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Oropharyngeal and Tonsillar Infections

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Introduction

Infections of the oropharynx and tonsils are common and account for significant health care expenditures. Acute pharyngitis occurs in both children and adults, and it is one of the most frequent reasons for a physician visit, with an estimated 15 million outpatient visits per year.[1] It is often considered a disease of the pediatric population, with some estimating that it accounts for 7.3 million pediatric visits each year and 37% of all children examined in outpatient clinics.[2,3] Children affected are commonly 5 to 12 years old, and the incidence is estimated to be 12.8/100,000 patient years.[4] It is also a relatively common complaint in the adult population, with an incidence of 4.7/100,000 patient years.[4]

Because pharyngitis accounts for such a large percentage of patient visits to a physician, its negative impact on the economy is significant. Most of the economic burden comes from time lost at work for parents of children with strep throat, and this has been estimated to be anywhere from 224 to 539 million dollars per year in the United States.[5,6]

A variety of infectious agents is responsible for acute oropharyngeal infections, and differentiating between the pathogens is a challenge for even the most experienced clinician. The constellation of symptoms is often concerning to the affected patient, but the disease is often self-limited. Viral causes of pharyngitis are more common than bacterial ones (Table 16-1).[7-9] Bacterial causes can have unwanted systemic and locally advanced sequelae if not treated appropriately. In an era of increasing antibiotic resistance, the workup for pharyngitis should be thorough, and the treatment options should be strongly considered. A more complete thought process on the part of the clinician will ultimately lead to improved diagnostic ability and a more judicious use of antibiotics.

Complications do occur with pharyngitis; they are uncommon overall, but can be life-threatening. Suppurative complications caused by rapid spread of infection to deeper spaces of the neck can result in airway compromise if not recognized in a timely fashion.[10] There are also systemic, nonsuppurative complications for bacterial and viral pharyngitis that need to be considered when evaluating acute oropharyngeal infections. Fortunately, improving antibiotic therapies and recognition of worsening symptoms have decreased the frequency of complications of pharyngitis.[10]

It is clear that acute infections of the oropharynx and tonsils play a significant role in pathologies of the head and neck. The topic of oropharyngeal infections is broad and has become much broader with the introduction of human papillomavirus as a causative agent in oropharyngeal cancer. In this chapter, we will focus our discussion on acute oropharyngeal infections. Appropriate workup and diagnostic measures will be reviewed along with medical and surgical therapies. Finally, we will discuss specific complications and how they can be avoided and managed.

Anatomy

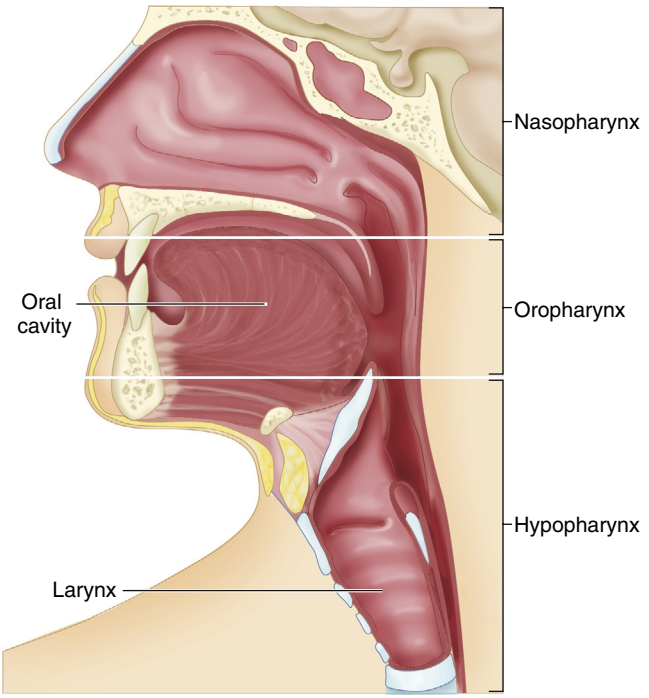
The anatomy of the pharynx can be cumbersome because of the great number of structures in a crowded anatomic space. There are three distinct regions of the pharynx: the nasopharynx, the oropharynx, and the hypopharynx. The oropharynx starts at the anterior tonsillar pillars bilaterally, which consist of the palatoglossus muscles. It includes the tonsils, thus making tonsillar infections a specific subsite of the oropharynx. Superiorly, it extends from the soft palate to the posterior pharyngeal wall, where it is separated from the nasopharynx. Inferiorly, its boundary is the hyoid bone to the posterior pharyngeal wall, where it lies above the hypopharynx (Figure 16-1). The major subsites of the oropharynx include the soft palate/uvula, tongue base, tonsils, and lateral/posterior pharyngeal walls.[11]

The blood supply of the oropharynx is provided primarily by the ascending pharyngeal branch of the external carotid. The sensory innervation is via the glossopharyngeal plexus and includes cranial nerves IX and X.[5] A majority of the lymphatic drainage is unilaterally to levels II, III, and IV in the neck, which explains why infections can manifest with anterior cervical adenopathy.

TABLE 16-1 Infectious Causes of Acute Pharyngitis

Bacteria	Viral	Atypical Bacteria
Group A β-hemolytic streptococci	Adenovirus	*Mycoplasma pneumonia*
Group C streptococci	Herpes simplex virus 1 and 2	*Chlamydophila pneumoniae*
Neisseria gonorrhoeae	Coxsackievirus	*Chlamydophila psittaci*
Corynebacterium diphtheriae	Rhinovirus	
Fusobacterium necrophorum	Coronavirus	
Francisella tularensis	Influenza A and B	
Yersinia pestis	Parainfluenza	
Treponema pallidum	Respiratory syncytial virus	
Mixed anaerobes	Epstein-Barr virus	
	Cytomegalovirus	
	HIV	

Data adapted from Weber R: Pharyngitis, *Prim Care Clin Office Pract* 41:91-98, 2014.



• **Figure 16-1** Anatomy demonstrating the boundaries of the oropharynx in relation to other upper aerodigestive anatomy. (Adapted from Goldman L, Schafer AI: *Goldman's Cecil medicine,* ed 24, Philadelphia, 2012, Saunders.)

Etiologies

Viral

Viruses are the most common cause of oropharyngeal and tonsillar infections.[1,4-6,12,13] These infections occur as a constellation of symptoms related to the common cold or upper respiratory illness, but there are some that warrant particular attention and different treatments. The viruses most often responsible are respiratory viruses: rhinovirus, adenovirus, coronavirus, parainfluenza, influenza, and respiratory syncytial virus. These organisms are the ones that cause some variation of the common cold. They are usually self-limited and of little clinical significance because they do not require any intervention on the part of the clinician. The viral causes of oropharyngeal infections that have more clinically significant implications are Epstein-Barr virus (EBV), human immunodeficiency virus (HIV), cytomegalovirus (CMV), and herpes simplex virus.

EBV (mononucleosis) is a herpesvirus. The virus infects B cells, which serve as a reservoir for the virus. These infected B cells circulate throughout a person's lifetime. The body's T cells respond by attacking the infected B cells, and in the acute setting it often causes an infection that can have severe complications involving a variety of organ systems. It often manifests in the second decade of life with nonspecific symptoms of fatigue and cervical adenopathy in addition to pharyngotonsillitis. Data suggest that up to 95% of adults worldwide are infected with EBV.[14] In some cases, the complications can become life-threatening, with upper airway obstruction or splenic rupture.[12,14]

HIV is the causative agent of acquired immunodeficiency syndrome and can appear in the acute setting with an acute retroviral syndrome.[12,13] Symptoms include fever, pharyngitis, rash, headache, and adenopathy.[15] These symptoms can appear within a few days following incubation of the virus, but are often 3 to 5 weeks after acquisition of the infection.[12] They occur as a result of the immune system's response to a large viral load. There is cytokine release and inflammatory mediators that manifest initially as nonspecific symptoms. HIV can mimic EBV and mononucleosis with its symptoms of sore throat and pharyngitis in addition to malaise and fatigue.

Herpes simplex virus-1 (HSV-1) is another viral cause of acute oropharyngeal infection. HSV-1 is an infection that

manifests with oral lesions, pharyngitis with a prodrome, and adenopathy.[16] This infection is termed *herpetic gingivostomatitis,* and it can be severe and cause pain and dehydration. It is often seen in children with painful swollen vesicles on an erythematous base, but there is also asymptomatic seroconversion in many people.[16] The vesicles of this virus often help to differentiate it from other causes of pharyngitis or tonsillitis.

CMV is an infection that often manifests itself in immunocompromised patients; however, it can appear in patients with a competent immune system. In fact, it has been reported that the seroprevalence of CMV ranges from 60 to 100% worldwide. Most patients with a competent immune system have a benign course, but in severe cases, it can mimic a mononucleosis-type infection with pharyngitis.[17]

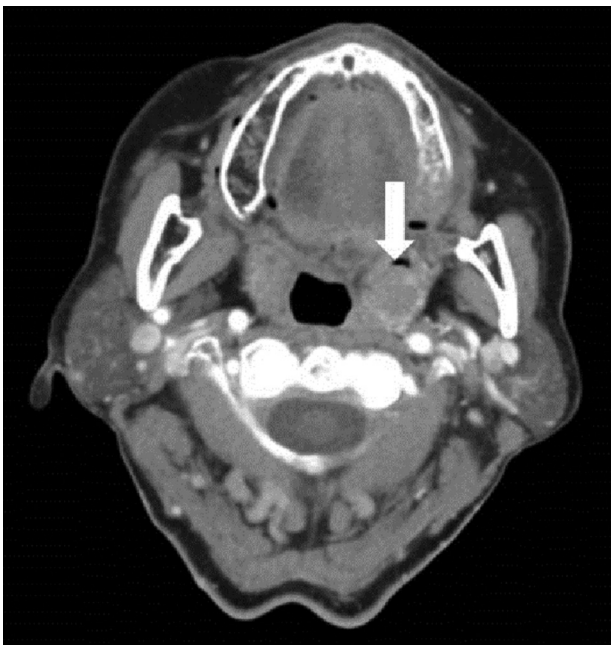
Bacterial

A number of bacteria cause pharyngitis and tonsillitis, but the overwhelming majority of cases are caused by group A *Streptococcus* (GAS). In children, this organism is estimated to be responsible for 15 to 36% of cases of sore throat,[9,18] whereas in adults it is reported to account for 5 to 15% of cases of pharyngitis. Overall, GAS account for 15 to 30% of pharyngitis regardless of age.[12]

This pathogen occurs among children who are 5 to 15 years old,[10] and it is frequently seen in the winter and early spring months. Unlike viral causes, it presents without any prodrome, cough, or nasal congestion. One reason that GAS is of such great clinical concern is that it can cause nonsuppurative complications of rheumatic fever and poststreptococcal glomerulonephritis. In fact, prevention of rheumatic fever is one of the most compelling reasons to treat GAS pharyngitis. Fortunately, these complications are rare, especially in developed countries.[6,7,19]

Streptococcal species such as groups C and G β-hemolytic streptococci are also thought to be responsible for about 5% of pharyngitis and oropharyngeal infections,[4,12] but the clinical presentation is often milder. These have also been reported to cause nonsuppurative complications such as rheumatic fever.[7] Other bacterial species that should be considered in cases of oropharyngeal infections are *Actinomycetes* species, *Neisseria gonorrhoeae, Corynebacterium diphtheriae, Chlamydia pneumoniae,* and *Mycoplasma pneumoniae,* all of which account for about less than 1% of pharyngitis in all patients.[12]

Diagnosis of these other bacterial causes of pharyngitis can be difficult, and often a clinical suspicion is necessary to make these diagnoses. *Actinomycetes* species is a bacteria that is part of the oral cavity flora; however, it can present with a picture of acute infections with suppurative complications in the oral cavity and oropharynx. Typically, an infection is caused in an immunocompromised host, but it can manifest as recurrent tonsillitis in children.[20] Diagnosis of actinomycosis infection requires biopsy and tissue that shows yellow, sulfur granules.[21] This can also mimic a tonsillar mass and adenopathy, which increases suspicion for malignancy in many patients (Figure 16-2). For patients in whom *N. gonorrhoeae* is considered, an adequate sexual history must be obtained. The advent of childhood vaccinations against diphtheria has been monumental in preventing *C. diphtheriae* as a cause of often life-threatening pharyngeal infections. It will manifest with a gray membrane coating the oropharynx that causes respiratory distress often requiring intubation and airway protection. A history of "walking pneumonia" is a likely clue to the diagnosis of chlamydia or *M. pneumoniae*.



• **Figure 16-2** *Actinomycetes*. Note the left-sided asymmetry and rim enhancement *(white arrow)*. Biopsy specimen showed sulfur granules and actinomycosis without evidence of malignancy.

History and Examination

The history and physical examination are essential to making an accurate diagnosis. An acute oropharyngeal infection and tonsillitis caused by a bacteria or a virus often exhibit subtle differences, and distinguishing between them is challenging. Acute infections often occur in younger populations, but when they do occur in adults, the organisms are often different and the strains have a tendency to be more resistant to treatment with different disease manifestations.[4,22] Asking whether someone has been exposed to a sick contact may help the clinician to diagnose an infection, but it does not necessarily indicate the causative organism. Many of the symptoms of sore throat, fever, fatigue, and dysphagia are overlapping. It is important to ask how long the symptoms have been present and whether episodes are recurrent, because these are key points that can alert the physician to the source of infection and the need for different management. Timing and seasonality of the symptoms can also be helpful in determining a specific organism. GAS and many of the respiratory viruses occur in the winter or early fall, whereas EBV and HIV can occur at any time.

Examination findings often are similar between both bacteria and viruses. Examination findings include erythema of the oropharynx, tonsillar exudates, uvular swelling, and cervical adenopathy. It is important when examining patients who have suspected oropharyngeal infections not to overlook signs of trismus, neck pain, and voice changes, which can indicate complications of pharyngitis.

The importance of differentiating GAS from other causes of oropharyngeal infections is essential because one of the reasons to treat streptococcal pharyngitis is to prevent nonsuppurative complications, such as rheumatic fever caused by GAS. Often GAS infections appear with sore throat without cough.[10] Clinicians have tried to create a set of clinical criteria to help diagnose streptococcal pharyngitis, but its utility is uncertain. These criteria, the Centor criteria, include a four-point scoring scale based on signs and symptoms suggestive of GAS bacterial pharyngitis. This scoring system has been shown to have a high negative predictive value in some reports (81%), as opposed to its positive predictive value (48%).[5] Some studies show that even patients with all four criteria have less than a 60% chance of having a positive throat culture, which is the gold standard for diagnosis.[1] The utility of a scoring system in making a diagnosis of GAS pharyngitis is that it helps to stratify patients into high, medium, or low probability of having the disease. These criteria are used to guide further workup and should be used with additional diagnostic information to confirm GAS.[1,5] The use of these criteria alone can lead to an incorrect diagnosis of GAS and can increase the use of unnecessary antibiotics. It is important to note that GAS often manifests differently in children/adolescents and adults; therefore, the criteria do not necessarily apply equally to all patients. However, there is a newer scoring system that accounts for a patient's age (Table 16-2).

For many of the respiratory viral causes of oropharyngeal and tonsillar infections, the history will be slightly different and will include symptoms of upper respiratory illness, such as cough, coryza, and congestion. For more severe viral causes such as EBV and HIV, there will be a stronger history of fatigue and systemic symptoms. EBV often affects patients in the second decade of life, with the highest incidence in patients who are 15 to 24 years old, and it occurs in college students or patients in close contact.[14] A strong suspicion on the part of the clinician is often needed to diagnose these viruses, because the symptoms initially closely mimic more benign, self-limited diseases.

Examination findings in these more virulent viruses can also be more diffuse and can involve organ systems outside the head and neck. Thus, if there is any suggestion of EBV, CMV, or HIV, a full examination is indicated. EBV can appear with bilateral tonsillar hypertrophy and exudates, palatal petechiae, rash, and splenomegaly, which occur in 15 to 65% of patients (Figure 16-3).[14] HIV can mimic a mononucleosis-like infection in an acute retroviral syndrome. If there is any suggestion of HIV based on the patient's history, a workup should be performed because after the acute phase, there is a latent period for the virus, in which there are no systemic symptoms for a number of years typically.[15] CMV can cause pharyngitis with symptoms of vasculitis, liver disease, and fatigue.[17]

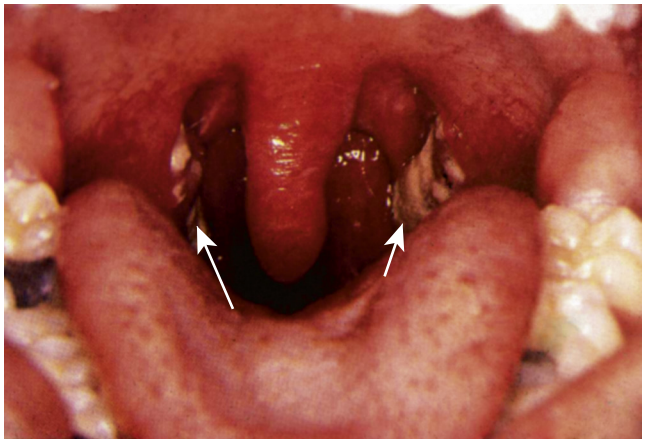
An adequate history needs to be taken if *N. gonorrhoeae* is suspected. Systemic symptoms and findings such as arthritis or genitourinary symptoms such as pain and discharge can be relevant for patients with pharyngitis, and should not be ignored if discussed in the history.

C. diphtheriae is a historical point in developed countries since the advent of vaccination; however, the symptoms should be considered in patients who have not been immunized or are from underdeveloped countries. The oropharynx will be coated with a thick, gray membrane. It can be scraped off, and it causes bleeding and edema of the tissues beneath the membrane. The membrane over the oropharynx is often life-threatening because of upper airway obstruction. It is associated with cardiotoxicity and neurotoxicity; therefore, a full history and examination are mandated.[12]

TABLE 16-2 Centor Criteria

Criterion*	Points
Fever	1
Absence of cough	1
Anterior cervical adenitis	1
Tonsillar exudate	1
Age (yr)	
2-14	1
15-44	0
≥45	-1

*Note the modified version accounts for age.
Data adapted from Weber R: Pharyngitis, *Prim Care Clin Office Pract* 41:91-98, 2014.



• **Figure 16-3** Bilateral tonsillar exudates *(white arrows)*. This is an example of mononucleosis with erythema and exudates of the tonsils. (Adapted from Belleza W, Kalman S: Otolaryngologic emergencies in the outpatient setting, *Med Clin North Am* 90:329-353, 2006. Courtesy Joydeep Som, MD.)

Diagnosis

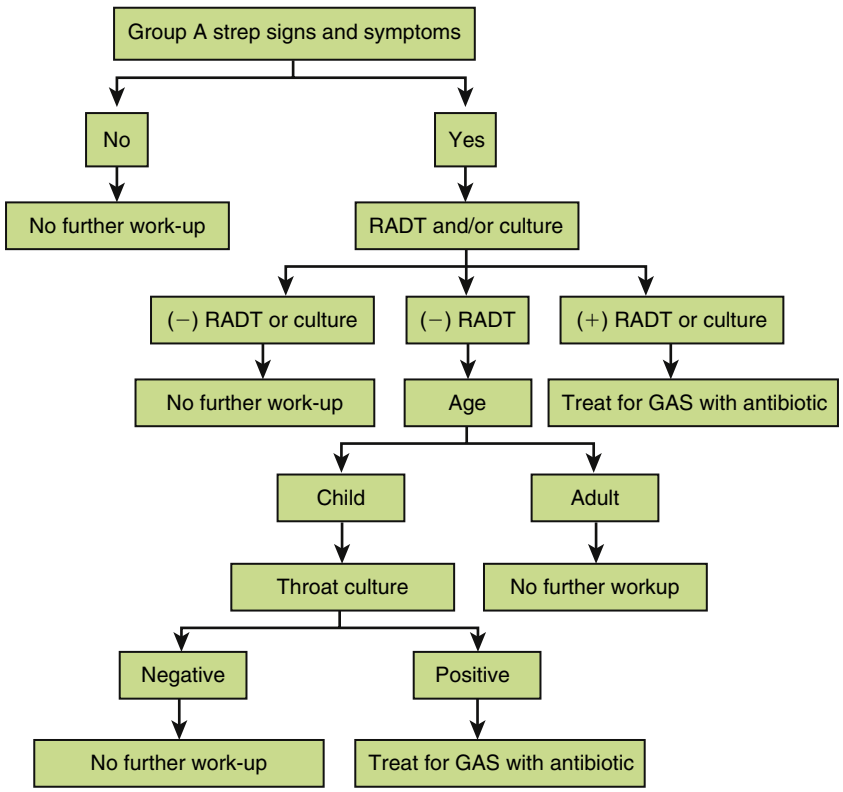
Bacterial Causes

While the diagnosis of acute oropharyngeal infections can often be made based on the history and examination, it is important to determine the organism involved. It is essential to rule out GAS to avoid nonsuppurative complications and rheumatic heart disease. Because the symptoms are nonspecific for GAS, and clinical judgment is not an effective means of accurate diagnosis,[6] different laboratory tests have been created to make this diagnosis.

The appropriate use of clinical scoring systems can help to guide the next step in treatment. If two or three of the Centor criteria are met, a rapid antigen detection test (RADT) should be performed. If four of the Centor criteria are met, it has been suggested that empiric treatment for GAS can be started or RADT can be performed.[1] The RADT is a throat swab that is used to detect cell wall carbohydrate antigens with specific enzyme-immunoassay antibodies.[10,12] The sensitivities of this test range from 70 to 90%[1,10,12]; however, the specificity of this test is extremely high at greater than 95%.[1,7,10] Thus, patients who have a positive RADT and symptoms of pharyngitis should have antibiotic therapy initiated. Patients without any symptoms do not need to be tested because a positive test without symptoms would indicate carrier status as opposed to being acutely infected. The diagnostic ability of the test increases if there is a greater likelihood of the patient having GAS pharyngitis.[7] If a RADT result is negative, then a throat culture should be used for a more definitive test. Throat culture is ultimately the gold standard by which the diagnosis of GAS pharyngotonsillitis is made. The throat swab for culture needs to be collected from the surface of the pharynx or tonsils, because collections from other sites in the oral cavity reduce diagnostic accuracy.[1,10] When this algorithm is used, the diagnostic sensitivity and specificity are both greater than 95%,[1] and it is the most cost-effective management[10] (Figure 16-4).

Throat cultures take 24 to 48 hours to return a result. In the situation with a negative RADT result, antibiotics do not necessarily need to be prescribed before a positive throat culture result. The delay in treatment does not affect the rates of nonsuppurative complications, such as rheumatic heart disease or post–streptococcal glomerulonephritis.[1,10] Currently the question of whether to treat GAS has been raised because there are such low rates of rheumatic heart disease and renal involvement following GAS in the developed world.[7,10] This algorithm of RADT followed by culture may also be more useful in children and unnecessary in adults. Some reports recommend against a throat culture in the face of a negative RADT in adults because the incidence of GAS is lower, and the incidence of rheumatic heart disease is minimal.[1]

Other less common bacterial causes should be worked up with throat culture to confirm the diagnosis. *N. gonorrhoeae* can be obtained using a throat culture on Thayer-Martin agar. It should be noted that asymptomatic colonization with *N. gonorrhoeae* can occur, however.[2] Culture of the



• **Figure 16-4** Algorithm for workup of acute pharyngitis. (Adapted from Kociolek LK, Shulman ST: In the clinic. Pharyngitis, *Ann Intern Med* 157:ITC3-1–ITC3-16, 2012.)

pseudomembrane of *C. diphtheriae* should be performed on Loeffler or tellurite selective media.[6,12]

Viral Causes

For many of the respiratory viruses that cause acute oropharyngeal and tonsillar infections, there is no diagnostic test available. Because most of the viral causes of the infection are self-limited, it is neither cost effective nor necessary to determine the organism; however, workup of EBV and HIV warrant special attention.

If EBV is suggested as a cause of acute pharyngotonsillitis, workup with laboratory tests is a necessary part of the evaluation. Because EBV often causes an infectious mononucleosis, a workup with a complete blood cell count and differential is necessary. The complete blood cell count will often show a marked lymphocytosis,[5] which suggests EBV mononucleosis, as opposed to a left-shifted leukocytosis of bacterial causes of oropharyngeal infections. Some reports indicate that a lymphocyte count of greater than 4.0×10^9 in patients with symptoms that are strongly suggestive of EBV is a reliable predictor of the infection; however, it should be still further confirmed with more specific testing.[23] Peripheral blood smears with greater than 10% atypical lymphocytes also strongly suggest infection with EBV.

Further testing involves antigen–antibody interaction. EBV induces heterophile antibodies against viral antigens that cross-react with antigens from sheep and horse red cells, and these are present in approximately 90% of infected individuals within the first 2 to 3 weeks of illness.[12,14] The reported sensitivity and specificity of the heterophile antibody test are 85 and 94%, respectively.[14] There are also rapid monospot tests available as screening for patients with possible EBV. Children often do not produce heterophile antibodies; therefore, false-negative results are more common in this age group.[12] Some reports indicate only 25 to 50% of 12 year olds will be positive for this antibody.[14] It is important to note that these test results may be negative in patients with symptoms early in the viral course; therefore, a negative test result does not necessarily rule out infection with EBV.

The diagnosis of EBV mononucleosis can be made with a combination of clinical presentation, atypical lymphocytosis, and the presence of heterophile antibody. The confirmatory test is antibody titers to viral capsid antigens. Immunoglobulin (Ig) M antibodies are seen within the first 4 to 8 weeks of a primary infection, and if detected in circulation, acute infection can be diagnosed. IgG can be present in the blood throughout one's lifetime; however, it is not present early in the infection, and so will not help much in the acute setting.

If a patient presents with mononucleosis-like symptoms, but is EBV negative with a negative heterophile antibody, HIV and CMV infections should be suspected. CMV is often the cause, and it is particularly important in pregnant women because of the risk to the fetus. This can be confirmed with testing for IgM and IgG antibodies.[5,17] The Centers for Disease Control and Prevention recommends that testing begin with a combination immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen. All specimens reactive on this initial assay undergo supplemental testing with an immunoassay that differentiates HIV-1 from HIV-2 antibodies. Specimens that are reactive on the initial immunoassay and nonreactive or indeterminate on the antibody differentiation assay proceed to HIV-1 nucleic acid testing for resolution.

Treatment (Medical versus Surgical)

The treatment of acute oropharyngeal and tonsillar infections depends on the causative organism. Bacterial infections require antibiotics, whereas viral causes are self-limited. Treating oropharyngeal infections and tonsillitis is controversial because increased use of antibiotics has led to the concern of increased resistance among organisms. Thus, it is suggested that treatment be started only for culture-proven cases, including GAS.[19] The rationale behind treatment is to prevent complications from the infection and to shorten the duration of symptoms. Studies of cost-effectiveness of treatments indicate that starting empiric antibiotics for symptomatic adult patients is ineffective, and it leads to unnecessary overuse of antibiotics and increased medication side effects.[10]

Medical

Group A *Streptococcus* is the most common cause of pharyngotonsillitis; therefore, treatment options have been well studied for this organism. In fact, it is the only commonly occurring organism for which antibiotic therapy is indicated.[18] It has been shown that even bacterial infections are often self-limited; therefore, treatment goals are essentially to avoid complications of the oropharyngeal infection.[1,12] Penicillin used to be the mainstay of antibiotic classes used for management of this organism, and there has yet to be a case of reported penicillin resistance in GAS.[4-6] Initiation of a 10-day course of penicillin dosing three to four times per day can be used as first-line therapy for penicillin-tolerant patients.[4,6,24] Amoxicillin is often used as a first-line therapy for GAS because of the once-daily dosing regimen. A 10-day course of amoxicillin has been shown to be just as effective as penicillin against GAS eradication in the oropharynx of acutely infected individuals.[1,25] If a patient has EBV and is being treated with antibiotics for a presumed bacterial pharyngitis, he or she will often exhibit a maculopapular rash when given amoxicillin or ampicillin; this can be used as a clue to aid in the diagnosis of EBV.

Oral cephalosporins are a reasonable second option for treatment, because they have good coverage against GAS and eradicate the organism completely.[26] In patients who are allergic to penicillin, oral macrolide antibiotics are the best options for coverage of GAS oropharyngitis. The most commonly prescribed macrolides are azithromycin and clarithromycin because of their lower side effect profile compared with

erythromycin. Duration of treatment with azithromycin is typically only 5 days with dosing once daily, which makes it an attractive therapy for convenience. The downside of treatment with macrolides is that resistance has been reported with short-term use of the antibiotic, which has not been seen with penicillins.[12,26] It is also a more expensive family of antibiotics; therefore, it is typically reserved for penicillin-allergic patients and is not used as a first-line therapy.

In addition to antibiotic therapy to treat the infectious agent in oropharyngitis, there is a role for adjuvant use of steroids in patients with GAS pharyngitis. Steroid use has been thoroughly studied in adult patients as a single dose during an acute infection. The mechanism of their action is believed to be mediated through an antiinflammatory effect, which helps to reduce pain symptoms associated with severe oropharyngeal infections. Therapy can be administered either orally or intramuscularly to help reduce symptoms of pain in acute infections, and this often leads to a quicker recovery.[27-29] The data on their use are mixed, however, and in GAS pharyngitis only a small clinical improvement can be expected.[30] There can also be unwanted side effects in some patients; therefore, the decision regarding their use can be left to the clinical judgment of the clinician.

For EBV infections and mononucleosis, the use of steroids is also an area of uncertainty. The data evaluating its efficacy in uncomplicated cases are mixed, and in uncomplicated cases steroids do not provide much therapeutic benefit. However, the most benefit appears to be derived in patients with severe tonsillar hypertrophy causing obstruction. Antivirals have been shown to be ineffective in treating EBV.[12,14] As with other viruses, the diseases are typically self-limited, and steroid treatment is for symptom relief and is not routinely required.

Surgical

For patients who have recurrent episodes of acute pharyngotonsillitis that continue despite multiple antibiotic courses, there is a surgical option of a tonsillectomy. Other indications for surgical management with tonsillectomy include suppurative complications of a pharyngotonsillitis, such as a peritonsillar abscess. The criteria for tonsillectomy in a patient with recurrent infection are debated. However, current recommendations suggest a tonsillectomy for patients with seven episodes of pharyngitis in one year, five episodes in two consecutive years, and three episodes in three consecutive years[31,32]; this is known as the *Paradise criteria*. Much of the debate around this topic is centered on the fact that there is no universal definition for an acute pharyngotonsillitis based on clinical criteria. In the studies used to define these surgical criteria, it was not necessary to document a cause of the infection.[32]

The expected benefit of having a tonsillectomy is a reduction in the frequency and severity of oropharyngeal infections for up to 2 years.[33] This benefit may be underestimated, however, because the researchers reporting this value included only severe cases of recurrent infection in the surgical arm of their study.[32]

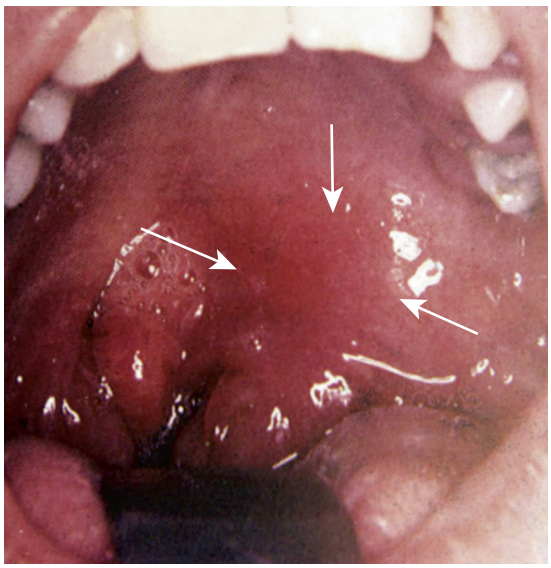
Surgical management is not without risk. A tonsillectomy has the known risks of pain, dehydration, and bleeding that may require an additional surgical procedure to control it. Thus, the options for management need to be strongly considered. Often a 12-month observation period is an option before tonsillectomy is performed.

Complications

The complications of acute oropharyngeal infections and tonsillitis can be broken down into two different types of complications: suppurative and nonsuppurative. The suppurative causes occur more frequently, whereas the nonsuppurative causes are rare in industrialized countries. The rate of all complications has been reduced dramatically with the introduction of antibiotics; however, serious sequelae can occur if these complications are not identified.

Suppurative

The complications often seen with acute pharyngitis are abscesses and deep space neck infections. The complex anatomy and fascial planes of the head and neck create a number of pathways for spread of infection. There are many types of deep space neck infections, but the most common one in both children and adults is a peritonsillar abscess (PTA; Figure 16-5).[34] However, the infection of an acute pharyngitis can spread to the parapharyngeal space, the buccal space, the masticator space, the retropharyngeal space, the danger space, the prevertebral space, and the carotid space. Each of these spaces is its own distinct plane, and infection



• **Figure 16-5** Left-side peritonsillar abscess demonstrating bulging and erythema of the soft palate *(white arrows)* with the uvula deviated to the right. (Adapted from Belleza W, Kalman S: Otolaryngologic emergencies in the outpatient setting, *Med Clin North Am* 90:329-353, 2006. Courtesy Joydeep Som, MD.)

in some of these spaces can be life threatening if not treated appropriately. One series review of the literature from 1994 to 2004 found a mortality rate of 6.1 to 41.7% when life-threatening complications occurred.[35]

Acute pharyngitis is becoming a less frequent cause of these complications since the advent of penicillins, while there has been an increase in deep space neck infection of odontogenic origin.[8,35] This emphasizes the need for a thorough evaluation of the dental structures during the history and physical examination. Similarly, patients with complex medical histories such as diabetes or HIV tend to have atypical complications.[8]

Diagnosis of these complications can often be suggested on history and physical examination. When evaluating for deep space involvement, neck pain and range of motion, in addition to any trismus or voice changes, help to raise the suggestion of complications. Studies have tried to use clinical data as predictors of who will develop suppurative complications; however, this has not been shown to be useful as a predictive tool.[36] The diagnosis often relies on imaging with computed tomography with contrast enhancement, which has essentially become the standard of care to identify deep space suppurative infections.[8] Imaging is especially important in evaluating for retropharyngeal, danger space, and prevertebral infections because they can spread into the thoracic cavity. The one exception to that would be for an uncomplicated PTA, which often does not require imaging.

One other suppurative complication for the clinician to be aware of is Lemierre syndrome, which results from PTA extension to the tonsillar veins and the internal jugular vein (Figure 16-6). The spread of infection into the venous system will cause thrombosis in the vein, which leads to septic embolization and respiratory failure.[37] This complication was much more common in the pre-antibiotic era, but it still occurs. The organism that is classically associated with this syndrome is the anaerobe *Fusobacterium necrophorum*; however, other organisms and polymicrobial infections can be responsible as well (Figure 16-7).

The diagnosis of these suppurative complications and deep neck infections caused by an acute pharyngitis is important because management often requires procedural or surgical intervention. Intravenous antibiotics with penicillins such as ampicillin–sulbactam or clindamycin are considered first-line antibiotics. Clindamycin provides good anaerobic coverage for the polymicrobial environment of the abscess. Studies analyzing the complications of a deep neck infection found that the only prognostically significant factor contributing to complications was the involvement of more than one neck space, whereas hospital stays were likely to be increased in patients with medical comorbidities, leukocytosis, and the need for both medical and surgical treatment.[35]

The role of the clinician in knowing when to suspect a deep space neck infection cannot be overemphasized. Despite the fact that medical treatments are improving the rates of these complications, they do occur and can have serious sequelae if not diagnosed in a timely manner.

Nonsuppurative

Acute rheumatic fever and glomerulonephritis are the nonsuppurative complications that are most concerning following an acute infection of the oropharynx. It is beyond the scope of this chapter to discuss how to manage these complications or perform a workup; however, it is essential to be aware of the fact that there are systemic complications. These complications are typically a result of a GAS pharyngitis. The mechanism is due to cross-reactivity and molecular mimicry of the streptococcal antibody within different organs.[38] Traditionally, the nonsuppurative complications of acute pharyngotonsillitis are the reason that this often self-limited disease is treated. With the use of antibiotics, some studies have reported 80% reduction in the incidence of acute rheumatic fever when compared with no antibiotics.[10]

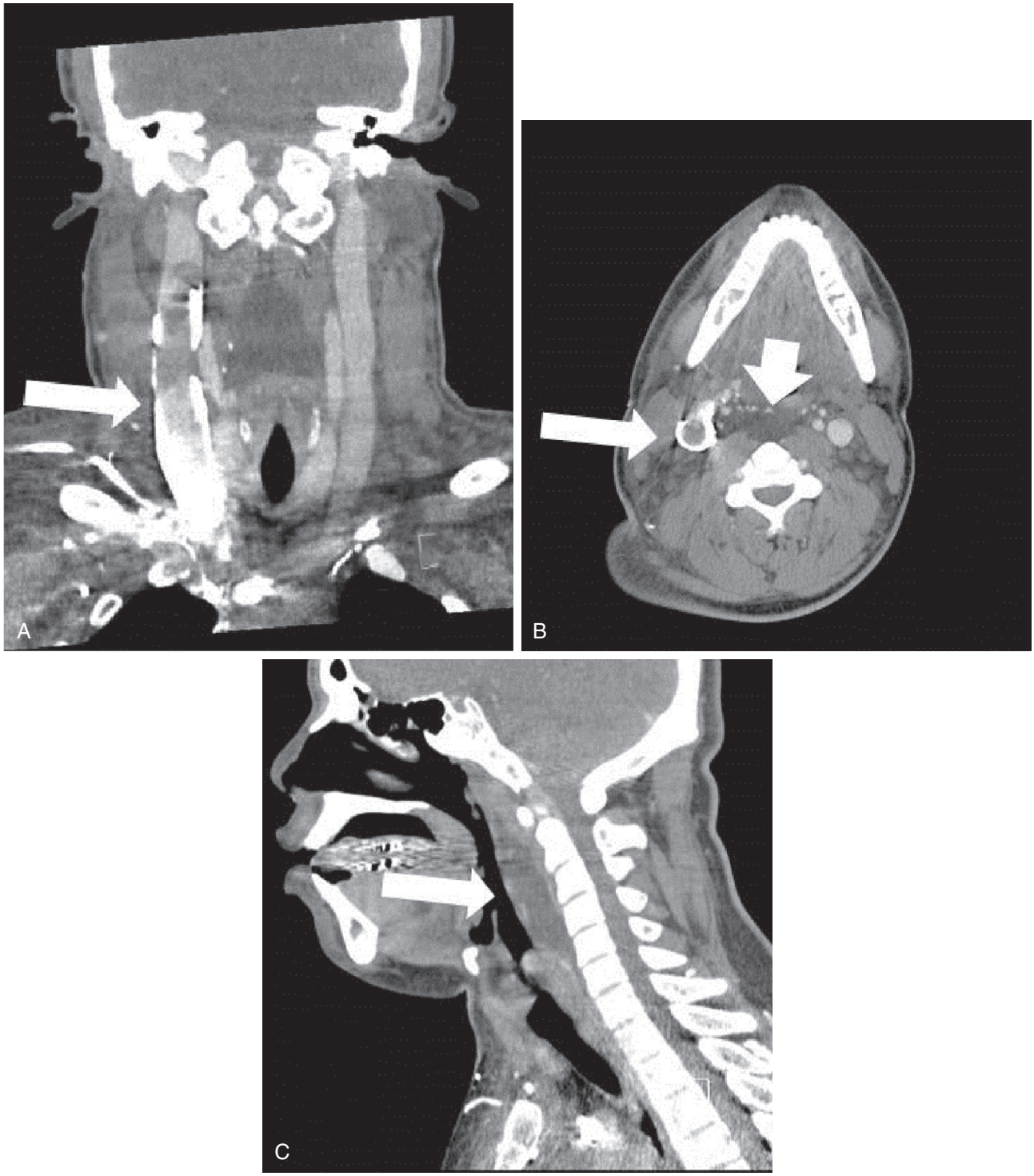
Acute rheumatic fever can cause a wide constellation of nonspecific symptoms that include arthritis, carditis, subcutaneous nodules, and chorea. Symptoms usually appear 2 to 3 weeks after an acute GAS pharyngitis. It is rare in developed countries; however, rheumatic heart disease following an acute GAS oropharyngeal infection is the leading cause of acquired heart disease in many areas, such as sub-Saharan Africa, India, and Australia,[10] and it is the leading cause of cardiovascular death in some developing areas of the world.[38] There is little evidence to support the idea that treatment of acute pharyngitis caused by GAS prevents acute glomerulonephritis.[10,12]

Nonsuppurative complications can also occur in conjunction with acute pharyngotonsillar infections not caused by GAS. In EBV infections, systemic complications such as splenic rupture occur in 0.5 to 1% of cases of primary EBV infection.[14] EBV has the potential to cause multiple hematologic complications, such as hemolytic anemia, thrombocytopenia, and hemolytic-uremic syndrome.[14] There can also be superimposed bacterial pharyngitis, with EBV pharyngotonsillitis causing deep space neck abscess.

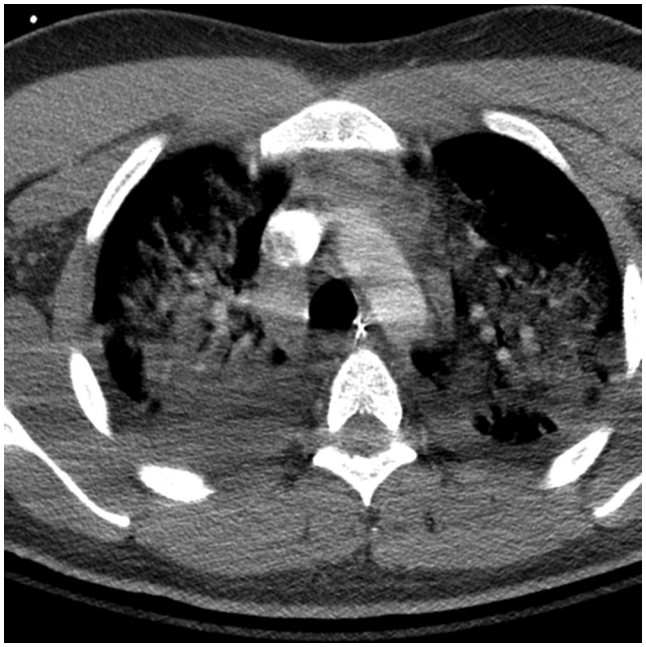
Awareness of these potential nonsuppurative complications is essential, because their management can be complex and can involve multiple medical teams. Timely diagnosis is necessary to prevent complications or organ failure resulting from the systemic involvement.

Conclusion

Oropharyngeal and tonsillar infections are responsible for a large percentage of visits to the physician each year. The causative organisms can be bacterial, viral, or both. Although viral causes are more common, the bacterial causes often require a more involved workup because failure to treat them can have more severe consequences. Viral causes are treated with supportive care, but particular care should be taken not to overlook EBV and HIV as potential viral organisms causing pharyngitis. GAS pharyngitis is the most common bacterial cause of oropharyngeal infection. Fast and accurate diagnosis of GAS is essential because antibiotic therapy will help to



• **Figure 16-6** Twenty-four-year-old male patient with a history of recurrent tonsillitis. **A,** Coronal cut of soft tissue neck computed tomographic scan with contrast demonstrating thrombosis of right internal jugular vein *(white arrow)* owing to acute tonsillitis leading to retropharyngeal phlegmon. **B,** Axial cut demonstrating retropharyngeal phlegmon *(short white arrow),* tonsillar edema, and right internal jugular vein thrombosis *(long white arrow).* **C,** Sagittal cut demonstrating retropharyngeal phlegmon *(white arrow).*



• **Figure 16-7** Extensive bilateral airspace opacities consistent with acute respiratory distress syndrome in a 17-year-old male patient with anaerobic tonsillitis *(Fusobacterium necrophorum)* and sepsis.

prevent both suppurative and nonsuppurative complications. This diagnosis can be facilitated with rapid antigen detection test and confirmed with throat culture. Once the causative organism is identified, prompt initiation of antibiotics with either penicillin or cephalosporin should be started. For recurrent infections or suppurative complications, surgical intervention should be given consideration as well. For the clinician, the balance must be weighed between treating promptly and being too aggressive and increasing antibiotic resistance. This area of study will continue to make acute pharyngitis and tonsillitis a topic of discussion in the future.

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