STATE-OF-THE-ART CLINICAL ARTICLE

Acute Community-Acquired Sinusitis

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Classification

Acute sinusitis can be classified into categories on the basis of several characteristics, including the immune status of the patient; infectious or noninfectious nature; occurrence in the community or hospital setting; and viral, bacterial, or fungal etiology (table 1). These categories are of both theoretical and practical importance for understanding the pathogenesis and clinical expression of the infection and for optimizing approaches to diagnosis and treatment. This review is confined to sinus infections of viral and bacterial etiology acquired in the community.

Introduction

Managing acute community-acquired sinusitis (ACAS) has been a continuing challenge for physicians, who frequently have trouble making the diagnosis with accuracy and evaluating the effectiveness of treatment with precision. These problems would not exist if the paranasal sinuses were accessible to direct examination and to noninvasive sampling for microbial culture. Because they are not, for diagnosis physicians have had to rely on clinical evaluations that are either insensitive or nonspecific [1] and on imagining studies, which are also insensitive or nonspecific.

The problem can be explained in large part by the recent finding that sinus disease is an inherent part of the common cold syndrome itself, in that 87% of patients with colds have sinus cavity disease [2]. Thus, the common cold is in reality a viral rhino*sinusitis* (VRS), not simply a rhinitis as traditionally held. Not appreciating this difference has led to confusion, since historically the term *acute sinusitis* has been used to identify what is considered a bacterial infection of the sinus. Undoubtedly this term has often been misapplied to cases of viral etiology or of a combined viral-bacterial etiology. Without the benefit of sinus puncture, these distinctions cannot be made with accuracy.

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In cases of combined viral-bacterial infection, the clinical features of the illness will reflect its dual nature. The viral component will contribute to the overall severity and duration of the illness and thus complicate the diagnosis and confound the assessment of antimicrobial effectiveness. Likewise, cases of pure VRS that are misdiagnosed as acute bacterial sinusitis will be a cause of confusion in case management, and these cases will contaminate patient samples in clinical trials of antimicrobial therapy. The perspective provided by the new information on VRS leads to a better understanding of the pathogenesis of ACAS and permits the development of improved approaches to diagnosis and management, which will be discussed in this review.

History

The maxillary antrum was described by Vesalius (1514–1564) and later by Highmore (*Antrum Highmori*), who died in 1664 [3]. In 1707, William Cowper developed a method of treating sinusitis by draining the antrum through the alveolus after removal of a tooth. Following this, John Hunter (1728–1793) recommended opening the antrum by way of the middle meatus, and Gooch, who died in 1780, and later, Mikulicz (1896) introduced antral puncture through the inferior meatus [4]. In this same period, Caldwell (1893) and Luc (1897) described an approach to the maxillary antrum via the canine fossa. These procedures were used for diagnosis and treatment of acute and chronic maxillary sinus infection. Drainage and irrigation were a mainstay of treatment for acute and subacute cases, while creation of a permanent drainage site was employed for cases that had become chronic.

Scandinavian investigators began using sinus aspiration to obtain specimens for bacterial culture in the 1940s [5–9]. This work established that the maxillary sinus cavity is sterile under normal conditions and disclosed the bacterial species that are the most important causes of bacterial ACAS (ACABS). When antibiotics became available, pretherapy and posttherapy sinus-aspirate cultures were used to evaluate (and thus demonstrate the effectiveness of) antimicrobial treatment for ACABS [10].

More recently, the nature of the bacterial etiology of ACABS has been confirmed by investigators in the United States [11, 12], who also recovered respiratory viruses from sinus aspirates of patients with ACAS [11, 13]. In addition, the recent development of computed tomography (CT) has provided a powerful tool for studying the pathogenesis of sinus infections and for

Table 1. Classification of acute sinusitis.

Patient with normal immunity:
Infectious
Community-acquired
Viral
Viral/bacterial
Bacterial
Fungal (noninvasive)
Nonallergic
Allergic
Fungus ball
Nosocomial
Bacterial
Fungal
Noninfectious
Allergic
Toxic
Immunocompromised patient:
Viral
Bacterial
Fungal (invasive)

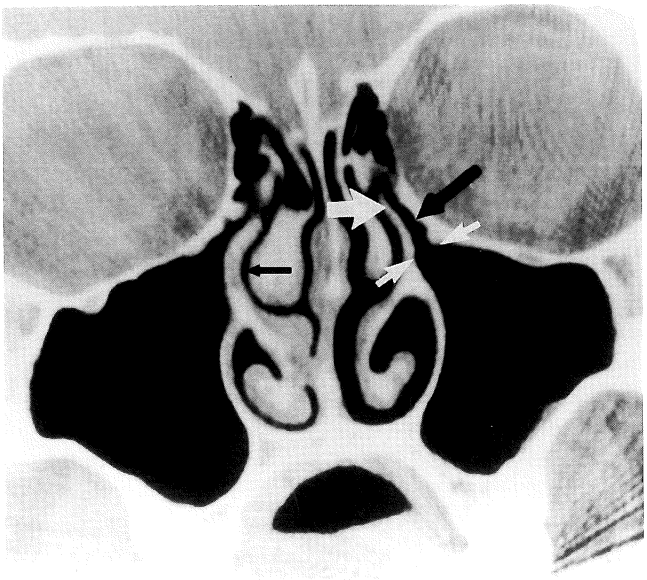

Figure 1. Selected features of the anatomy of the drainage system of the maxillary sinus, as shown on CT scan. The ostium (*between small white arrows*) opens into a tubular structure, the infundibulum (*large black arrow*). The upper part of the uncinate process (*large white arrow*) forms the inferior portion of the infundibulum. The infundibulum empties into the middle meatus. The contralateral middle meatus (*small black arrow*) is narrowed as a result of turbinal distension from the normal nasal cycle.

improved management of cases, especially those of chronic sinus disease. As discussed above, sinus CT scanning has demonstrated the importance of common cold viruses in causing acute disease of the sinuses [2].

Anatomy and Physiology

Paranasal pneumaticity originated in animals that lived somewhat earlier than the common ancestor of the dinosaurs [14]. In the dinosaurs, an air sac is believed to have filled a large paranasal space, the antorbital cavity. The derivative of this structure, the antorbital or cavionchal sinus, is present in birds and crocodilians, respectively, but not in lizards, snakes, and turtles. A similar structure, the maxillary sinus, arose in the evolutionary line leading to humans and is present in placental mammals but not in marsupials and egg-laying mammals.

The ethmoid, frontal, and sphenoid sinuses are of more recent origin and have been described as characteristic of conventional mammals [15]. Despite this long history, the function of the paranasal sinuses remains somewhat in doubt. It has been proposed that these structures reduce the bony mass and weight of the skull, participate in warming and humidification of inspired air, and add resonance to the voice.

The maxillary sinus is a bony cavity located within the maxilla (figure 1) [16, 17]. The chamber has a pyramidal shape, and the base of the pyramid is formed by the lateral wall of the nasal cavity, with the apex extending toward the zygomatic process. In the adult, the maxillary sinus cavity has a volume of 15–30 mL. The sinus is lined with ciliated pseudostratified epithelium and is covered with a mucus blanket. The epithelium is well supplied with goblet cells (table 2) [18, 19]. In contrast, seromucous gland densities in the sinus cavity are low in comparison with those in the nasal passages [20].

The maxillary ostium is located on the highest part of the medial wall of the sinus cavity (figure 1) [21]. It is connected to the nasal cavity by a small tubular passage, the infundibulum, which is encased in bone and lies directly under the lamina papyracea of the orbit. The infundibulum leads to the hiatus semilunaris of the middle meatus, which is posterolateral to the uncinate process in a shielded location. The anterior ethmoid and frontal sinuses also empty into the middle meatus. This area and the region of the anterior ethmoid are described together as the ostiomeatal complex.

The infundibulum is ~6 mm in length and has an average diameter of 3 mm, which is of adequate size to drain 30 mL (the maxillary sinus volume) of water by gravity in ~11 seconds. Mucus and other fluids produced in the maxillary sinus

Table 2. Density (quantity per mm^2) of mucus-producing structures in the nasal passages and paranasal sinuses.

Variable	No. of goblet cells*	No. of seromucous glands†
Nasal passages	5,700–11,000	8
Sinuses		
Maxillary	9,700	0.2
Ethmoid	6,500	0.5
Frontal	5,900	0.08
Sphenoid	6,200	0.05

* Data are from [20].
† Data are from [18, 19].

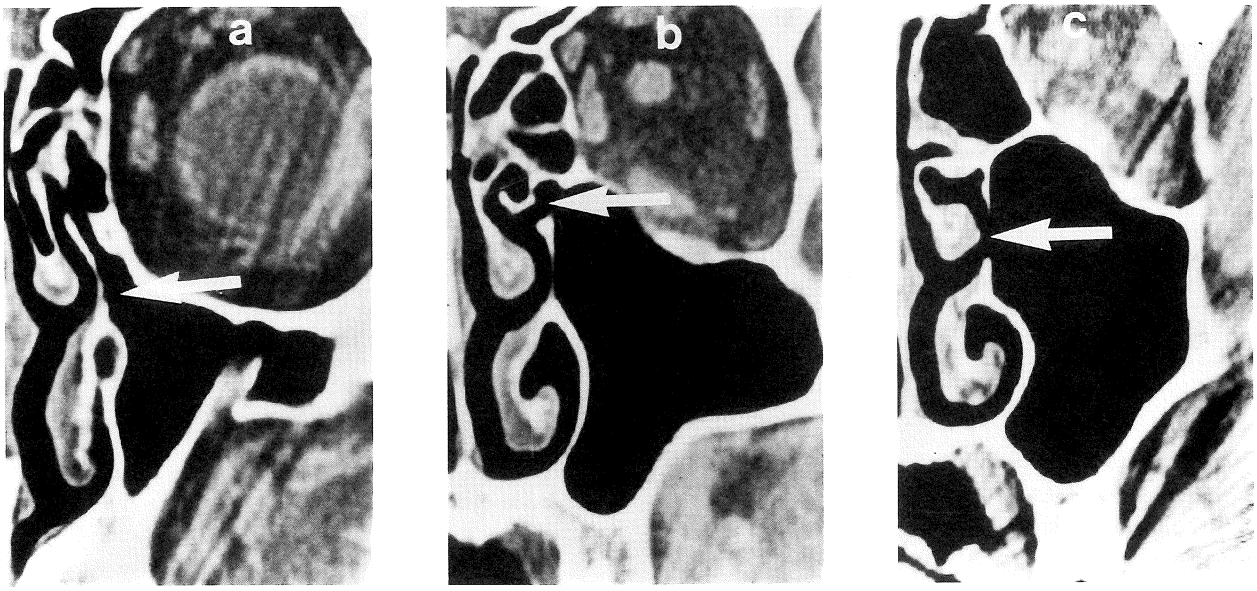

Figure 2. CT scan views of the maxillary sinus of a patient: *a,* the natural ostium opening into the infundibulum; *b,* an accessory ostium located posteriorly and superiorly on the medial wall of the sinus and emptying into the middle meatus; and *c,* a second accessory ostium located further posteriorly at the level of the middle turbinate and emptying into the nasal passage.

cavity are transported by ciliary action in a spiral direction up to and through the infundibulum and delivered into the hiatus semilunaris of the middle meatus [22, 23]. Mucociliary transit times of 4.6–12.3 mm/min have been measured in the nose [24], and transit times are presumably similar in the sinus. The mucous blanket changes 2–3 times each hour [25], and normally mucus does not accumulate in the sinus cavity.

In 10%–30% of adults, the maxillary sinus cavity is connected to the nasal passage by one or more accessory ostia that are located inferiorly to the infundibulum in the area of the anterior and posterior nasal fontanelles (figure 2). It is not known if these accessory ostia are congenital in origin or are acquired as a result of rupture during sinus infection in early life. Rupture of an anterior nasal fontanelle has been observed by endoscopy to occur during the course of an acute sinus infection (D. Kennedy, personal communication).

The fontanelles are areas of very thin bone or membrane located in the lateral nasal wall at the level of the middle meatus and lying anteriorly and posteriorly to the uncinate process. If accessory ostia are present, fluid may enter or leave the maxillary sinus cavity through these openings, although ciliary transport remains directed to the natural ostium.

The paranasal sinuses, although directly connected to the nasal passages, which are colonized with bacteria [26], are themselves sterile under normal conditions [6, 11, 27, 28]. Sterility is maintained in the sinus by mechanisms that are not fully understood but are believed to include the mucociliary clearance system and, possibly, antibacterial concentrations of nitric oxide gas in the sinus cavity [29]. Components of the humoral and cellular immune systems also probably have a role in maintaining sterility in the sinus. The composition of nasal secretions has received considerable study, but secretions from the sinus cavity itself have not received comparable attention because of the difficulty of obtaining them, especially from healthy persons. Constituents of human nasal secretions include a variety of mucous and serous products, plasma proteins, and inflammatory mediators [30].

Epidemiology and Economic Impact

The epidemiology of VRS is the well-characterized epidemiology of common colds and related acute viral respiratory illnesses. In the United States, the incidence of acute respiratory illness in children is 6–8 illnesses per person per year, and in adults, 2–3 [31]. In temperate areas, acute respiratory illness rates follow a well-established seasonal pattern, with annual epidemics in the fall, winter, and spring and periods of relative inactivity during the summer months. The different virus families tend to have characteristic periods of high prevalence, which for rhinovirus are early fall and late spring and for coronavirus, respiratory syncytial virus, and influenza virus are winter and early spring.

If the published findings are representative [2], then ~90% of patients with colds would be expected to have viral sinusitis as part of the basic illness. A small proportion of colds are, in turn, complicated by an acute bacterial infection of the sinus. This has been reported to occur in 0.5%–2% of cases (table 3) [32, 33]. It should be pointed out that in these studies sinus aspirate cultures were not performed and, thus, the incidence of secondary bacterial sinusitis complicating VRS cannot be precisely determined from this work.

The seasonal trends in the incidence of presumed bacterial sinusitis have been shown to correlate with those of common colds [34]. In addition to VRS-related cases, ACABS occurs

Table 3. Presumed cases of acute bacterial sinusitis complicating the common cold.

Population	Method of diagnosis	No. of patients: With colds	No. of patients: With sinusitis
Cleveland families*	Clinical	11,134	53 (0.5%)
Adult patients with ENT infections†	Sinus puncture	89	2 (2.2%)

* Data are from [32].
† Data are from [33]; ENT = ear, nose, and throat.

throughout the year and is associated with allergy, swimming, and nasal obstruction due to polyps, foreign bodies, and tumors. Other, less common risk factors are immune deficiencies such as agammaglobulinemia and AIDS; abnormalities of WBC function, as found in chronic granulomatous disease; structural defects, especially cleft palate; and disorders of mucociliary clearance, including cilial dysfunction and cystic fibrosis.

On the basis of the epidemiological findings described above, ~1 billion cases of VRS can be expected to occur annually in the United States (260 million people [adults and children] ×4 acute respiratory illnesses = ⩾1 billion cases of VRS annually) and, in turn, to be complicated by 20 million cases of ACABS, assuming a 2% complication rate. Data from the National Ambulatory Medical Care Survey for 1991 indicated the occurrence of 11,570,000 physician-patient contacts per year for acute upper respiratory illness and 2 million patient visits per year for presumed acute bacterial sinusitis [35]. Thus, in the United States, an estimated 1 in 100 patients with VRS and 1 in 10 patients with ACABS seek the care of a physician for their illness.

In the survey [35], upper respiratory tract infection (URI) was the second most frequent diagnosis after essential hypertension. However, physician-patient contact for normal pregnancy, general medical examination, and child-health supervision also ranked above URI on the list of most frequent reasons for visits. The total annual nonprescription cost of medications for acute URI in the United States is >3 billion dollars [36]. Expenditures for antibiotics, for other drugs requiring prescriptions, and for physician visits add substantially to this amount. Additional large costs to society result from time lost from work and school, of which acute respiratory illness is the leading cause.

Pathogenesis

Viral Infection

Most investigative work in the area of the pathogenesis of colds has been done with rhinovirus. A central feature of the pathogenicity of the rhinovirus is its ability to evade the host's protective defenses in the upper airway. The vulnerability of the nose to rhinovirus is shown by the fact that intranasal inoculation of virus in nonimmune volunteers routinely leads to a ⩾90% infection rate [37]. Following infection, however, only three-quarters of persons have symptoms of a cold; the rest have an inapparent infection. The fact that these asymptomatic infections are apparently terminated as efficiently as those that are associated with illness suggests that, in this situation, the symptoms of a cold do not result from any beneficial activity of the immune system.

Key factors in initiation of infection include viral deposition in the nose, followed by presumed transport to the posterior nasopharynx [38] and attachment to rhinovirus receptor (ICAM-1) [39]. In biopsy specimens from uninfected volunteers, ICAM-1 has been located on clusters of M (membranous) cells present in the adenoid crypts but not on adjacent ciliated epithelial cells [40, 41]. After initiation of infection, there is stimulation of several inflammatory pathways and of the parasympathetic nervous system. These events, rather than direct viral cytopathogenicity, are believed to be the major causes of symptom generation [42].

Studies of rhinovirus with use of nucleic acid probes have shown only sparse and widely scattered foci of infection in biopsy specimens of nasal turbinates of experimentally infected volunteers [43]. The activation of inflammatory pathways results in engorgement of the capacitance vessels in the venous erectile tissue of the nasal turbinates, intercellular leakage of plasma into the nose and (presumably) sinuses, discharge of seromucous glands and goblet cells, and stimulation of pain nerve and sneeze and cough reflexes.

Sinus cavity abnormalities were seen in 87% of patients with early natural colds and included all of the different sinuses (table 4) [2]. The nature of the abnormality in the sinus cavity has not been well defined. The typical finding observed by imaging in cases of acute sinusitis has traditionally been labeled "mucosal thickening," except when a classic air-fluid level is present. However, the presence of gaseous bubbles in the material seen on CT and its irregular distribution on the walls of the sinus suggest that it is, in reality, a highly viscous substance that is adherent to the floor, the sides, and—in some cases—the ceiling of the sinus cavity (figure 3).

Because goblet cells but not seromucous glands are prevalent in the sinus cavity (table 2), the material probably consists of excess amounts of mucus discharged from these cells. In addi-

Table 4. Frequency of sinus abnormalities, as revealed by CT scans, in adults with early common colds.

Sinus abnormality	Percentage of Adults
Occlusion of infundibulum	77
Abnormality of sinus cavity	
Maxillary	87
Ethmoid	65
Frontal	32
Sphenoid	39

NOTE. Data are from [2].

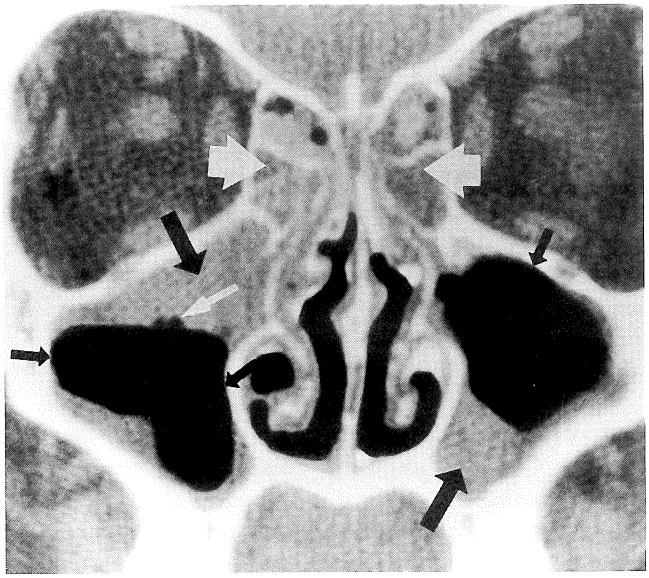

Figure 3. A CT scan of the sinuses of an adult with a common cold of 4 days' duration. Abnormalities of the roof and floor of the maxillary sinuses (*large black arrows*) are evident. Gaseous bubbles in the material (*small white arrow*) and its irregular distribution along the walls of the sinus cavity suggest that it is thick exudate adherent to the sinus wall rather than mucosal swelling. Portions of the air-bone interfaces of the sinus wall are normal (*small black arrows*). The uneven distribution of the abnormalities is not compatible with mucosal swelling, which would be expected to be more uniform. Bilateral disease of the ethmoid sinuses is also present (*large white arrows*).

tion, transudation of plasma into the sinus cavity may contribute to the amount and viscosity of the material. Sinus ostial obstruction is often cited as a major cause of sinusitis. By CT scan, the infundibulum was occluded in 77% of patients with VRS, and the ostiomeatal complex was also frequently congested (table 4) [2].

However, this may not be the major cause of the cavity disease. Observations from paired scans, performed over a span of hours, include failure of the cilia to move deposits of the material toward the ostium (figure 4) [44]. Thus, a major part of the disease process appears to be malfunction of mucociliary clearance as a result of increased amounts of the viscous material, which occurs in addition to infundibular and ostiomeatal obstruction from mucosal swelling.

Another possible cause of failure to clear the material would be cilial slowing or paralysis. Nasal mucus transit times were shown to be moderately delayed in subjects with experimental rhinovirus colds [45], but the amount of slowing observed does not appear to be sufficient to explain the degree of stasis seen on the CT scans. Furthermore, cilial dysfunction seems unlikely as the major problem because of the patchy nature of the cavitary abnormalities, as discussed below. With other, more destructive viral infections, such as influenza, epithelial damage is a more likely possibility.

The actual mechanisms by which virus causes disease in the sinus cavity are not known. Viruses have been recovered from sinus cavity aspirates taken from patients with ACAS [13], but it is not clear if viral invasion of the cavity is necessary to cause the disease. The erratic distribution of the abnormalities among the different sinuses in the same patient (figure 5) seems more compatible with random viral invasion of a sinus than with a response to generalized activation of inflammatory mediators in the nasal passage. The latter might be expected to cause a more uniform distribution of disease among the various sinuses.

Bacterial Infection

The nasal passages and nasopharynx are colonized with the same bacterial species that cause ACABS [26], and, undoubtedly, the bacteria in these areas serve as the reservoir for such infection (table 5). The specific factors that determine whether bacterial invasion of the sinus will occur during VRS are unknown. Sneezing, coughing, and nose-blowing may create pressure differentials that cause deposition of bacteria-containing nasal secretions into the sinus. In a rabbit model, introduction of *Streptococcus pneumoniae* or *Haemophilus influenzae* into an acutely obstructed maxillary sinus led to infection and disease, while obstruction of the sinus ostium without bacterial instillation did not [46]. Experimental obstruction of the sinus in rabbits leads to reduced oxygen tension and increased concentrations of lactic acid [47].

Once bacteria are deposited into the cavity of an obstructed sinus, growth conditions are favorable, as indicated by the high titers measured in sinus aspirates at concentrations of $\geq 10^7$ cfu/mL [11]. In these cases, the infection was associated with leukocytosis ($\geq$10,000 WBCs/mm^3) in sinus aspirates; however, granulocyte phagocytosis may be impaired by the reduced oxygen tension in an obstructed sinus.

In a rabbit model, maxillary sinus infection with *S. pneumoniae* or *H. influenzae* resulted in a modest increase in ciliary-beat frequency for 2 to 3 days, which was followed by marked destruction of ciliated epithelial cells, starting on day 2 (*S. pneumoniae*) and day 4 (*H. influenzae*) [46]. By the fourth day, there was a 70%–80% reduction in viable ciliated cells. By the fifth day, the sinus was completely filled with extremely viscous material described as ''mucopus.''

The authors of that study point out that reversing the disease process would involve more than just relieving ostial obstruction and that generation of new ciliated epithelium would be necessary to remove the considerable debris and bacteria present. In other studies using rabbit sinusitis models, squamous cell metaplasia and increased numbers of goblet cells were observed as part of the process [48, 49].

There is evidence that ACAS in humans is a process of sufficient severity to require several weeks to heal. Studies using serial sinus imaging have shown slowly resolving sinus-cavity abnormalities that persist after clinical complaints have resolved [11, 50, 51]. In one study of 13 previously healthy adults in which serial sinus MRI was performed, mean aeration

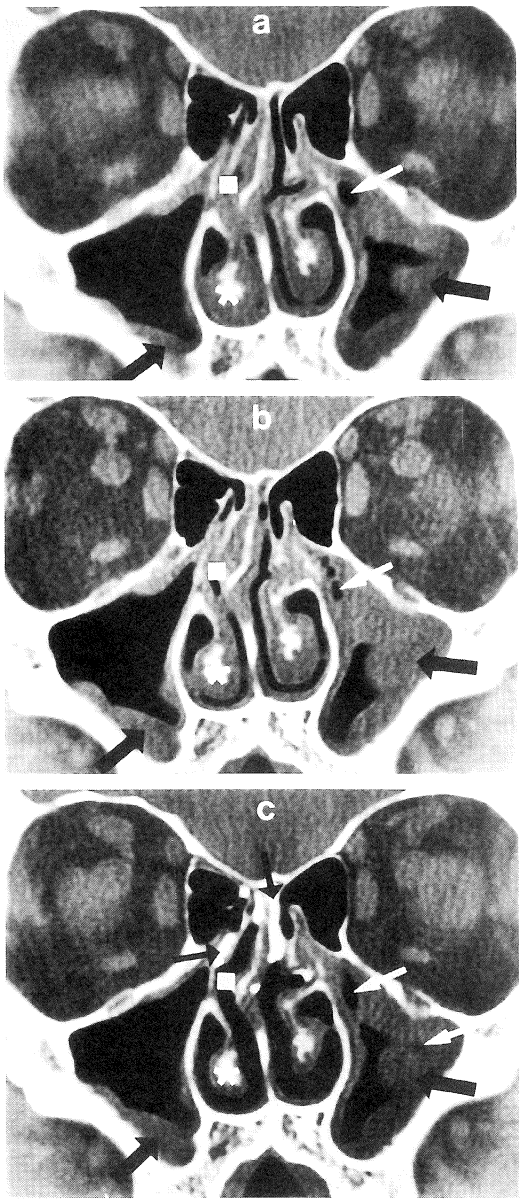

Figure 4. Serial sinus CT scans of an adult with a common cold of 4 days' duration. The first scan (*a*) was obtained at 2:00 p.m. There are abnormalities in both maxillary sinuses (*black arrows*). A gaseous bubble is present on the left (*white arrow*), indicating that the material causing the abnormality is thick fluid. The nasal turbinates are engorged (*asterisk*), and the middle meatus is congested (*square*). Immediately after the scan was obtained, the patient was given 60 mg of pseudoephedrine orally. The second scan (*b*) was obtained at 4:00 p.m. on the same day. The material in the maxillary sinuses (*black arrows*) has not moved, and the findings are essentially unchanged after treatment with pseudoephedrine. The turbinates remain engorged (*asterisk*) and the middle meatus congested (*square*). Immediately after the scan was obtained, the patient was given two intranasal sprays of .05% oxymetazoline. The third scan (*c*), obtained 10 minutes after oxymetazoline administration, shows shrinkage of the turbinates (*asterisk*) and decongestion of the middle meatus (*square*). Omnipaque dye was given intranasally immediately before the scanning while the patient was supine and is present in the middle meatus and olfactory recess (*small black arrows*). The location of the material in the maxillary sinus cavities (*large black arrows*) has not changed.

of the sinus showed a steep increase up to day 10 and then a more gradual improvement up to day 56, the last day of observation [51]. However, there was still a mean aeration of only ~80% when observations were discontinued. Sinus aspirate cultures were not performed in that study, but the clinical presentation with fever and facial pain and the radiological finding of an air-fluid level in some cases make it probable that at least some of the patients had bacterial infection.

Microbial Etiology

Specimen Collection

Specimen collection has an important influence on the accuracy of sinus culture results. Unless sinus-cavity specimens are collected without contamination by nasal secretions, there is always the danger that the specimens will yield bacteria that are growing in the nose instead of the sinus. For this reason, culture of sinus-cavity samples obtained by puncture and aspiration has been the ''gold standard'' for microbial diagnosis.

Sinus puncture is a relatively painless and safe procedure when performed by an experienced operator, although it is not suitable for routine clinical use (table 6). More recently, a spring-loaded device has become commercially available for performing sinus puncture. The bacteria recovered from sinus aspirates have shown features indicating a causal relation to disease, including high titers on quantitation, correlation with simultaneous gram stains, and association with leukocytosis in the aspirate [11].

The development of modern endoscopes has raised the possibility of collecting sinus specimens endoscopically. This presents several difficulties. First, it is not possible to enter the sinus cavities by way of the natural ostia with an endoscope. With the maxillary sinus, the sheltered location of the hiatus semilunaris behind the turbinate and uncinate process [21] and the small diameter of the infundibulum and its acute angle relative to the lower nasal passage (figure 1) make it physically impossible to pass an endoscope into the cavity.

It may be possible to enter the maxillary sinus cavity in some of the 10%–30% of persons with accessory ostia (figure 2), but it is still very difficult to do so without contaminating the specimen with nasal secretions. Therefore, most efforts at endoscopic sampling have focused on collecting secretions from the middle meatus and shielding the endoscope in an attempt to prevent specimen contamination. Secretions obtained from the middle meatus have been considered to contain material that has been discharged from the sinus cavity, but it is not clear whether the middle meatus is normally sterile or is colonized or contaminated with nasopharyngeal bacteria.

In one study of 47 patients with ACABS, endoscopic sampling was associated with a sensitivity of 65% and a specificity of 40% in comparison with the ''gold standard'' of sinus aspirate culture [52]. The sensitivity and specificity increased (to 79% and 85%) when the data were analyzed for only *S. pneumoniae, H. influenzae,* and *Moraxella catarrhalis.* Further work

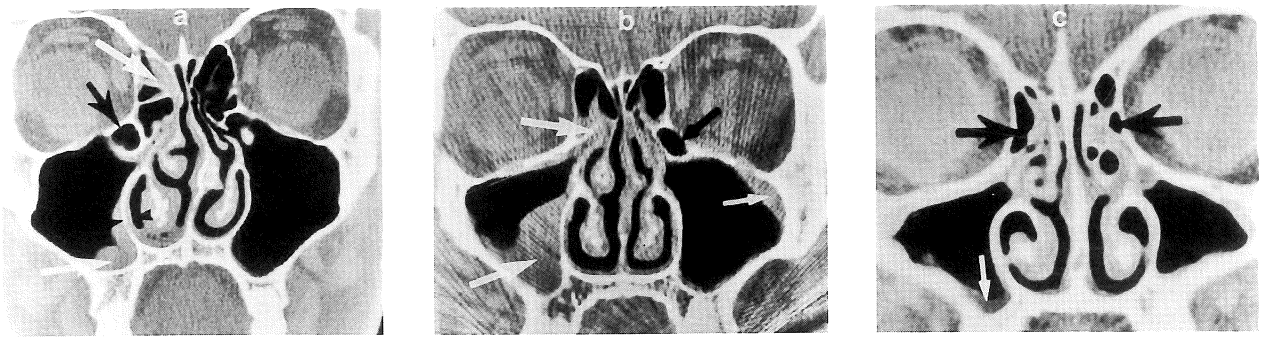

Figure 5. Sinus CT scans of three patients with early common colds show examples of the irregular distribution of sinus-cavity abnormalities in cases of viral rhinosinusitis. In *a,* there are abnormalities in the right maxillary and ethmoid sinus cavities (*white arrows*) but none on the left. A large infraorbital ethmoid cell (Haller's cell) is present on the right (*black arrow*). In *b,* moderate to marked abnormalities are evident in the right maxillary and ethmoid sinus cavities (*large white arrows*), with minimal abnormality in the left maxillary sinus cavity (*small white arrow*). A large infraorbital ethmoid cell (Haller's cell) is present on the left (*black arrow*). In *c,* bilateral ethmoid sinus abnormalities (*black arrows*) can be seen, with minimal abnormality in the right maxillary sinus cavity (*white arrow*).

is necessary to determine the ultimate utility of endoscopic sampling in sinus disease. The limited amount of information from direct comparisons of aspiration and endoscopy does not permit replacement of aspirate cultures as the ''gold standard'' for microbiological diagnosis at this time.

Viral Etiology

Only a limited number of sinus aspirates from patients with acute sinusitis have been tested for virus. Viruses were recovered from 11 (16%) of 70 positive aspirates (table 7) [13]. Most of these specimens were collected after the first 3 days of illness, when the chance of isolating the virus declines. Rhinovirus, parainfluenza virus, and influenza virus were identified, findings that support the role of viruses in the pathogenesis of sinusitis.

Bacterial Etiology

The etiology of ACABS has been well defined by puncture studies since the late 1940s and 1950s [5–12]. There has been good agreement among the results. Consistently, *S. pneumoniae* and *H. influenzae* have been the most important pathogens, accounting for a combined percentage of >50% of cases (table 7). *M. catarrhalis,* other streptococcal species (including *Streptococcus pyogenes, Streptococcus intermedius,* and other α-hemolytic streptococci), *Staphylococcus aureus,* and anaerobic bacteria each account for a small proportion of cases. *M. catarrhalis* is more prevalent in children than in adults, while anaerobic infections are infrequent in children [12].

Most sinusitis due to anaerobic bacteria arises from infection of the roots of the premolar teeth, thus representing a pure bacterial infection. Some of the anaerobic infections have involved up to six different species of microaerophilic and anaerobic bacteria. As discussed above, most acute bacterial infections of the sinuses are a complication of VRS. Viruses and bacteria have been recovered simultaneously from the same sinus aspirate, confirming the dual nature of the infection (table 8).

The relative importance of the different bacteria has not changed in the last half century, but there have been important changes in their antimicrobial susceptibilities. The appearance of penicillin resistance in *S. aureus* was followed by the emergence of resistance to β-lactam agents in strains of

Table 5. Indigenous bacterial flora of the nose, in adults.

Site, organism	Frequency of recovery (percentage of adults)
Nasal vestibule	
Staphylococcus aureus	25–40
Posterior nasopharynx	
Streptococcus pneumoniae	15–25
Haemophilus influenzae	6–40
Streptococcus pyogenes	6
Staphylococcus aureus	12

NOTE. Data are from [26].

Table 6. Method of sinus puncture and aspiration for specimen collection.

(1) Disinfect the anterior nares and the area below the inferior turbinate (puncture site).
(2) Anesthetize the puncture site with a topical anesthetic.
(3) Puncture the medial wall of the antrum with a 12-gauge needle (or spring-loaded puncture device).
(4) Aspirate the sinus contents into a syringe; if necessary, add 1–2 mL of sterile normal saline (without preservatives) to obtain a specimen.
(5) Cap the syringe and transport the specimen in the syringe to the laboratory.
(6) Have quantitative bacterial cultures performed, if possible.

Table 7. Viral and bacterial etiology of acute community-acquired maxillary sinusitis.

Etiologic agents	Mean % of cases involving: Adults	Children
Viruses*		
Rhinovirus	15	...
Influenza virus	5	...
Parainfluenza virus	3	2
Adenovirus	...	2
Bacteria† (range)		
Streptococcus pneumoniae	31 (20–35)	36
Haemophilus influenzae (unencapsulated)	21 (6–26)	23
S. pneumoniae and *H. influenzae*	5 (1–9)	...
Anaerobic bacteria (e.g., *Bacteroides, Peptostreptococcus,* or *Fusobacterium* species)	6 (0–10)	...
Moraxella catarrhalis	2 (2–10)	19
Staphylococcus aureus	4 (0–8)	...
Streptococcus pyogenes	2 (1–3)	2
Gram-negative bacteria‡	9 (0–24)	2

* Data are from [13].
† Data are from [5–12].
‡ One study had a 24% rate of isolation of gram-negative bacteria, but in four other studies the recovery rate was ≤5%. Gram-negative bacteria recovered included *Pseudomonas aeruginosa, Klebsiella pneumoniae,* and *Escherichia coli.*

H. influenzae and *M. catarrhalis*. The most recent and serious event has been the emergence of multiply resistant strains of *S. pneumoniae.*

Only ~60% of sinus aspirates in suspected cases of ACABS yield bacteria [53]. The etiology of the culture-negative cases is not clear, but undoubtedly many are due to viruses. *Chlamydia pneumoniae* has been identified in patients with respiratory illness that includes features of sinusitis [54]. However, until *C. pneumoniae* is identified in sinus aspirates, its role as a cause of sinusitis cannot be considered established.

Mycoplasma pneumoniae also has been suggested as a cause of ACABS, but there are no reports of attempts to isolate it in cultures of sinus aspirates. Atypical pneumonia and bronchitis are the characteristic syndromes associated with *M. pneumoniae* infection [55]. The clinical features of sinusitis have not been described with this infection. On the other hand, fungi are well established as a cause of occasional cases of ACAS [56]. Most of these fungal cases present with pressure changes such as masses, proptosis, and bony erosion. Community-acquired fungal sinusitis and nosocomial sinusitis are beyond the scope of this report.

Clinical Features

Because most cases of ACABS are superimposed on pre-existing VRS, the clinical features of the illness reflect the dual nature of the infection. The profiles of natural and experimental rhinovirus colds have been described in detail and include the well-known upper and lower respiratory tract symptoms of the common cold (figure 6) [57, 58]. It is not possible to separate the symptoms associated with nasal vs. sinus pathology, but sneezing, rhinorrhea, nasal obstruction, facial pressure, and headache are common sinonasal complaints.

The clinical presentation of ACABS has traditionally been described as including these same complaints, with the addition of purulence or color to the nasal discharge, a temperature of ≥38°C, and facial pain or erythema. Cough has been reported as characteristic of ACABS in children [12] and is also a common complaint in adults with acute sinusitis. Hyposmia may also be noted. When the sinusitis follows dental infection, molar pain and a foul odor to the breath are additional characteristic features.

Patients with bacterial infection of the sphenoid sinus have presented with severe frontal, temporal, or retro-orbital headache that radiates to the occipital region and hypesthesia or hyperesthesia of the ophthalmic or maxillary dermatomes of the fifth cranial nerve [59]. Lethargy and the clinical findings of cavernous sinus or cortical-vein thrombosis may also be present, as well as signs of orbital cellulitis and abscess. With severe frontal sinusitis, pus may collect under the periosteum of the frontal bone, causing swelling and edema of the forehead, which is known as Pott's puffy tumor [60].

Diagnosis

Diagnosis of ACAS continues to present a difficult challenge to the physician, despite modern technology. An initial distinction must be made between infectious and allergic or other noninfectious syndromes. Differentiation must then be made between a viral, combined viral-bacterial, or pure bacterial etiology, and finally, when possible, the specific microbial cause must be determined. An allergic etiology can usually be established by a history of paroxysmal sneezing, itching eyes, allergen exposure, and similar prior episodes. In one small study, adult patients were accurate in making the distinction between allergy and infection by self-diagnosis [61].

Table 8. Examples of mixed viral-bacterial sinus infections in cases of acute community-acquired sinusitis.

Isolates (cfu/mL)
Rhinovirus, *S. pneumoniae* ($>10^5$)
Rhinovirus, *H. influenzae* ($>10^5$)
Influenza A_2, *S. pneumoniae* ($>10^5$)
Influenza A_2, *S. pneumoniae* ($>10^5$) and non–group A *β-Streptococcus* ($>10^5$)
Influenza A_2, *M. catarrhalis* ($>10^4$)

NOTE. Isolates were recovered from aspirates of the maxillary sinus. Data are from [11].

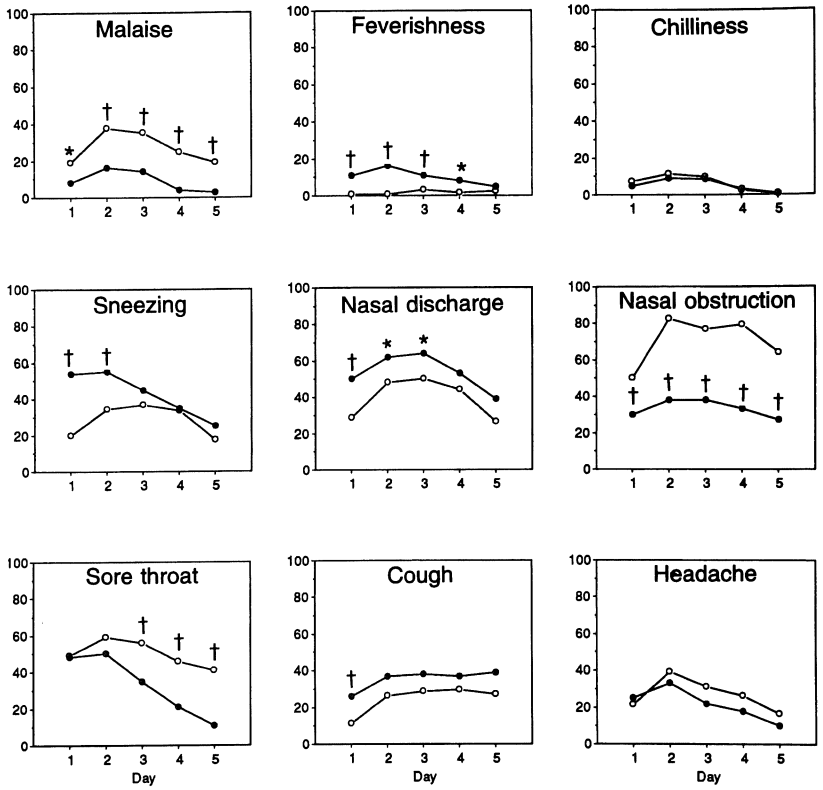

Figure 6. Prevalence (percentage of cases) of symptoms associated with natural (●, $n = 133$) and experimental (○, $n = 125$) rhinovirus colds in adults (*, $P < .05$; †, $P < .01$) [58]. The greater frequency of nasal obstruction and sore throat in subjects with experimental colds may have resulted from the irritation associated with daily nasal washes.

Separating viral from viral-bacterial or bacterial infections is a more difficult problem. Evaluation of symptoms and signs with use of either a positive sinus roentgenogram or the presence of purulent secretions (not cultured for bacteria) in a sinus aspirate as the comparison standards showed that no parameters were both sensitive and specific for this purpose (table 9) [1, 33]. The results might have been somewhat different if the "gold standard," sinus aspirate culture, had been used, but the general conclusions of the study would probably have been similar.

Another study examined adults with paranasal symptoms in whom pus was observed coming from the middle meatus; a purulent sinus aspirate (not cultured for bacteria) was used as the comparison standard [62]. The presence of two of three

Table 9. Sensitivity and specificity of clinical findings in adults with acute community-acquired sinutitis.

Population	Criterion standard	Finding	Sensitivity (%)	Specificity (%)
Males with nasal discharge*	Positive sinus radiology	History of colored nasal discharge	72	52
		Cough	70	44
		Sneezing	70	34
		Poor response to decongestants	41	80
		Maxillary toothache	18	93
		Purulent secretion	51	76
		Sinus tenderness	48	65
		Temperature of >38°C	16	85
Emergency ward patients with paranasal symptoms†	Purulent sinus aspirate‡	Purulent rhinorrhea, unilateral	48	...
		Pain, unilateral	37	...
		Purulent rhinorrhea, bilateral	35	...
		Sinus tenderness on percussion	43	...
		Pus in nasal cavity	41	...

* Data are from [1].
† Data are from [33].
‡ Bacterial culture was not performed.

Table 10. Categories of severity and management plans for suspected acute community-acquired sinusitis.*

Category	Features	Management plan
Emergent	Signs and symptoms suggesting intracranial (meningitis, brain abscess) or orbital extension	Emergency diagnostic measures: head CT, lumbar puncture, surgical consultation Intravenous antibiotic therapy (vancomycin and a 3rd-generation cephalosporin) while awaiting culture and susceptibility results Surgical decompression as needed
Urgent	Fever (temperature of ≥38°C), facial pain, edema, and erythema; maxillary toothache; classic air-fluid level	Cefuroxime axetil (250 mg b.i.d.)† or amoxicillin/clavulanate (500/125 mg three times daily) plus an oral decongestant (pseudoephedrine; phenylpropanolamine), a 1st-generation antihistamine, and a mucoevacuant (guaifenesin)
Elective	A cold or "flu"-like illness that has persisted for 8–10 days or more with no improvement or with worsening	Antibiotic and supportive treatment (as for urgent cases)

* In the setting of an illness beginning as a common cold, "flu"-like illness, or allergic rhinitis or associated with swimming or other risk factors.

† Or other antibiotics with a favorable profile of activity against intermediately resistant *S. pneumoniae;* adult dosages are given.

findings—local pain with unilateral predominance, unilateral purulent rhinorrhea, and an erythrocyte sedimentation rate of >12 mm/h—were associated with a sensitivity of 79% and a specificity of 83%.

In another study of adult patients from a general practice, in which a purulent maxillary sinus aspirate was the criterion standard, the finding of an elevated C-reactive-protein concentration (>10 mg/L) combined with an elevated erythrocyte sedimentation rate (10 mm/h for men and 20 mm/h for women) was associated with a sensitivity of 82% and a specificity of 57% [63]. Other standard laboratory tests such as WBC and differential cell counts are not useful because of their lack of sensitivity and specificity.

CT scanning is a very sensitive method of detecting disease in the paranasal sinuses and has largely supplanted conventional roentgenography as the imaging method of choice. The cost of a CT scan limited to the sinuses is comparable to that of plain sinus roentgenography in many clinics and hospitals. However, imaging studies are not recommended for the routine diagnosis of community-acquired sinusitis because of their lack of specificity.

Most patients with VRS have sinus CT scan abnormalities that cannot be distinguished from those associated with ACABS [2]. However, if a classic air-fluid level with a flat meniscus (indicating thin fluid in the cavity) is observed, there is a good correlation with a positive bacterial aspirate culture. In one study of adults, the finding of an air-fluid level on a conventional sinus roentgenogram had a specificity of 89% when compared with a positive aspirate-culture result, although such a level was noted in only 37.5% of 48 positive examinations [13].

Without help from imaging or the laboratory, short of sinus aspirate culture, the physician must continue to depend on clinical parameters for the differential diagnosis. Three diagnostic categories of ACABS can be recognized (table 10). The first presentation, which is rarer than the other presentations, is that in which the sinusitis has been complicated by meningitis, brain abscess, or orbital infection. In these cases, the clinical features of the sinus infection are overshadowed by the more serious illness.

The second presentation is that in which the classic and relatively specific features of ACABS are present. These include fever (temperature of ≥38°C) and facial pain, marked tenderness, erythema, or swelling. Also in this category are patients with molar pain or other evidence of an odontogenic cause of the infection.

The third presentation, which is the most common, is that in which an illness with sinonasal symptoms of VRS has continued for 8–10 days or more and the symptoms of colored nasal discharge, nasal obstruction, facial pressure, and sometimes cough are no better or are worse. Uncomplicated rhinovirus colds have a median duration of 1 week (figure 7) [64, 65]. Most colds, if still symptomatic, are improved by the end of 1 week, so the worsening or persistence of symptoms raises the suspicion of a complication. In addition, sinus-puncture studies have shown that for ~60% of patients who initially present with VRS and whose sinonasal symptoms do not abate after 1 week, a bacterial aspirate culture will be positive [53].

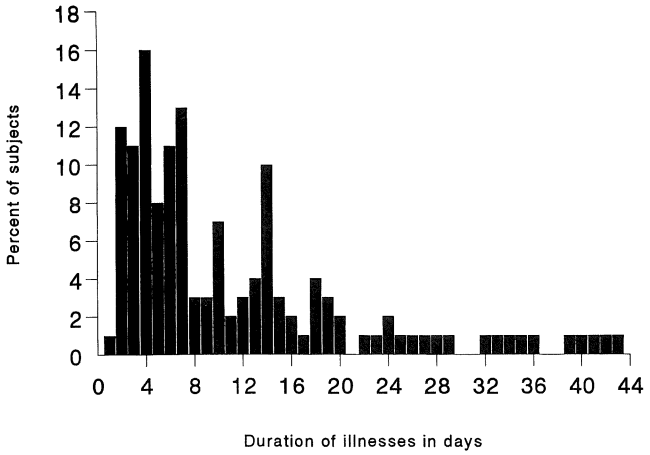

Figure 7. Duration of natural rhinovirus colds in 139 adults [65].

Complications

ACABS may lead to intracranial, orbital, and respiratory complications. The intracranial complications include meningitis, brain abscess, subdural empyema, and cavernous-sinus and cortical-vein thrombosis. Orbital complications are most common in young children and include orbital cellulitis, subperiosteal abscess, and orbital abscess. Sinusitis also is associated with the onset or exacerbation of asthma and bronchitis. Sinopulmonary disease is a well-recognized combination, especially when the condition has become chronic.

Whether the usual type of ACABS is a cause of chronic sinus disease is unknown. Certain specific microorganisms might predispose to chronic sinus disease, or chronic sinus disease may be an entirely different process related to allergy or other, as-yet-undetermined risk factors of the host.

Therapy

Antimicrobial Therapy

General considerations. Randomized placebo-controlled trials of antimicrobial therapy for ACABS with use of pretreatment and posttreatment sinus aspirate cultures have not been conducted. However, in several nonrandomized studies, such aspirate cultures have been done [10, 13, 53, 66]. The findings of these studies show that antimicrobials with appropriate antibacterial spectra and given in adequate doses are highly effective in eradicating or substantially reducing bacterial titers in the sinus cavity, while those with an inadequate spectrum or given in an inadequate dose are not (table 11).

Correlations of bacterial titers and histopathologic findings in the sinus mucosa of humans have not been reported, but if epithelial damage occurs in humans with acute bacterial sinusitis as it does in rabbits [46–48], then early eradication of a bacterial infection in the sinus cavity is an important treatment goal.

Table 11. Comparative bacteriologic cure rates (as determined by sinus puncture) among patients with acute community-acquired bacterial sinusitis.

Reference, comment regarding treatment	No. (%) of bacteriologic cures/no. of cases
[10]	
Antibiotic concentration* was ⩾ MIC of causative bacteria	19/21 (90)
Antibiotic concentration* was < MIC of causative bacteria	15/33 (45)
[13]	
Appropriate antimicrobial and dose given	47/49 (96)
Inappropriate antimicrobial given†	0/6
[66]	
Appropriate antimicrobial and dose given	105/115 (91)
Suboptimal dose given‡	37/50 (74)
[53]	
Appropriate antimicrobial and dose given	126/136 (93)
Suboptimal dosage given‡	1/5 (20)
Suboptimal dosage given§	15/21 (71)

* Antibiotic concentration in sinus aspirate after 2–3 days of treatment.
† Clindamycin, against *H. influenzae.*
‡ Cefaclor, 500 mg b.i.d.
§ Cefaclor, 500 mg t.i.d.

Over the past 20 years, a number of antimicrobials have been tested in cases of ACABS with use of pretreatment and posttherapy aspirate cultures. When a 10-day course of therapy with an antimicrobial that has an appropriate [53] antibacterial spectrum has been used (at the correct dosage), a ⩾90% bacteriologic cure rate has been routinely obtained (table 12).

Table 12. Findings of pretreatment and posttreatment aspirate studies in cases of acute maxillary sinusitis.

Study year(s), treatment	No. of bacteriologic cures/no. of evaluations	Cure rate (%)
1975–1981		
Ampicillin, 500 mg q.i.d.	12/13	92
Amoxicillin, 500 mg t.i.d.	14/14	100
TMP-SMZ DS, 160/800 mg b.i.d.	18/19	95
1983		
Bacampicillin, 800 mg b.i.d.	18/19	95
1986		
Cyclacillin, 500 mg t.i.d.	23/26	88
Amoxicillin, 500 mg t.i.d.	25/27	93
1989		
Cefuroxime axetil, 250 mg b.i.d.	36/38	95
1990		
Amoxicillin/clavulanate, 500/125 mg t.i.d.	11/12	92
Loracarbef, 400 mg b.i.d.	13/14	93
1995		
Levofloxacin, 500 mg q.d.	14/14	100

NOTE. Data are from [53]. TMP-SMZ DS = double-strength trimethoprim-sulfamethoxazole.

In formal clinical trials of antimicrobial therapy for ACABS, pretreatment bacterial aspirate culture is desirable to exclude the cases of pure VRS that will invariably contaminate the patient sample if inclusion criteria are based solely on clinical and imaging parameters. Posttreatment aspirate culture is also necessary to determine effectiveness of therapy because of the recognized difficulty in accurately monitoring the clinical course of sinusitis [67].

This difficulty is due to the dual viral-bacterial etiology of the infection and to its self-limited natural history. Currently the U.S. Food and Drug Administration does not require post-treatment aspirate cultures for approval of a sinusitis-treatment indication. In addition, some reports of ''bacteriologic cures'' have appeared in the literature, involving cases in which post-therapy aspirate cultures were not performed; the ''bacteriologic cure'' assessment was based on clinical response, not findings of aspirate culture.

Recommendations for the treatment of ACABS have changed as the antimicrobial susceptibility of the causative bacteria continues to evolve. The emergence of methicillin-resistant *S. aureus* was not a major problem because of the relative infrequency of ACABS due to this species, especially methicillin-resistant strains. The emergence of β-lactamase-producing strains of *H. influenzae* and *M. catarrhalis* was a more important event that reduced the usefulness of ampicillin. A number of other effective antimicrobials are still available (table 12), although the cost of most is considerably more than that of ampicillin. The recent emergence of intermediately and highly resistant strains of *S. pneumoniae* is a much more serious problem that is not satisfactorily addressed with currently available antimicrobials.

Current recommendations. Because treatment with the most effective antimicrobials against multiply resistant *S. pneumoniae*—vancomycin and third-generation cephalosporins—is not appropriate for ACABS, the currently recommended first-line therapy is dependant on drugs with unreliable activity. Susceptibility testing has shown that of the drugs proven effective in previous sinus-aspirate studies (table 12), cefuroxime axetil and amoxicillin clavulanate are currently the most active against strains of intermediately resistant *S. pneumoniae* [68–71]. Cefprozil and cefpodoxime have shown in vitro activity similar to that of cefuroxime axetil against intermediately resistant pneumococci. In addition, some of the new quinolones under development have good activity against intermediately resistant pneumococci. A 10-day course of treatment with one of these antibiotics is recommended when the diagnosis of ACABS is made (table 10).

The symptoms of ACAS usually abate following 2 or 3 days of treatment and are generally resolved by 7–10 days [51]. *However, it is important to be aware that the symptoms of patients with acute sinusitis may be substantially diminished despite the persistence in the sinus of purulent material containing high titers of bacteria* [11]. In patients with evident severe infection or in whom intracranial or orbital extension of infection is suspected, intravenous therapy should be started with vancomycin and ceftriaxone or cefotaxime until the results of culture and susceptibility testing are available for directing treatment (table 10). Patients in these latter categories should have emergency evaluations by CT and/or MRI and may also require diagnostic lumbar puncture and/or surgical decompression and drainage. Recommendations for the treatment of the complication of ACABS are beyond the scope of this review.

Ancillary Treatment

Ancillary treatment should be directed at drainage of the nasal passages and sinuses and the relief of sneezing, coughing, and systemic complaints [72]. The traditional approach to improving drainage has been the use of decongestants and drugs that are believed to aid in evacuation of mucus. This approach has a theoretical basis, but evidence of its effectiveness in cases of sinus disease in controlled clinical trials is lacking. Topical and, to a lesser extent, oral decongestants are rapidly effective in shrinking the erectile vascular tissue of the turbinates and thus in helping relieve ostiomeatal and nasal obstruction (figure 4) [44]. However, sequential CT scans have shown that decongestants have little or no effect in promptly draining the sinuses.

CT scans emphasize how different the anatomy of the sinus drainage passages is from that of the nose. In the maxillary sinus, for example, the drainage passage (infundibulum) is encased in bone, has a very small diameter (3 mm) compared with that of the nasal passage, and is lined with a thin nonerectile mucosa (figure 1). Scans taken before and after topical or oral decongestant treatment failed to show an increase in the diameter of the infundibulum or the relief of its obstruction (figure 4).

Compounding the problem is the observation that the material in the sinus cavity of patients with VRS is too viscous to be moved by mucociliary clearance (figure 4). Therefore, it is not surprising that immediate clearance of the sinus cavity was not detected by CT scans performed before and after decongestant treatment. In another study, manometric measurements in patients with acute rhinosinusitis failed to show a significant increase in the functional size of the infundibulum after administration of 100 mg of phenylpropanolamine [73].

On the other hand, after nasal decongestion, even thick secretions can be cleared from the nasal passages by sneezing and nose-blowing. Oral decongestants are preferred over topical preparations. Although their activity is less immediate and potent, oral decongestants avoid rebound vasodilatation and obstruction and the pharyngeal irritation that often accompanies the use of nasal decongestants. Oral decongestants are safe for patients with stable hypertension who are receiving antihypertensive treatment [74].

Topical and sometimes oral steroids have been used as decongestants (to reduce inflammation), but the effectiveness of this form of treatment has not been rigorously evaluated [72]. Intranasal beclomethasone used alone had little, if any, beneficial effect on nasal symptoms and nasal mucus weights in volunteers with rhinosinusitis due to experimental rhinovirus

infection [75]. Steroids are not recommended for use against ACABS unless there is evidence of an allergic component to the patient's illness. The value of mucoevacuant drugs such as guaifenesin in sinusitis is also not established, but they are used on theoretical grounds. Nonsteroidal antiinflammatory drugs are useful in treating systemic complaints such as fever and malaise and may also help in reducing cough [76, 77]. More traditional cough suppressants such as dextromethorphan and codeine may be needed for cough control.

First-generation antihistamines have not been widely recommended in the past for treating VRS or ACABS because of their anticholinergic activity and the possibility of their drying secretions and thus impairing drainage. While this is a reasonable theoretical consideration, testing under randomized, controlled, blinded conditions has shown a reduction of ~50% in sneezing and a 30% reduction in rhinorrhea and nasal mucus weights in volunteers with experimental rhinovirus colds [78]. In addition, there was no evidence of worsening of other symptoms or prolongation of the overall illness, indicating that drying of secretions and impairment of drainage were not problems.

The theoretical case can be made that by reducing sneezing, antihistamines reduce the chance for viral and bacterial dissemination in the nasal passages and for their deposition in the sinus cavity. In addition, experimental upper-airway challenge with histamine in volunteers stimulates the release of nasal secretions with an increased sulfate concentration characteristic of mucus, suggesting that histamine stimulates goblet-cell exocytosis [79]. Thus, there is the possibility that antihistamine therapy may reduce the amount of mucus that accumulates in the sinus cavity during acute sinusitis. However, controlled clinical trials of antihistamine treatment need to be done in patients with ACABS before its value can be accurately assessed.

Prevention

Preventing colds may be possible to some extent by avoiding contact with people who have colds and by hygienic measures such as handwashing when contact occurs between infected and noninfected persons. Covering the mouth with disposable nasal tissues when coughing or sneezing also is desirable. Vaccine is effective in preventing influenza, as is prophylactic amantadine or rimandatine during periods of epidemic influenza. There are no proven measures for preventing secondary bacterial infection of the sinuses, although suppression of sneezes and coughs can be considered of theoretical value.

Promotion of decongestion and drainage is possible in the lower nasal passages and ostiomeatal area, but as discussed above, its value in clearing the sinus cavity is problematic. Prophylactic antimicrobial administration to prevent recurrent ACABS is not recommended, and if used widely for such a common illness as VRS, it would undoubtedly hasten the emergence of bacteria with new patterns of antibiotic resistance.

Better treatments for colds may be available in the future, and these, when given early in the course of the illness, might modify the viral sinusitis and in turn lower the incidence of secondary bacterial sinusitis.

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1. Recent work suggests that disease in the paranasal sinuses occurs as part of the common cold in
   A. >10% of cases
   B. >30% of cases
   C. >50% of cases
   D. >80% of cases
   E. no cases
2. Sinus-cavity abnormalities in patients with common colds:
   A. involve the ethmoid twice as often as the maxillary sinus
   B. are probably due to marked and irregular swelling of the sinus cavity mucosa
   C. are most likely due to thick secretions because they often contain gaseous bubbles
   D. occur because of the high concentrations of seromucous glands in the sinus cavity
   E. clear within minutes with the use of topical decongestants
3. The rate of acute bacterial sinusitis complicating common colds is reported to be in the range of
   A. 0.5%–2%
   B. 5%–10%
   C. 15%–20%
   D. 20%–30%
   E. >50%
   F. zero
4. Pathogens causing acute community-acquired bacterial sinusitis include all but one of the following:
   A. α-hemolytic streptococci
   B. *Haemophilus influenzae*
   C. *Moraxella catarrhalis*
   D. *Staphylococcus epidermidis*
   E. mixtures of anaerobic bacteria
5. The differential diagnosis of acute viral vs. acute bacterial sinusitis is difficult because
   A. the conditions usually occur simultaneously
   B. the signs and symptoms of the two conditions have considerable overlap
   C. in the absence of an air-fluid level, sinus roentgenographic or CT examinations cannot reliably distinguish between the two conditions
   D. a therapeutic trial of antibiotics does not result in the rapid clearing of sinus abnormalities on roentgenographic or CT examination
   E. in bacterial cases, all of the above
6. In selecting antimicrobial treatment for acute community-acquired bacterial sinusitis, all but one of the following considerations are important:
   A. giving an adequate dose and duration of treatment
   B. dealing with β-lactamase production by some of the causative bacteria
   C. selecting a drug that covers *Mycoplasma pneumoniae*
   D. using oral drugs with the best available activity against pneumococci that are intermediately penicillin-resistant
   E. realizing that some strains of *Staphylococcus aureus* may be resistant to methicillin
7. In the acute bacterial sinusitis model in the rabbit:
   A. ciliary-beat frequency is markedly reduced by 24 hours after bacterial challenge
   B. goblet-cell density in the sinus mucosa decreases
   C. relieving ostial obstruction leads to healing within 72 hours
   D. a $\geq$70% reduction in viable ciliated cells occurs by the fourth day

E. rhinovirus is instilled into the sinus cavity before bacterial challenge

8. Collecting maxillary sinus cavity samples for bacterial culture
   A. can be done with ease by passing an endoscope through the natural ostium into the sinus cavity
   B. is possible by use of an endoscope but risks contamination of the specimen when the endoscope traverses the infundibulum
   C. still depends on sinus puncture and aspiration for providing valid culture results
   D. is an important part of the diagnostic workup in outpatient clinical practice
   E. is no longer important in antibiotic drug trials in patients with bacterial sinusitis since sinus CT scanning has become available
9. The common cold (viral rhinosinusitis)
   A. affects ~1 billion persons annually in the United States and is complicated by an estimated 20 million cases of acute bacterial sinusitis
   B. is the leading cause of time lost from school and work
   C. in recent surveys, was the second most frequent reason for patient-physician contacts in the United States
   D. leads to annual nonprescription drug costs of >3 billion dollars in the United States
   E. all of the above
10. Drugs that have been shown to be clinically useful in the ancillary treatment of viral rhinosinusitis (common cold) in controlled, blinded clinical trials include all but
   A. topical (intranasal) anticholinergics
   B. topical (intranasal) steroids
   C. first-generation antihistamines
   D. topical (intranasal) decongestants
   E. oral decongestants