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Chapter 5

Upper Airway Infections

DIAGNOSTIC APPROACH TO UPPER RESPIRATORY INFECTIONS

Acute Rhinosinusitis

Acute rhinosinusitis is the inflammation of the nasal mucosa and paranasal sinuses with obstruction of sinus ostia and impaired ciliary transport in the respiratory epithelium.¹ Viral infections are responsible for the majority of cases with superimposed bacterial infection in only 2% of cases. However, when acute bacterial infections occur, and caused by respiratory pathogens (Table 5.1), rhinosinusitis may be associated with important head and intracranial complications (Table 5.2). Oral corticosteroids combined with antibiotic may be associated with modest benefit for short-term relief of symptoms in adults with severe acute sinusitis.²

Acute Pharyngitis

There are many microorganisms capable of causing pharyngitis (sore throat) that could be a single disease manifestation or as part of a more generalized illness³ (Table 5.3). There are also noninfectious causes of pharyngitis that need to be considered in the differential diagnosis of “sore throat” syndromes. Pharyngitis may be part of the common cold and this is considered one of the most common reasons for outpatient medical consultation. Acute pharyngitis in adults is associated with *Streptococcus pyogenes* in 5–9% of cases with a similar number of cases in adolescents and young adults caused by *Fusobacterium necrophorum*. Acute pharyngitis due to *S. pyogenes* is always important to suspect when an individual reports with tonsillopharyngeal exudate, tender anterior cervical lymphadenitis, and fever greater than 100.4; absence of cough and coryza (ie, Centor criteria) make the possibility of group A streptococci infection likely; particularly if this occurs during winter and early spring and when it involves school-age children. Confirmation of streptococci through antigen testing and culture is recommended. Treating group A streptococci pharyngeal infection improves symptoms, prevent further transmission, prevents rheumatic fever, and probably prevent local and systemic spread of disease.

TABLE 5.1 Major Clinical Syndromes of the Upper Respiratory Tract

Disease	Etiologies	Core concepts
Rhinopharyngitis	<p><i>Viral</i> Common cold viruses (rhinoviruses, coronaviruses) Parainfluenza Influenza A and B Adenovirus Enterovirus</p> <p><i>Bacterial</i> <i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Staphylococcus aureus</i> <i>Moraxella catarrhalis</i> <i>Streptococcus</i> spp. Anaerobes</p>	<p>Fever is frequently present in children but rarely in adults. Other associated symptoms include nasal discharge that could be profuse with clear secretions that sometimes may become yellow or during the trajectory of the illness</p> <p>Less common than viral</p>
Pharyngitis	<p>Infectious</p> <p>Non-infectious</p>	<p>Bacterial, viral, chlamydial, mycoplasmal, or candida Drug induced, Still’s disease, Kawasaki’s disease, gastroesophageal reflux disease</p>
Pertussis	<p><i>Bordetella pertussis</i></p>	<p>Three clinical phases including the following:</p> <ol style="list-style-type: none"> 1. Catarrhal (7–10 days with predominant upper respiratory symptoms) 2. Paroxysmal (1–6 weeks with episodic cough) 3. Convalescent (7–10 Days) of gradual recovery
Otitis media	<p><i>Bacterial</i> <i>S. pneumoniae</i> <i>H. influenzae</i> <i>S. aureus</i> <i>M. catarrhalis</i> <i>Streptococcus</i> spp.</p> <p><i>Treponema pallidum</i> during secondary syphilis</p>	<p>Complications of acute otitis media include mastoiditis, brain abscess of the temporal lobe, lateral venous sinus thrombosis, and otitis media with effusion</p> <p>Otitis malignant externa is associated invasion of temporal bone via cartilage of external auditory canal <i>S. aureus</i> or <i>Pseudomonas aeruginosa</i> in patients with diabetes mellitus or severely immunocompromised (ie, HIV/AIDS)</p>

TABLE 5.1 Major Clinical Syndromes of the Upper Respiratory Tract (cont.)

Disease	Etiologies	Core concepts
Epiglottitis	Bacterial or viral <i>H. influenza</i> <i>S. aureus</i>	Rapid progression to high fever, toxic appearance, drooling, and respiratory distress with no coughing May occur in children 2–5 years of age but cases are also seen in adolescents and young adults. “Thumb sign” which corresponds to the large swollen epiglottis is present on lateral neck radiograph Management priority is establishing an airway and antibiotic coverage including vancomycin and usually a third generation cephalosporin to cover <i>H. influenzae</i> or other respiratory pathogens

Among adolescents and young adults (usually 15–18 years of age) presenting with acute pharyngitis, fever, tender cervical lymphadenopathy and a scarlatiniform rash and whose evaluation is negative for *S. pyogenes* or infectious mononucleosis, infection due to *Archaeobacterium haemolyticum* should be suspected.

TABLE 5.2 Complications of Bacterial Rhinosinusitis

Anatomic location	Complications
Maxillary	Possibly brain abscesses through emissary veins
Frontal	Potts puffy tumor associated with osteomyelitis and subperiosteal abscess of the frontal bone, brain abscess (frontal lobe), epidural abscess, subdural empyema, meningitis (trauma leading to CSF leakage)
Sphenoid	Posterior orbital abscess, cavernous sinus thrombosis, venous sinus thrombosis, meningitis
Ethmoid	Preseptal cellulitis (see chapter: Ocular Infections), subperiosteal abscess, orbital abscess, cavernous sinus thrombosis, meningitis

TABLE 5.3 Differential Diagnosis of Acute Pharyngitis^a

Etiologies	Syndrome	Core concepts
Bacterial	<p><i>S. pyogenes</i></p> <p><i>Streptococcus dysgalactiae</i> subspecies equisimilis (Group C streptococci)</p> <p><i>Neisseria gonorrhoeae</i></p> <p><i>A. haemolyticum</i></p> <p><i>Corynebacterium diphtheriae</i></p>	<p>Can cause pharyngitis, tonsillitis, scarlet fever, rheumatic fever, glomerulonephritis, reactive arthritis, PANDAS^b</p> <p>Patients usually have sore throat, cervical adenopathy but there is no rhinorea, coryza, or cough</p> <p>Pharyngitis and tonsillitis</p> <p>Glomerulonephritis (most commonly when it causes skin and soft tissue infections)</p> <p>Can cause pharyngitis and it is sexually acquired and maybe associated with disseminated gonococcal infection</p> <p>Pharyngitis and scarlatiniform rash</p> <p>Severe pharyngitis with peripheral neuropathy and myocarditis</p>
Viral ^c	<p>Human immunodeficiency virus (HIV)</p> <p>Epstein-Barr virus</p> <p>Cytomegalovirus</p> <p>Human Herpes Virus-6 (HHV-6)</p> <p>Adenovirus types 3, 4, 7, 14 and 21</p> <p>Herpes simplex types 1 and 2</p> <p>Coxsackievirus A types 2, 4, 5, 6, 8, and 10</p>	<p>Acute retroviral syndrome associated with HIV</p> <p>Infectious mononucleosis</p> <p>Infectious mononucleosis</p> <p>Mononucleosis-like illness with pharyngitis</p> <p>Pharyngoconjunctival fever</p> <p>Stomatitis, pharyngitis</p> <p>Herpangina</p>
Chlamydial	<i>Chlamydia pneumoniae</i>	Pneumonia, bronchitis, pharyngitis
Mycoplasmal	<i>Mycoplasma pneumoniae</i>	Pneumonia, bronchitis, pharyngitis
Inflammatory ^d	<p>Adult onset Still's disease</p> <p>Kawasaki's disease</p>	<p>Pharyngitis (although, there is some evidence that soreness maybe due to laryngeal cartilage inflammation)</p> <p>Mucocutaneous syndrome that may involve the pharynx</p>
Parasitic	<i>Toxoplasma gondii</i>	Mononucleosis-like illness that can include pharyngitis

TABLE 5.3 Differential Diagnosis of Acute Pharyngitis^a (cont.)

Etiologies	Syndrome	Core concepts
Fungal	<i>Candida albicans</i>	Oral and esophageal candidiasis
Drug induced	Angiotension converting enzyme inhibitors Erythema multiforme with mucosal involvement	
Miscellaneous noninfectious ^e	Smoking Snoring Endotracheal intubation Gastroesophageal reflux Air pollution	

^aBisno AL. Acute pharyngitis. N Engl J Med 2001;344(3):205–211.

^bPediatric autoimmune neuropsychiatric disorders associated with streptococcal infection.

^cInfluenza A and B may include some component of pharyngitis given its involvement of many segments of the upper and lower respiratory epithelium; similarly parainfluenza 1–4 may cause symptoms consistent with common cold and croup that could involve sore throat.

^dRenner B, Mueller CA, Shephard A. Environmental and non-infectious factors in the aetiology of pharyngitis (sore throat). Inflamm Res 2012;61:1041–1052.

^eOther processes that can cause pharyngitis include Epiglottitis (infectious) can cause pharyngitis if associated with severe inflammation) or Ludwig's angina or retropharyngeal abscess.

Chronic Cough Syndrome

The syndrome of chronic cough (>12 weeks) is also an important reason for infectious disease consultation and it can be caused by chronic smoking, post nasal drip due to chronic bacterial sinusitis, gastroesophageal reflux, anatomic abnormalities of the respiratory tract, drug-induced angiotensin-converting enzyme inhibitors (ACE), pertussis,⁴ asthma, and chronic interstitial lung disease. Diagnostic workup of chronic should consider this differential diagnosis.

Bronchorrhea

Bronchorrhea is defined as water sputum production of over 100 mL per day and sometimes it can be confused as a chronic cough syndrome. The most important considerations in the differential diagnosis include primary lung malignancies including bronchioloalveolar carcinoma since it involves some glandular component that produces excess mucous. Bronchorrhea can also be associated with lung metastases from adenocarcinomas of the colon, pancreas, or other glands. Nonmalignant conditions include endobronchial tuberculosis, and asthma. Patients with ruptured pulmonary echinococcosis (hydatid disease) into a bronchus may also present with bronchorrhea and often report a salty taste associated with expectoration.

TABLE 5.4 Odontogenic Infectious Syndromes

Syndrome/disease	Core concepts
Noma (cancrum oris) ^a	It is a polymicrobial infection that destroys the hard and soft tissues of the mouth and may involve the nose and other parts of the face Its an ulcerative disease of extreme poverty that occurs concomitantly or immediately after a debilitating illness such as measles, malaria, severe enterocolitis, tuberculosis, or necrotizing ulcerative gingivitis Most important pathogens are <i>F. necrophorum</i> and <i>Prevotella intermedia</i> and due to its effect on nutrition, its associated with stunt growth, malnutrition, and often death
Lemierre's syndrome ^b	Septic thrombophlebitis of the jugular vein that sometimes is associated with odontogenic infection with secondary seeding of the jugular vein. Patients often present with cavitary lung lesions due to multiple septic emboli to the lung or pleural effusions/empyemas
Submandibular abscesses and Ludwig's angina	Usually arise from the spread of periapical abscess of the mandibular molars, most typically from the second or third molar Periapical abscess involving the first molar initially infect the sublingual space, whereas infections originating from the 2nd or 3rd molar infect the submylohyoid space and this infection pushes the tongue against the epiglottis Ludwig's angina experience a rapid spreading woody inflammation of the submandibular area that can lead to insidious or rapidly progressive asphyxiation if left untreated
Brain abscess ^c	Connection through the valveless emissary veins leading to brain abscesses usually temporal or parietal lobes (see chapter: Central Nervous System Infections)

^aEnwonwu CO. Noma – the ulcer of extreme poverty. *N Engl J Med* 2006;**354**;(3):221–224.^bReynolds SC, Chow AW. Life-threatening infections of the peripharyngeal and deep fascial spaces of the head and neck. *Infect Dis Clin. N Am* 2007;**21**:557–576.^cBrouwer MC, Tunkel AR, McKhann II GM, van den Beek D. Brain abscess. *N Engl J Med* 2014;**371**(5):447–456; Darouiche RO. Spinal epidural abscess. *N Engl J Med* 2006;**355**(19):2012–2020.

Septic Thrombophlebitis of the Internal Jugular Vein (Lemierre's Syndrome)

Lemierre's syndrome is septic thrombophlebitis of the internal jugular vein.¹ *F. necrophorum* is the most common pathogen associated with this disease, and previously it was recognized as postanginal sepsis due to *S. pyogenes* pharyngitis.⁵ It most often steams from ear, nose, and throat infections that spread into the vasculature that drains through the jugular vein.⁶ Septic embolization to the

TABLE 5.5 Necrotizing Syndromes of the Nose and Nasopharynx^a

Infections and inflammatory conditions involving the nasal mucosa and cartilaginous portion	Saddle nose deformity	Syphilis Leprosy Granulomatosis with polyangiitis Relapsing polychondritis Midline granuloma
	Vestibulitis with or without abscess	Methicillin Resistant <i>S. aureus</i> (MRSA) usually community-associated and highly-associated with smoking Less frequently caused by <i>S. pneumoniae</i> or <i>Haemophilus</i> spp.
	Parasitic	Mucocutaneous leishmaniasis due to <i>L. braziliensis</i>
	Mycobacterial Rhinoscleroma ^b	<i>Mycobacterium leprae</i> <i>Klebsiella rhinoscleromatis</i> produces a chronic granulomatous disease of the nose or other parts of the respiratory system including palate, and larynx
	Noma (cancrum oris) ^c	Polymicrobial including oral anaerobes
	Fungal	Paracoccidioidomycosis, blastomycosis, histoplasmosis, and coccidioidomycosis
	Granulomatous Malignancy	Sarcoidosis Squamous cell carcinoma, basal cell carcinoma, lymphoma
	Miscellaneous	Chronic and frequent snoring of cocaine

^aReynolds SC, Chow AW. Life-threatening infections of the peripharyngeal and deep fascial spaces of the head and neck. *Infect Dis Clin N Am* 2007;**21**:557–576.

^bGaafar HA, Gaafar AH, Nour YA. Rhinoscleroma: An updated experience through the last 10 years. *Acta Oto-Laryngologica* 2011;**131**:440–446.

^cEnwonwu CO. Noma-The ulcer of extreme poverty. *N Engl J Med* 2006;**354**(3):221–224.

lungs is often considered part of this syndrome.⁶ These cases occurred in an era before antibiotics, when this illness had a mortality rate of 90%. After the introduction of antibiotics in the 1950s, Lemierre's syndrome vanished for several decades. Interestingly, in the past two decades, there have been at least 400 cases reported in the literature through case studies and many cases are caused by invasive community-acquired methicillin resistant *S. aureus* MRSA.⁶

The differential diagnosis of selected odontogenic infectious syndromes and necrotizing infectious processes of the nose are discussed in [Table 5.4](#) and [Table 5.5](#), respectively.

REFERENCES

1. Chow AW, Benninger MS, Brook I, Brozek JL, Goldstein EJC, Hicks LA, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis* 2012;**54**(8):1041–5.
2. Venekamp RP, Thompson MJ, Rovers MM. Systemic corticosteroid therapy for acute sinusitis. *JAMA* 2015;**313**(12):1258–9.
3. Bisno AL. Acute pharyngitis. *N Engl J Med* 2001;**344**(3):205–11.
4. Hewlett EL, Edwards KM. Pertussis – not just for kids. *N Engl J Med* 2005;**352**(12):1215–22.
5. Kizhner V, et al. Methicillin-resistant *Staphylococcus aureus* bacteraemia associated with Lemierre’s syndrome: case report and literature review. *J Laryngol Otol* 2013;**127**.7:721–3.
6. Chanin JM, Marcos LA, Thompson BM, et al. Methicillin-Resistant *Staphylococcus aureus* USA 300 clone as a cause of Lemierre’s syndrome. *J Clin Microb* 2011;**49**(5):2063–6.