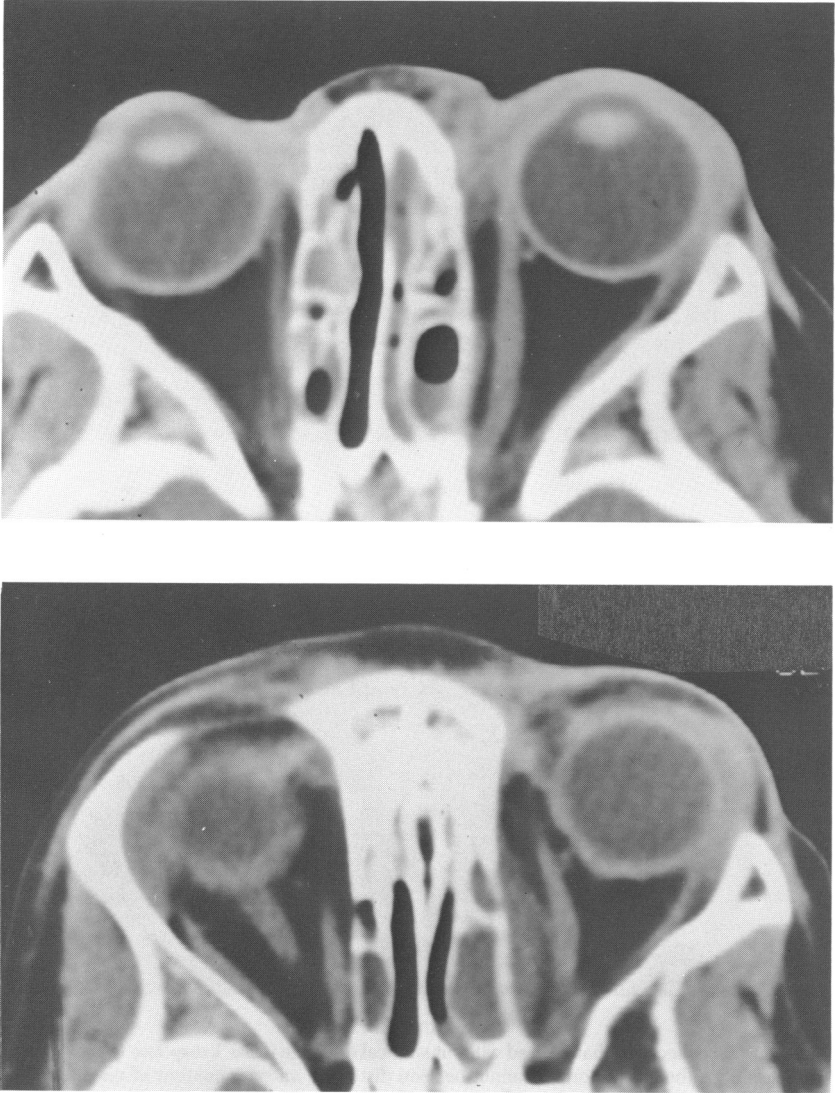


FIGURE 22

Case 4. Serial CT scans in patient who recovered completely without drainage (class 1). Top: Admission scan following 1 day of oral antibiotics, but prior to intravenous therapy. Bottom: After 4 days of intravenous antibiotics.



FIGURE 23

Case 4 (continued). Top: After 9 days of intravenous antibiotic therapy. Bottom: After total of 12 days of intravenous and 7 days of oral therapy. Note progressive enlargement of subperiosteal collection in initial phases of effective intravenous therapy. Subperiosteal location of process was confirmed by fat density between it and medial rectus muscle.

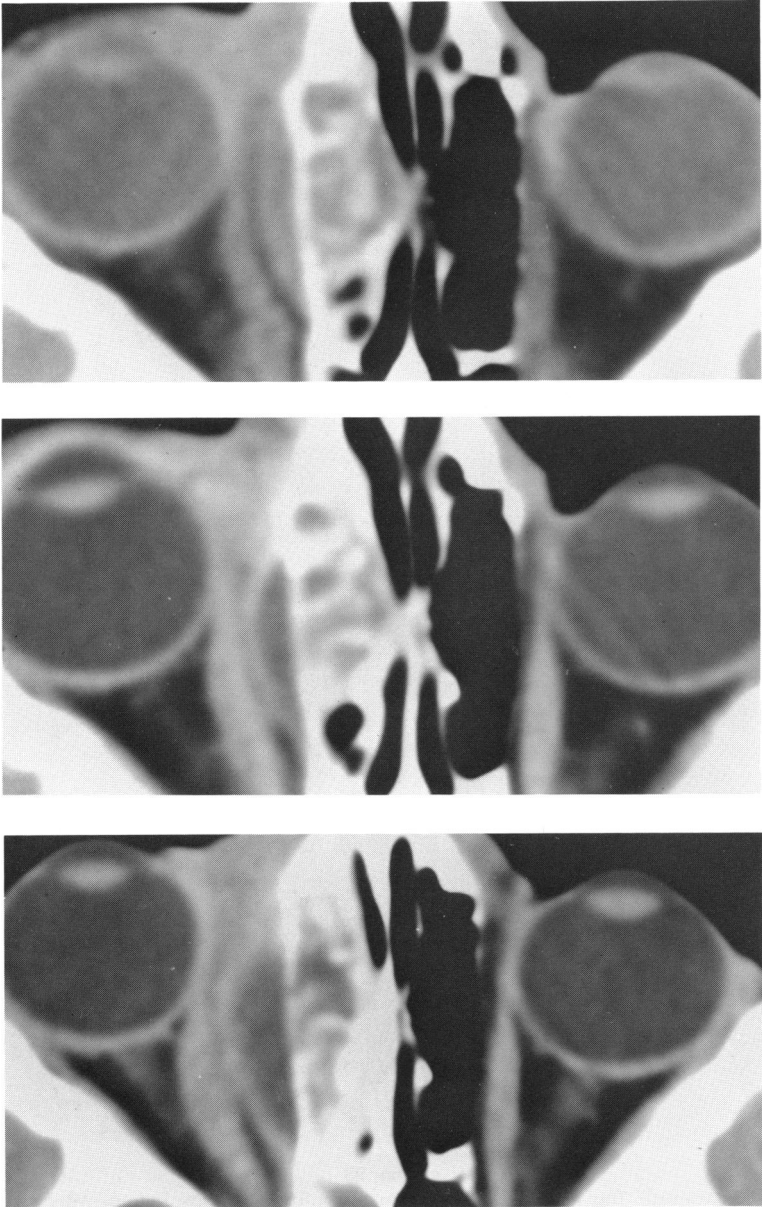


FIGURE 24

Case 9. Progression during effective antibiotic treatment. Top and Center: Before and after intravenous contrast infusion in same admission CT study. Bottom: Following 3 days of intravenous therapy and just prior to surgical evacuation, which yielded negative cultures (class 2 response to treatment).

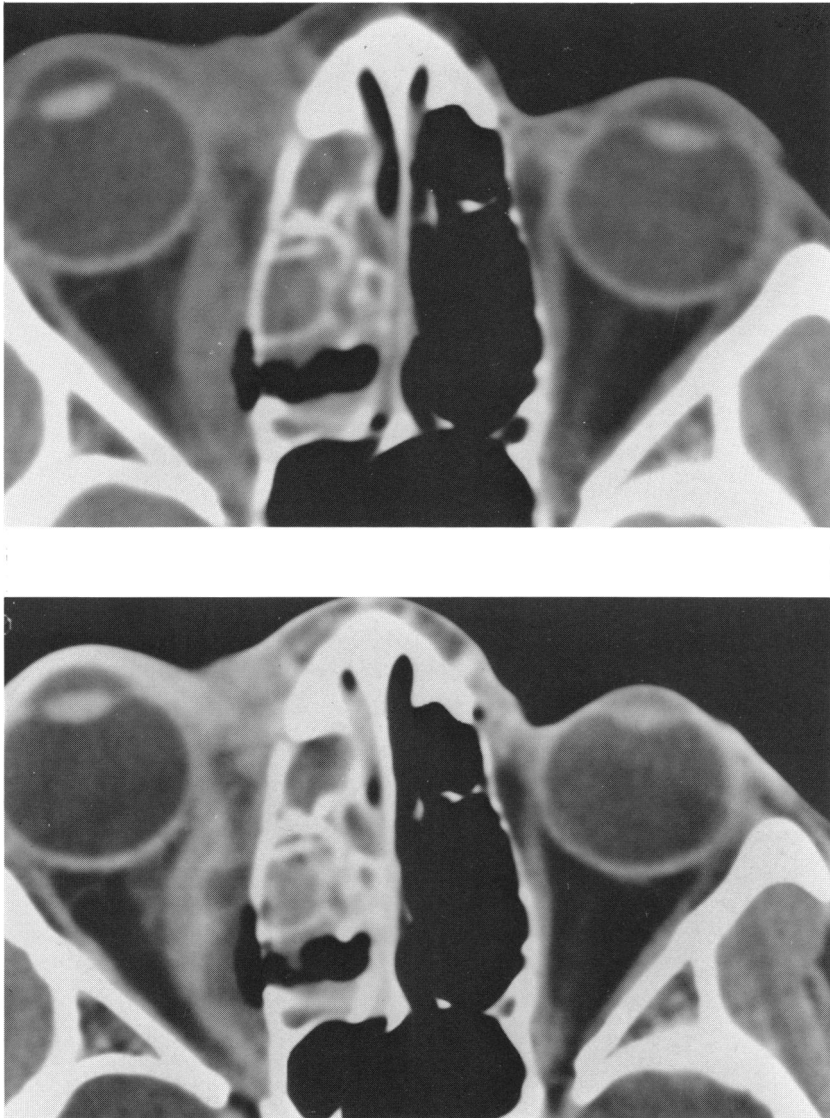


FIGURE 25

Case 16. Serial scans (class 3 response to treatment). Top: Admission scan, without contrast enhancement. Note continuity of air between ethmoid cells and subperiosteal space. Bottom: After 24 hours of intravenous antibiotics, with contrast enhancement.

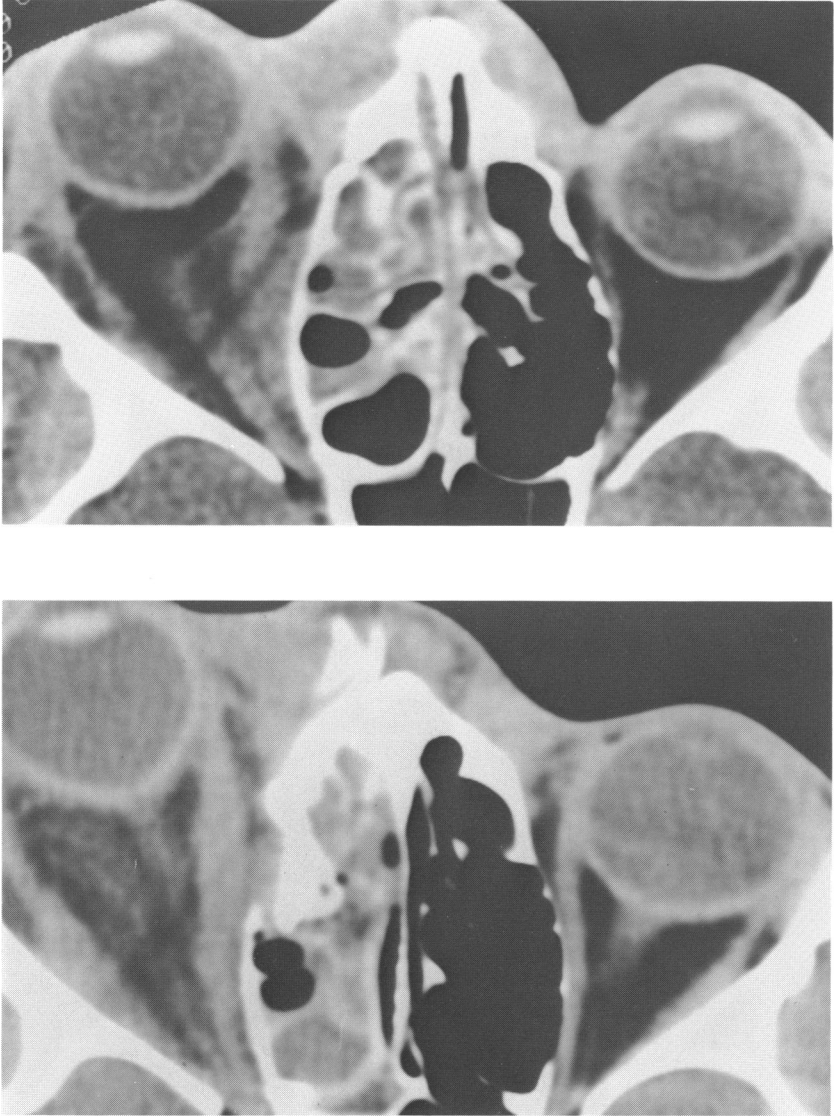


FIGURE 26

Case 16 (continued). Top: Following 2½ days of intravenous antibiotics, and just prior to surgical evacuation. Note decreased aeration of sinuses and subperiosteal space and enlargement of collection compared with admission scan. Cultures yielded alpha- and beta-streptococci and *Bacteroides intermedius*. Bottom: 3 days following surgical drainage. Note little qualitative change in findings at this postoperative stage. Full recovery ensued.

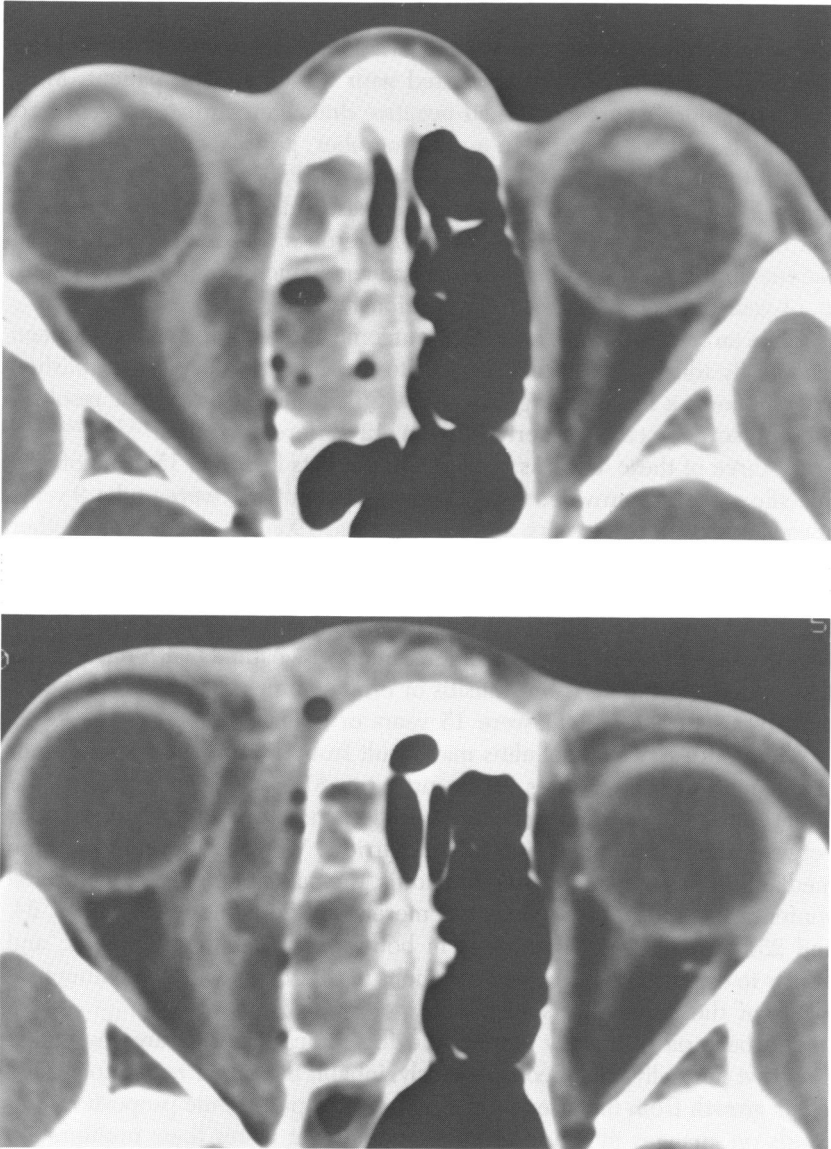


FIGURE 27

Case 33. Serial scans (class 4 response to treatment). Top: Admission scan shows severe proptosis related to a medial and inferior SPA (a large portion is below plane of scanning). Surgical drainage was performed on day of admission. Bottom: 3½ days after initiation of antibiotics and initial drainage. Proptosis has increased. Second surgical procedure yielded positive aerobic and anaerobic cultures.

DISCUSSION

In this series of 37 patients with SPA, variations in the bacteriology and the response to treatment were associated with the age of the patient. Most children under 9 years of age had negative drainage cultures or recovered completely without surgery. In a small number, positive cultures obtained early in the illness revealed only single aerobes. Patients 15 years of age or older all had positive cultures despite at least 3 days of antibiotic therapy that was generally effective *in vitro*. Anaerobes were isolated from all patients in this group, and all but one had a polymicrobial infection. The 9- to 14-year-old cohort showed a transition between these extremes.

While an association between SPA outcome and patient age has not been specifically addressed by other investigators, composite analysis of published data supports a linkage. A group of 44 CT-diagnosed SPAs that resolved without surgery can be derived from 12 different studies.^{1,17-24,26,64,65} Forty-three of these 44 SPAs occurred in patients less than 15 years of age. Specific ages were provided for 31 of the 44 patients: 19 were under 9 years of age; 11 were 9 to 14 years; and 1 patient was 19 years of age. At the other extreme, most patients with refractory or complicated SPAs have been older children or adults. Among 159 patients with orbital complications of sinusitis, 4 had permanent blindness.¹⁵ All four had surgically confirmed SPAs, and all were 15 years of age or older. Among 13 patients with intracranial abscesses that resulted from sinusitis or orbital abscesses, 2 patients were 9 to 14 years of age and 11 were 15 years or older.⁷⁴

While diffuse orbital cellulitis may result from the phlebitic extension of organisms from the sinuses to the orbit, an SPA seems to represent the direct spillage or overflow of bacteria and inflammatory products through or between the insubstantial sino-orbital barriers. Viewed differently, when a medial SPA has resulted from ethmoiditis, the partition between the orbital contents and the infected sinus has merely shifted laterally (Figs 2, 8, 24, and 25). The bacterial pathogens in both compartments are similar, and efforts to explain age-associated variations in SPA begin with the pathophysiology of the underlying sinusitis.

The bacteria ultimately responsible for clinical sinusitis are the varied flora that normally, and inconspicuously, inhabit the upper respiratory tract. Their growth from inconsequential numbers to pathogenic proportions depends on changes in the local environment that foster their proliferation (Table I).^{27,30,69,79-83} In sinusitis, the bacteria do not initiate the sinus obstruction: their proliferation results from it, and their inflammatory products potentiate it. This type of infection, in which the relationships within an already complex biosystem are altered by environmental changes, differs from many ophthalmic infections. The latter may involve the introduction of

a pathogenic inoculum of almost any organism into a previously sterile environment (eg, endophthalmitis), or a particularly virulent exogenous microbe in an area with a normal flora (eg, conjunctivitis). These differences also influence the manner in which the conditions can be investigated. For example, the diverse microbiology of the upper airway that ultimately generates acute sinusitis would minimize the clinical relevance of an experimental model of SPA that employed a single pathogen.

The predominant organisms associated with sinusitis vary with the degree of physiological derangement (Table I). As oxygen tension is reduced, anaerobic flora assert themselves and join aerobes to produce mixed infections. The potential virulence of these bacteria is only realized as the altered environment allows them to proliferate with abandon. As noted, the biphasic transition in sinus pathogens may be a function of time, but also of severity. These variations may explain the seeming contradictions between the microbiology of acute sinusitis as reported in classic studies, and the pathogens recovered directly from the subperiosteal space of many patients in this and other reports. Well-designed microbiologic studies of acute sinusitis employed pretreatment diagnostic aspiration of maxillary sinuses in ambulatory patients with uncomplicated sinusitis—which usually cleared rapidly with antibiotics.³³⁻³⁶ Those studies generally revealed monomicrobial infections caused by *S pneumoniae*, *H influenzae*, or *M catarrhalis*. On the other hand, SPA drainage cultures have been derived from patients with fulminant and complicated acute sinusitis who have come to both orbital and sinus surgery.^{2,3,14} In those studies, patients with positive cultures had mixed infections involving staphylococci, beta-streptococci, and anaerobes.

When the sequential factors in bacterial sinusitis are considered (Table I), the degree of obstruction of sinus ostia would seem to influence the gas tensions and the pathogens within the chambers. Complete obstruction with predominantly anaerobic conditions might follow severe allergic or viral inflammation of the mucosa that rims the ostia. In addition, patients with narrow ostia relative to the cavities that must be drained might be at greater risk.

In this series, anaerobes were not isolated from the drainage cultures of children under 9 years of age. The pathogenic constituencies in younger children were simpler in general, with single aerobes recovered from four of the six culture-positive patients aged 9 years or younger. In contrast, all patients older than 15 years had polymicrobial, mixed aerobic and anaerobic infections. While the reasons for these age-associated differences are not entirely clear, anatomic factors may play a role.

With increasing age, the sinus cavities enlarge markedly, but the ostia remain approximately the same size (Fig 28).^{47,97,98} Relative to the cavities

they must drain, the ostia of young children are wide, and those of older children and adults are narrow. The relative width of ostia in young children partially explains their greater incidence of acute sinusitis, since frequent upper respiratory infections tend to involve the nose and sinuses as a single structure.^{47,97} The same relative proportions between sinus ostia and cavities may prevent severe derangement of the physiology and promote rapid resolution. It is known, for example, that chronic sinusitis is relatively rare in patients under 16 years of age.¹² Further, by analyzing the ages of patients who *do* have chronic sinusitis, it can be seen that the frequency of anaerobic

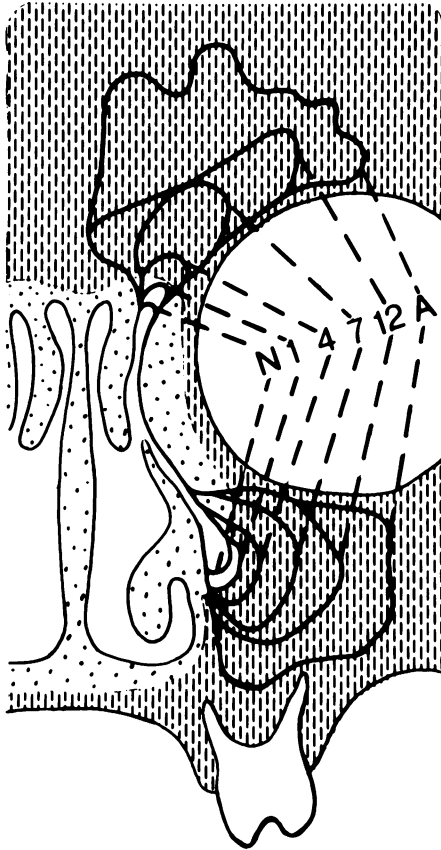


FIGURE 28

Normal enlargement of frontal and maxillary sinus cavities with increasing age (N, neonate; 1-12, age in years; A, adult) (modified from Arey LB: *Developmental Anatomy*, ed 7. Philadelphia, WB Saunders, 1974, p 528).

isolates increases with the mean age of patients in the series.^{37,67,71-73,75} We might speculate that younger children rarely achieve strict anaerobic conditions in their sinuses, while older children and adults are prone to more complete sequestration and more complex infections, even with a brief duration of symptoms.

The higher incidence of complicated SPAs in older patients may also be related to their potential for frontal sinus involvement. For the most part, orbital complications of sinusitis in the first decade result from disease in the ethmoid and maxillary sinuses.⁹ The frontal sinus appears between ages 5 and 7 years, but does not fully develop until late adolescence.^{9,86} Older children and adults can have SPAs related to ethmoid, maxillary, and/or frontal sinusitis—and the last may have a higher association with intracranial complications.⁹⁹

Although therapeutic protocols were not uniform in this series, it is still noteworthy that all of the 14 patients who recovered without drainage or had negative cultures at the time of surgery were under 15 years of age. These two responses to treatment are not equivalent, but both imply *in vivo* antibiotic efficacy. At the other end of the clinical spectrum were 14 patients with persistently viable bacteria in the subperiosteal space for more than 3 days after the initiation of antibiotics. In 13 of these 14 cases, at least one of the species isolated at surgery was sensitive *in vitro* to the previously administered antibiotics. Patients in this refractory category accounted for 8%, 25%, and 100%, respectively, among the three age groups studied (Table III).

The same anatomic differences might play a role in this trend toward more refractory infections with increasing age. An SPA and the underlying sinusitis represent a local conflict between interacting host, bacterial, and drug factors. While the correct choice of antibiotics favors the host, many other features can support the pathogens (Table II). Relative avascularity of the subperiosteal space and decreased sinus mucosal blood flow limit the penetration of antibiotics and host defense factors.^{79,90} Lack of ventilation and ischemia can reduce the effect of drugs and immune factors that do gain access.⁹¹ Among the many organisms recovered, several can enzymatically defend themselves against antibiotics and even surgical ventilation of the area.^{92,93} Mixed infections permit synergy: aerobes consume oxygen that would otherwise be toxic to most anaerobes⁷⁷; anaerobes may produce beta-lactamase, deactivating the antibiotics that are effective against aerobes in pure laboratory culture.⁹⁴

It should be noted that those factors that support the pathogens in this local conflict are strongest in mixed infections and anaerobic environments,

conditions that seem to characterize the SPAs and infected sinuses of older children and adults.

The medical management of SPA should be based on the bacteriology of that specific condition, rather than extrapolated from studies of uncomplicated sinusitis. While no simple regimen will cover every pathogen isolated in this series, several alternatives constitute reasonable presumptive intravenous therapy. Examples include ceftriaxone sodium, used alone for patients under 9 years of age, and used in combination with clindamycin phosphate for patients 9 years of age or older. This approach recognizes the role of anaerobes beyond the first decade. Single-drug options include ampicillin sodium/sulbactam sodium and ticarcillin disodium clavulanate potassium. These antibiotics are effective against beta-lactamase-producing aerobes and anaerobes, and they can be used for all age groups. Because the inventory of available drugs continually changes, knowledge of the responsible pathogens in each age group (Table IV) should help the ophthalmologist formulate an effective medical regimen with the aid of infectious disease consultants.

Surgical therapy for SPA should be influenced by several factors, including the visual status, the size and location of the SPA, intracranial complications, the sinuses involved, the presumed pathogens, and the anticipated bacterial response to antibiotic treatment. While simple algorithms cannot replace clinical judgment in integrating these variables, it should be noted that the last four factors are age-associated, and patient age can help direct therapeutic decisions.

Surgical intervention for SPA and sinusitis may involve three different approaches: (1) emergency drainage, (2) urgent drainage, and (3) expectant observation, with drainage reserved for failure to respond to antibiotics. Delayed surgery limited to sterile sinuses is a fourth option that may be elected by otolaryngologists in some cases. The management of all SPAs must involve close collaboration between ophthalmic and ENT specialists, and the specific surgical techniques were described earlier in this report.

EMERGENCY DRAINAGE

Patients of any age whose optic nerve or retinal function is compromised by the mass effect of an abscess constitute a true surgical emergency. While canthotomy and cantholysis may lower intraocular pressure, globe distortion and traction at the posterior pole will not be eliminated without evacuation of the subperiosteal space.⁵³ In such cases, surgical drainage as soon as possible is recommended.

URGENT DRAINAGE

Large SPAs that do not affect vision but cause significant discomfort should be drained promptly. Superior or inferior SPAs that have extended some distance from the ethmoid sinuses may be less likely to resolve completely, even if the sinuses clear with medical therapy (Figs 12 and 19). In these cases, drainage is performed within the first 24 hours of presentation, without regard to patient age.

All patients with intracranial complications or frontal sinusitis are also managed with prompt drainage. For those with intracranial infection, the central nervous system penetration of presumptive antibiotics must be considered, and the SPA should be drained for specific identification of the pathogens. These patients, as well as those with high-risk frontal sinusitis, are likely to be beyond the first decade of life.

If complex infections that include anaerobes are suspected, prompt drainage and ventilation are important to restore the aerobic conditions that discourage bacterial proliferation and enhance defense mechanisms. The youngest patient in this series with anaerobic isolates was 9 years 10 months of age. Therefore, this approach is used for patients 9 years of age or older and for all patients with a known dental source of the infection.

EXPECTANT OBSERVATION

While arguments have been advanced for draining all SPAs, the full recovery with antibiotics alone of almost 50 patients with CT criteria for SPA cannot be ignored.^{1,17-24,26,64,65} Concerns that surgical drainage may have seeded intracranial abscesses also must be considered.^{1,22} Based on the age-related bacteriologic findings of this study and the clinical outcomes reported by others, an expectant approach is taken to patients under 9 years of age, in whom simple infections might be predicted. This approach requires careful monitoring for an afferent pupillary defect, at least as often as every 6 hours, while the patient is hospitalized for intravenous antibiotics. In the course of close observation, the surgical option would still be pursued: if an afferent defect developed at any time, if fever did not abate within 36 hours of appropriate intravenous antibiotics, if there was clinical deterioration despite 48 hours of such treatment, or if there was no improvement despite 72 hours of appropriate therapy.

In making these judgments, CT improvement should be expected to lag behind that of the clinical picture. In fact, the CT findings may worsen during the first few days of hospitalization despite successful treatment with antibiotics alone. The time-dependent pharmacokinetics of antibiotic therapy must be considered. For example, there may be some clinical deterioration during the first 12 to 24 hours of antibiotic therapy, as tissue levels

increase and drugs are incorporated into microbial growth cycles. Gradual improvement may follow. A follow-up CT scan obtained 2 to 3 days after the admission scan may show SPA progression that occurred prior to sterilization of the subperiosteal space and sinuses (Figs 20 and 22 through 24). Contraction of the subperiosteal space will occur very slowly, over several days to weeks, despite obvious clinical improvement. While CT scans should not take precedence over clinical judgement in dictating therapy, at least one follow-up scan should be performed to rule out frontal lobe abscesses that may be clinically silent.

The decision to perform an elective ethmoidectomy on patients under 9 years of age whose SPAs have resolved with antibiotic therapy rests with the otolaryngologist. This option might be pursued if there have been repeated episodes of ethmoiditis, with or without orbital complications.

The criteria for expectant observation may seem fairly restrictive: no visual compromise; medial SPAs of modest size; no intracranial or frontal sinus involvement; under 9 years of age. However, about one fourth of the patients in this retrospective review would have conformed to that profile.

SUMMARY

The clinical course of SPA of the orbit is associated with the age of the patient. That association might be explained through a series of intermediate relationships: the clinical course correlates with the bacterial constituency, the bacterial constituency is related to physiologic derangement within the sinuses, the physiologic derangement may vary with the degree of obstruction of the sinus ostia, and the ostial caliber relative to the volume of the cavity that must be drained decreases with patient age into late adolescence.

The controversy between pediatricians and surgeons over the appropriate indications for drainage might be resolved with the acknowledgment that each side is correct on the basis of the patient populations treated. It is hoped that recognition of the age-related variations in SPA will permit a more systematic approach to the management of this complex infectious disease.

REFERENCES

1. Goodwin WJ Jr, Weinshall M, Chandler JR: The role of high resolution computerized tomography and standardized ultrasound in the evaluation of orbital cellulitis. *Laryngoscope* 1982; 92:728-731.
2. Schramm VL Jr, Curtin HD, Kennerdell JS: Evaluation of orbital cellulitis and results of treatment. *Laryngoscope* 1982; 92:732-738.

3. Goodwin WJ: Orbital complications of ethmoiditis. *Otolaryngol Clin North Am* 1985; 18:139-147.
4. Chandler JR, Langenbrunner DJ, Stevens ER: The pathogenesis of orbital complications in acute sinusitis. *Laryngoscope* 1970; 80:1414-1428.
5. Smith AF, Spencer JF: Orbital complications resulting from lesions of the sinuses. *Ann Otol Rhinol Laryngol* 1948; 57:5-27.
6. Hubert L: Orbital infections due to nasal sinusitis: Study of 114 cases. *NY State J Med* 1937; 37:1559-1564.
7. Harris GJ: Subperiosteal abscess of the orbit. *Arch Ophthalmol* 1983; 101:751-757.
8. Fairbanks DNF, Milmoe GJ: The diagnosis and management of sinusitis in children. Complications and sequelae: An otolaryngologist's perspective. *Pediatr Infect Dis* 1985; 4:575-578.
9. Hornblass A, Herschorn BJ, Stern K, et al: Orbital abscess. *Surv Ophthalmol* 1984; 29:169-178.
10. Spires JR, Smith RJH: Bacterial infections of the orbital and periorbital soft tissues in children. *Laryngoscope* 1986; 96:763-767.
11. Teele DW: Management of the child with a red and swollen eye. *Pediatr Infect Dis* 1983; 2:258-262.
12. Bluestone CD, Stool SE (eds): *Pediatric Otolaryngology*. Philadelphia, WB Saunders, 1983, pp 793-794.
13. Hirst LW, Thomas JV, Green WR: Periocular infections, in GC Mandell, RG Douglas Jr, JE Bennett (eds): *Principles and Practice of Infectious Diseases*, ed 2. New York, John Wiley & Sons, 1985, p 770.
14. Jackson K, Baker SR: Clinical implications of orbital cellulitis. *Laryngoscope* 1986; 96:568-574.
15. Patt BS, Manning SC: Blindness resulting from orbital complications of sinusitis. *Otolaryngol Head Neck Surg* 1991; 104:789-795.
16. Gutowski WM, Mulbury E, Hengerer AS, et al: The role of CT scans in managing the orbital complications of ethmoiditis. *Int J Pediatr Otorhinolaryngol* 1988; 15:117-128.
17. Catalano RA, Smoot CN: Subperiosteal orbital masses in children with orbital cellulitis: Time for a reevaluation? *J Pediatr Ophthalmol Strabismus* 1990; 27:141-142.
18. Rubin SE, Rubin LG, Zito J, et al: Medical management of orbital subperiosteal abscess in children. *J Pediatr Ophthalmol Strabismus* 1989; 26:21-26.
19. Towbin R, Han BK, Kaufman RA, et al: Postseptal cellulitis: CT in diagnosis and management. *Radiology* 1986; 158:735-737.
20. Tanenbaum M, Tenzel J, Byrne SF, et al: Medical management of orbital abscess. *Surv Ophthalmol* 1985; 30:211-212.
21. Hammerschlag SB, Hesselink JR, Weber AL: *Computerized Tomography of the Eye and Orbit*. Norwalk, CT, Appleton-Century-Crofts, 1983, pp 159-181.
22. Souliere CR, Antoine GA, Martin MP, et al: Selective non-surgical management of subperiosteal abscess of the orbit: Computerized tomography and clinical course as indication for surgical drainage. *Int J Pediatr Otorhinolaryngol* 1990; 19:109-119.
23. Noël LP, Clarke WN, MacDonald N: Clinical management of orbital cellulitis in children. *Can J Ophthalmol* 1990; 25:11-16.
24. Rubin SE, Slavin ML, Rubin LG: Eyelid swelling and erythema as the only signs of subperiosteal abscess. *Br J Ophthalmol* 1989; 73:576-578.
25. Eustis HS, Armstrong DC, Buncic JR, et al: Staging of orbital cellulitis in children: Computerized tomography characteristics and treatment guidelines. *J Pediatr Ophthalmol Strabismus* 1986; 23:246-251.
26. Harris GJ: Subperiosteal inflammation of the orbit: A bacteriological analysis of 17 cases. *Arch Ophthalmol* 1988; 106:947-952.
27. Evans FO Jr, Sydnor JB, Moore WEC, et al: Sinusitis of the maxillary antrum. *N Engl J Med* 1975; 293:735-739.
28. Gwaltney JM Jr, Sydnor A Jr, Sande MA: Etiology and antimicrobial treatment of acute sinusitis. *Otol Rhinol Laryngol* 1981; 90:68-71.

29. Wald ER, Milmoë CJ, Bowen AD, et al: Acute maxillary sinusitis in children. *N Engl J Med* 1981; 304:749-754.
30. Gwaltney JM: Acute sinusitis in adults. *Am J Otolaryngol* 1983; 4:422-423.
31. Wald ER: Acute sinusitis and orbital complications in children. *Am J Otolaryngol* 1983; 4:424-427.
32. Kallings LO: Bacteriological aspects of infections of the upper respiratory tract. *Scand J Infect Dis (Suppl)* 1983; 39:9-13.
33. Wald ER, Reilly JS, Casselbrant M, et al: Treatment of acute maxillary sinusitis in childhood: A comparative study of amoxicillin and cefaclor. *J Pediatr* 1984; 104:297-302.
34. Wald ER: Sinusitis in children. *N Engl J Med* 1992; 326:319-323.
35. ———: Sinusitis in infants and children. *Ann Otol Rhinol Laryngol (Suppl)* 1992; 155:37-41.
36. Wald ER, Byers C, Guerra N, et al: Subacute sinusitis in children. *J Pediatr* 1989; 115:28-32.
37. Berg O, Carenfeldt C, Kronvall G: Bacteriology of maxillary sinusitis in relation to character of inflammation and prior treatment. *Scand J Infect Dis* 1988; 20:511-516.
38. Gamble RC: Acute inflammations of the orbit in children. *Arch Ophthalmol* 1933; 10:483-497.
39. Gans H, Sekula J, Wlodyka J: Treatment of acute orbital complications. *Arch Otolaryngol* 1974; 100:329-332.
40. Jarrett WH II, Gutman FA: Ocular complications of infection in the paranasal sinuses. *Arch Ophthalmol* 1969; 81:683-688.
41. Sty JR, Babbitt DP, Aronow CB: Diagnosis of an orbital abscess with ultrasonography. *Wis Med J* 1980; 79:33-34.
42. Batson OV: Relationship of the eye to the paranasal sinuses. *Arch Ophthalmol* 1936; 16:322-323.
43. Williamson-Noble FA: Diseases of the orbit and its contents, secondary to pathological conditions of the nose and paranasal sinuses. *Ann R Coll Surg Engl* 1954; 15:46-64.
44. Clairmont AA, Per-Lee JH: Complications of acute frontal sinusitis. *Am Fam Physician* 1975; 11:80-84.
45. Jones DB, Steinkuller PG: Microbial preseptal and orbital cellulitis, in W Tasman, EA Jaeger (eds): *Duane's Clinical Ophthalmology*. Vol 4, Philadelphia, JB Lippincott, 1989, Chap 25.
46. Rubinstein JR, Handler SD: Orbital and periorbital cellulitis in children. *Head Neck Surg* 1982; 5:15-21.
47. Haynes RE, Cramblett HG: Acute ethmoiditis: Its relationship to orbital cellulitis. *Am J Dis Child* 1967; 114:261-267.
48. Robie C, O'Neal R, Kelsey DS: Periorbital cellulitis. *J Pediatr Ophthalmol* 1977; 14:354-363.
49. Cellady AM, Shulman ST, Ayoub EM: Periorbital and orbital cellulitis in children. *Pediatrics* 1978; 61:272-277.
50. Jackson K, Baker SR: Periorbital cellulitis. *Head Neck Surg* 1987; 9:227-234.
51. Krohel GB, Krauss HR, Christiansen RE, et al: Orbital abscess. *Arch Ophthalmol* 1980; 98:274-276.
52. Zimmerman RA, Bilanuk LT: CT of orbital infection and its cerebral complications. *AJR* 1980; 134:45-50.
53. Dolman PJ, Glazer LC, Harris GJ, et al: Mechanisms of visual loss in severe proptosis. *Ophthalmic Plast Reconstr Surg* 1991; 7:256-260.
54. Harley MJ, Guerier TH: Orbital cellulitis related to an influenza A virus epidemic. *Br Med J* 1978; 1:13-14.
55. Amies DR: Orbital cellulitis. *J Laryngol Otol* 1974; 88:559-564.
56. El Shewy TM: Acute infarction of the choroid and retina: A complication of orbital cellulitis. *Br J Ophthalmol* 1973; 57:204-205.
57. Morgan PR, Morrison WV: Complications of frontal and ethmoid sinusitis. *Laryngoscope* 1980; 90:661-666.

58. Brook I, Friedman EM, Rodriguez WJ, et al: Complications of sinusitis in children. *Pediatrics* 1980; 66:568-572.
59. Moloney JR, Badham NJ, McRae A: The acute orbit: Preseptal (periorbital) cellulitis, subperiosteal abscess and orbital cellulitis due to sinusitis. *J Laryngol Otol (Suppl)* 1987; 12:1-18.
60. Harris GJ, Beatty RL: Acute proptosis in childhood, in JV Linberg (ed): *Oculoplastic and Orbital Emergencies*. Norwalk, Appleton & Lange, 1990, pp 87-103.
61. Harris GJ, Massaro BM: Acute proptosis in childhood, in W Tasman, EA Jaeger (eds): *Clinical Ophthalmology*. Vol 2. Philadelphia, JB Lippincott, 1991, Chap 27, pp 1-24.
62. Goldberg F, Berne AS, Oski FA: Differentiation of orbital cellulitis from preseptal cellulitis by computed tomography. *Pediatrics* 1978; 62:1000-1005.
63. Harris GJ, Syvertsen A: Multiple projection computed tomography in orbital disorders. *Ann Ophthalmol* 1981; 13:183-188.
64. Lemke BN, Gonnering RS, Harris GJ, et al: Orbital cellulitis with periosteal elevation. *Ophthalmic Plast Reconstr Surg* 1987; 3:1-7.
65. Gold SC, Arriagg PG, Hedges TR III: Computerized tomography in the management of acute orbital cellulitis. *Ophthalmic Surg* 1987; 18:753-756.
66. Wald ER: Acute sinusitis in children. *Pediatr Infect Dis* 1983; 2:61-68.
67. Frederick J, Braude AI: Anaerobic infection of the paranasal sinuses. *N Engl J Med* 1974; 290:135-137.
68. Karma P, Jokipii L, Sipila P, et al: Bacteria in chronic maxillary sinusitis. *Arch Otolaryngol Head Neck Surg* 1979; 105:386-390.
69. Su WY, Liu C, Hung SY, et al: Bacteriological study in chronic maxillary sinusitis. *Laryngoscope* 1983; 93:931-934.
70. Brook I: Bacteriologic features of chronic sinusitis in children. *JAMA* 1981; 246:967-969.
71. Carenfelt C, Lundberg C, Nord CE, et al: Bacteriology of maxillary sinusitis in relation to quality of the retained secretion. *Acta Otolaryngol* 1978; 86:298-302.
72. Muntz HR, Lusk RP: Bacteriology of the ethmoid bullae in children with chronic sinusitis. *Arch Otolaryngol Head Neck Surg* 1991; 117:179-181.
73. Orobello PW Jr, Park RI, Becher LJ, et al: Microbiology of chronic sinusitis in children. *Arch Otolaryngol Head Neck Surg* 1991; 117:980-983.
74. Maniglia AJ, Goodwin WJ, Arnold JE, et al: Intracranial abscesses secondary to nasal, sinus, and orbital infections in adults and children. *Arch Otolaryngol Head Neck Surg* 1989; 115:1424-1429.
75. Brook I: *Pediatric Anaerobic Infection*, 2nd ed. St Louis, CV Mosby, 1989, Chap 4, p 17.
76. Jones DB, Robinson NM: Anaerobic ocular infections. *Trans Am Acad Ophthalmol Otolaryngol* 1977; 83:309-331.
77. Gorbach SL, Bartlett JG: Anaerobic infections (third of three parts). *N Engl J Med* 1974; 290:1289-1294.
78. Bartlett JG: Recent developments in the management of anaerobic infections. *Rev Infect Dis* 1983; 5:235-245.
79. Brook I: Aerobic and anaerobic bacterial flora of normal maxillary sinuses. *Laryngoscope* 1981; 91:372-376.
80. Shapiro ED, Wald ER, Doyle W, et al: Bacteriology of the maxillary sinus of rhesus monkeys. *Ann Otol Rhinol Laryngol* 1982; 91:150-151.
81. Lundberg C, Engquist S: Pathogenesis of maxillary sinusitis. *Scand J Infect Dis (Suppl)* 1983; 39:53-55.
82. Carenfelt C, Lundberg C: Purulent and non-purulent maxillary sinus secretions with respect to pO₂, pCO₂, and pH. *Acta Otolaryngol* 1977; 84:138-144.
83. Blayney AW, Frootko NJ, Mitchell RG: Complications of sinusitis caused by *Streptococcus milleri*. *J Laryngol Otol* 1984; 98:895-899.
84. Carenfelt C, Lundberg C: The role of local gas composition in pathogenesis of maxillary sinus empyema. *Acta Otolaryngol* 1978; 85:116-121.
85. Ginsburg CM: Aerobic microbiology of upper respiratory infections in infants and children. *Pediatr Infect Dis* 1987; 6:843-847.

86. Quick CA, Payne E: Complicated acute sinusitis. *Laryngoscope* 1972; 82:1248-1263.
87. Clark GM: Acute frontal and ethmoid sinusitis with subperiosteal abscess. *Aust NZ J Surg* 1969; 38:347-348.
88. Weiss W, Flippin HF: Treatment of acute nonspecific lung abscess: Use of orally administered penicillin G. *Arch Intern Med* 1967; 120:8-11.
89. Berg B, Franklin G, Cuneo R, et al: Nonsurgical care of brain abscess: Early diagnosis and follow-up with computerized tomography. *Ann Neurol* 1978; 3:474-478.
90. Tramont EC: General or nonspecific host defense mechanisms, in GL Mandell, RG Douglas Jr, JE Bennett (eds): *Principles and Practice of Infectious Diseases*, ed 2. New York, John Wiley & Sons, 1985, pp 25-31.
91. Gorbach SL: (Anaerobic bacteria) General concepts, in GL Mandell, RG Douglas Jr, JE Bennett (eds): *Principles and Practice of Infectious Diseases*, ed 2. New York, John Wiley & Sons, 1985, pp 1349-1355.
92. Gorbach SL: *Bacteroides* species, in GL Mandell, RG Douglas Jr, JE Bennett (eds): *Principles and Practice of Infectious Diseases*, ed 2. New York, John Wiley & Sons, 1985, pp 1368-1373.
93. Jedrzynski MS, Bullock JD, Elder BL, et al: Anaerobic orbital cellulitis: A clinical and experimental study. *Trans Am Ophthalmol Soc* 1991; 89:313-347.
94. Hackman AS, Wilkins TD: Influence of penicillinase production by strains of *Bacteroides melaninogenicus* and *Bacteroides oralis* on penicillin therapy of an experimental mixed anaerobic infection in mice. *Arch Oral Biol* 1976; 21:385-389.
95. Bauer AW, Kirby WMM, Sherris JC, et al: Antibiotic susceptibility testing by a standardized single disk method. *Am J Clin Pathol* 1966; 45:493-496.
96. Neumann M, Sahn D, Thornsberry C, et al: *New Developments in Antimicrobial Agent Susceptibility Testing*. Washington, DC, American Society for Microbiology, 1991.
97. English GM: Sinusitis, in GM English (ed): *Otolaryngology*. Vol 2, Hagerstown, Harper & Row, 1980, Chap 21.
98. Arey LB: *Developmental Anatomy*, ed 7. Philadelphia, WB Saunders, 1974, p 528.
99. Hawkins DB, Clark RW: Orbital involvement in acute sinusitis. *Clin Ped* 1977; 16:464-471.