

signs and symptoms of nonspecific URI include rhinorrhea (with or without purulence), nasal congestion, cough, and sore throat. Other manifestations, such as fever, malaise, sneezing, lymphadenopathy, and hoarseness, are more variable, with fever more common among infants and young children. This varying presentation may reflect differences in host response as well as in infecting organisms; myalgias and fatigue, for example, sometimes are seen with influenza and parainfluenza infections, whereas conjunctivitis may suggest infection with adenovirus or enterovirus. Findings on physical examination are frequently nonspecific and unimpressive. Between 0.5% and 2% of colds are complicated by secondary bacterial infections (e.g., rhinosinusitis, otitis media, and pneumonia), particularly in higher-risk populations such as infants, elderly persons, and chronically ill or immunosuppressed individuals. Secondary bacterial infections usually are associated with a prolonged course of illness, increased severity of illness, and localization of signs and symptoms, often as a rebound after initial clinical improvement (the “double-dip” sign). Purulent secretions from the nares or throat often are misinterpreted as an indication of bacterial sinusitis or pharyngitis. These secretions, however, can be seen in nonspecific URI and, in the absence of other clinical features, are poor predictors of bacterial infection.

TREATMENT NONSPECIFIC UPPER RESPIRATORY INFECTIONS

Antibiotics have no role in the treatment of uncomplicated nonspecific URI, and their misuse facilitates the emergence of antimicrobial resistance; in healthy volunteers, a single course of a commonly prescribed antibiotic like azithromycin can result in macrolide resistance in oral streptococci many months later. In the absence of clinical evidence of bacterial infection, treatment remains entirely symptom based, with use of decongestants and nonsteroidal anti-inflammatory drugs. Clinical trials of zinc, vitamin C, echinacea, and other alternative remedies have revealed no consistent benefit in the treatment of nonspecific URI.

INFECTIONS OF THE SINUS

Rhinosinusitis refers to an inflammatory condition involving the nasal sinuses. Although most cases of sinusitis involve more than one sinus, the maxillary sinus is most commonly involved; next, in order of frequency, are the ethmoid, frontal, and sphenoid sinuses. Each sinus is lined with a respiratory epithelium that produces mucus, which is transported out by ciliary action through the sinus ostium and into the nasal cavity. Normally, mucus does not accumulate in the sinuses, which remain mostly sterile despite their adjacency to the bacterium-filled nasal passages. When the sinus ostia are obstructed or when ciliary clearance is impaired or absent, the secretions can be retained, producing the typical signs and symptoms of sinusitis. As these secretions accumulate with obstruction, they become more susceptible to infection with a variety of pathogens, including viruses, bacteria, and fungi. Sinusitis affects a tremendous proportion of the population, accounts for millions of visits to primary care physicians each year, and is the fifth leading diagnosis for which antibiotics are prescribed. It typically is classified by duration of illness (acute vs. chronic); by etiology (infectious vs. noninfectious); and, when infectious, by the offending pathogen type (viral, bacterial, or fungal).

ACUTE RHINOSINUSITIS

Acute rhinosinusitis—defined as sinusitis of <4 weeks’ duration—constitutes the vast majority of sinusitis cases. Most cases are diagnosed in the ambulatory care setting and occur primarily as a consequence of a preceding viral URI. Differentiating acute bacterial from viral sinusitis on clinical grounds is difficult. Therefore, it is perhaps not surprising that antibiotics are prescribed frequently (in 85–98% of all cases) for this condition.

Etiology The ostial obstruction in rhinosinusitis can arise from both infectious and noninfectious causes. Noninfectious etiologies include

allergic rhinitis (with either mucosal edema or polyp obstruction), barotrauma (e.g., from deep-sea diving or air travel), and exposure to chemical irritants. Obstruction can also occur with nasal and sinus tumors (e.g., squamous cell carcinoma) or granulomatous diseases (e.g., granulomatosis with polyangiitis, rhinoscleroma), and conditions leading to altered mucus content (e.g., cystic fibrosis) can cause sinusitis through impaired mucus clearance. In ICUs, nasotracheal intubation and nasogastric tubes are major risk factors for nosocomial sinusitis.

Viral rhinosinusitis is far more common than bacterial sinusitis, although relatively few studies have sampled sinus aspirates for the presence of different viruses. In the studies that have done so, the viruses most commonly isolated—both alone and with bacteria—have been rhinovirus, parainfluenza virus, and influenza virus. Bacterial causes of sinusitis have been better described. Among community-acquired cases, *S. pneumoniae* and nontypable *Haemophilus influenzae* are the most common pathogens, accounting for 50–60% of cases. *Moraxella catarrhalis* causes disease in a significant percentage (20%) of children but a lesser percentage of adults. Other streptococcal species and *Staphylococcus aureus* cause only a small percentage of cases, although there is increasing concern about methicillin-resistant *S. aureus* (MRSA) as an emerging cause. It is difficult to assess whether a cultured bacterium represents a true infecting organism, an insufficiently deep sample (which would not be expected to be sterile), or—especially in the case of previous sinus surgeries—a colonizing organism. Anaerobes occasionally are found in association with infections of the roots of premolar teeth that spread to the adjacent maxillary sinuses. The role of atypical organisms like *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* in the pathogenesis of acute sinusitis is unclear. Nosocomial cases commonly are associated with bacteria prevalent in the hospital environment, including *S. aureus*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Klebsiella pneumoniae*, and *Enterobacter* species. Often, these infections are polymicrobial and can involve organisms that are highly resistant to numerous antibiotics. Fungi also are established causes of sinusitis, although most acute cases are in immunocompromised patients and represent invasive, life-threatening infections. The best-known example is rhinocerebral mucormycosis caused by fungi of the order Mucorales, which includes *Rhizopus*, *Rhizomucor*, *Mucor*, *Lichtheimia* (formerly *Mycocladius*, formerly *Absidia*), and *Cunninghamella* (Chap. 242). These infections classically occur in diabetic patients with ketoacidosis but can also develop in transplant recipients, patients with hematologic malignancies, and patients receiving chronic glucocorticoid or deferoxamine therapy. Other hyaline molds, such as *Aspergillus* and *Fusarium* species, also are occasional causes of this disease.

Clinical Manifestations Most cases of acute sinusitis present after or in conjunction with a viral URI, and it can be difficult to discriminate the clinical features of one from the other, with timing becoming important in diagnosis (see below). A large proportion of patients with colds have sinus inflammation, although, as previously stated, true bacterial sinusitis complicates only 0.2–2% of these viral infections. Common presenting symptoms of sinusitis include nasal drainage and congestion, facial pain or pressure, and headache. Thick, purulent or discolored nasal discharge is often thought to indicate bacterial sinusitis but also occurs early in viral infections such as the common cold and is not specific to bacterial infection. Other nonspecific manifestations include cough, sneezing, and fever. Tooth pain, most often involving the upper molars, as well as halitosis are occasionally associated with bacterial sinusitis.

In acute sinusitis, sinus pain or pressure often localizes to the involved sinus (particularly the maxillary sinus) and can be worse when the patient bends over or is supine. Although rare, manifestations of advanced sphenoid or ethmoid sinus infection can be profound, including severe frontal or retroorbital pain radiating to the occiput, thrombosis of the cavernous sinus, and signs of orbital cellulitis. Acute focal sinusitis is uncommon but should be considered with severe symptoms involving the maxillary sinus and fever, regardless of illness duration. Similarly, patients with advanced frontal sinusitis can