Acute Pharyngitis, Tonsillitis, and Peritonsillar Abscess

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Anatomy and Pathophysiology

The pharynx is a fibromuscular tube extending from the skull base to the lower border of the cricoid cartilage connecting the oral cavity to the esophagus. Portions of the pharynx lie posterior to the nasal cavity (nasopharynx), oral cavity (oropharynx), and larynx (laryngopharynx) (Fig. 17.1a). The muscular components include three pharyngeal constrictor muscles and the stylopharyngeus, salpingopharyngeus, and palatopharyngeus muscles. The circular structure of lymphoid tissue located in the nasopharynx and oropharynx is known as Waldeyer's ring. It is formed by two palatine tonsils (commonly called tonsils) in the lateral walls of the tonsillar fossa, a pharyngeal tonsil (commonly called the adenoid), two tubal tonsils, and the lingual tonsil. The adenoid tonsil is large between ages 3 and 8 and then regresses. The tubal tonsils are located near the Eustachian tube openings. The lingual tonsil is located at the base of the tongue. Peritonsillar abscess refers to infection adjacent to one of the palatine tonsils (Fig. 17.1b).

The tympanic branch of the glossopharyngeal nerve is responsible for referred pain present with tonsillar inflammation. The palatoglossus muscle forms the anterior tonsillar pillar, the palatopharyngeus muscle forms the posterior tonsillar pillar, and the pharyngeal constrictors form the base of the tonsillar fossa. The tonsil capsule attaches to the pharyngeal muscles [1].

When patients present to medical care with a "sore throat" due to an infection, they can be experiencing pharyngitis, tonsillitis, or pharyngotonsillitis. The exact mechanism that leads to pain with inflammation in this region is incompletely understood; however, studies have demonstrated that bradykinin and prostaglandin may play a role in mediating a pain response [2–4].

Epidemiology

Sore throat is a very common complaint, generating 12 million ambulatory visits annually in the U.S. [5]. The highest burden of acute pharyngitis and tonsillitis occurs in children and young adults. A Swedish study found that 66.5% of cases of streptococcal tonsillitis and 65% of

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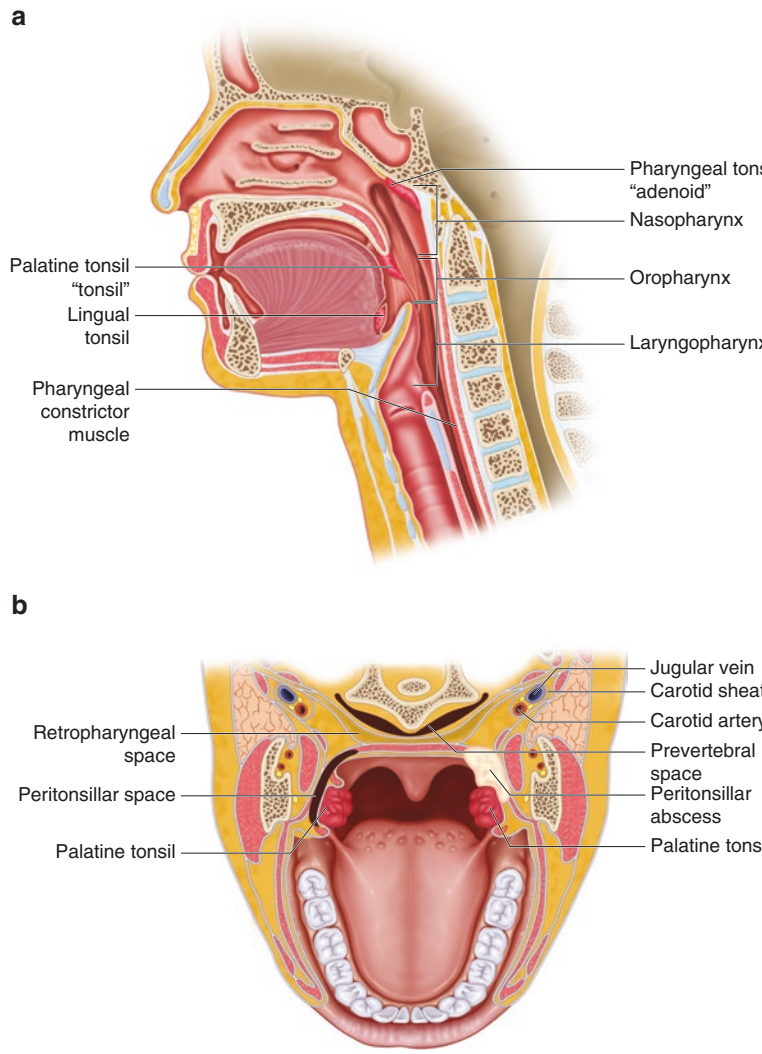

Fig. 17.1 (**a**) Sagittal view of the pharynx. (**b**) Peritonsillar abscess and its relationship to other structures in the throat

acute pharyngitis cases occurred in those aged 5–35 years old, with the 5–14 year olds having the highest burden of disease in this population sampled for both the conditions [6]. Similarly, in a study using national survey data from the U.S., the majority of outpatient pharyngitis visits were by patients under the age of 19 [7]. Viral agents are the most common cause of pharyngitis, and in temperate climates, pharyngotonsillitis tends to be more prevalent in the winter and early spring, corresponding to circulation of these respiratory viruses.

Clinical History

Acute pharyngitis and tonsillitis are clinical diagnoses. Patients with acute pharyngitis and tonsillitis report irritation or pain in the posterolateral oropharynx which tends to be exacerbated by swallowing. Depending on the infectious agent causing their disease, they may also variably report associated fever, rhinorrhea, cough, tender or enlarged lymph nodes, or rash. It is important to inquire about associated symptoms, sick contacts, travel, vaccination history, sexual history,

including history of oral sex, and other risk factors for human immunodeficiency virus (HIV) acquisition. This detailed information may aid the clinician in narrowing the differential diagnosis and allow targeted diagnostic testing (Table 17.1).

Table 17.1 History and physical examination findings suggesting possible pathogens causing pharyngitis or tonsillitis

Historical clues	**Suggestive etiologies**
Epidemic pharyngitis	Adenovirus (water exposure), group G *Streptococcus* (dairy/eggs)
Daycare exposure	Adenovirus, Enterovirus, Parainfluenza virus, Rhinovirus, Respiratory syncytial virus (RSV), group A *Streptococcus* (GAS)
Intravenous drug use	Human immunodeficiency virus (HIV)
High risk sexual behaviors	HIV, Herpes simplex virus (HSV), *Chlamydia trachomatis, Neisseria gonorrhoeae*
Unvaccinated	*Corynebacterium diphtheriae*

Clinical signs/ symptoms	**Suggestive etiologies**
Cough	*C. pneumoniae*, *Mycoplasma pneumoniae*, respiratory viruses
Rhinorrhea	Adenovirus, Parainfluenza virus, Rhinovirus, RSV
Weight loss	HIV
Nausea, abdominal pain	GAS

Physical exam findings	**Suggestive etiologies**
Rash	GAS, *Arcanobacterium haemolyticum*, HIV, Epstein Barr Virus (EBV), Adenovirus, Coxsackievirus, Enterovirus
Conjunctivitis	Adenovirus
Adenopathy	GAS, Adenovirus, EBV (posterior, axillary, inguinal chains), HSV
Palatal petechiae	GAS, EBV
Oral ulcers	Coxsackievirus, Enterovirus, HIV, HSV
Tonsillar exudates	GAS, *Fusobacterium*, group C *Streptococcus, N. gonorrhoeae*, Adenovirus, EBV, HSV; *Corynebacterium diphtheriae* commonly causes pseudomembranes over the tonsils that bleed on scraping
Splenomegaly	EBV

Patients who have developed a peritonsillar abscess as a complication of tonsillitis may report a sore throat that becomes progressively severe and may be unilateral, as well as fever, a change in voice, difficulty with swallowing secretions leading to drooling, and difficulty opening their mouth. It is important to elicit other symptoms that may reflect more severe illness such as lightheadedness or syncope, which may indicate hypotension and sepsis, or difficulty with breathing, which may portend impending respiratory failure.

Examination

The examination of a patient with a sore throat should include measurement of vital signs. A fever is variably present depending on the pathogen. Tachycardia, hypotension, or tachypnea may be clues that the patient is systemically unwell. Examining the nares and nasal mucosa may reveal rhinorrhea or hyperemia, often associated with viral agents causing sore throat, such as rhinovirus, adenovirus, or parainfluenza virus. Pharyngeal edema and erythema is visible with pharyngitis. Tonsillar edema or erythema is present with tonsillitis. Exudates on the posterior pharynx or tonsillar pillars are more commonly seen with group A *Streptococcus* (GAS), Epstein Barr Virus (EBV), *Neisseria gonorrhea*, and diphtheria (see Chap. 19). Petechiae on the soft palate may be seen in GAS. Unilateral peritonsillar swelling with displacement of the tonsil suggests peritonsillar abscess (Fig. 17.2). A rash may be present with certain infections, including GAS, *Arcanobacterium haemolyticum*, HIV, and EBV. Tender adenopathy in the cervical chain is commonly described with pharyngotonsillitis (Table 17.1). Swelling of or difficulty with rotating the neck may suggest a more extensive deep neck space infection (see Chap. 27).

There is considerable overlap between the infectious causes of pharyngitis and tonsillitis. Specific infectious agents and the clinical syndromes they cause will be reviewed here along with diagnostic and therapeutic considerations for each. Viruses are the most common cause of pharyngitis [8–10].

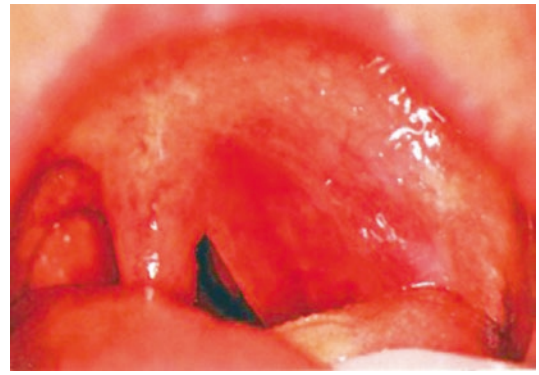

Fig. 17.2 A view of the oropharynx in a patient with a peritonsillar abscess. From: Flint, Paul W. Throat disorders. In: Goldman L, Schafer AI (eds). Goodman-Cecil Medicine, 25th edition. Elsevier, Inc. 2016, with permission

Viral Etiologies of Pharyngitis

Adenovirus

Adenovirus is a common cause of pharyngotonsillitis. In an Italian study, extensive diagnostic testing of children presenting with acute pharyngitis revealed adenovirus to be the most common single viral agent [9]. A retrospective study of children in Spain with positive pharyngeal cultures for adenovirus demonstrated that 88% had tonsillitis and 52% of those had exudates [11]. Cervical lymphadenopathy and a rash may also be present. Pharyngoconjunctival fever syndrome is classically associated with adenovirus serotypes 3 and 7. Patients present with pharyngitis and conjunctivitis in the spring or summer, usually after swimming. This is highly contagious and may spread to up to 50% of close contacts [12]. Direct fluorescent antibody testing of nasopharyngeal swabs can confirm the diagnosis. Treatment is supportive.

Respiratory Syncytial Virus

Respiratory syncytial virus (RSV), a member of the *Paramyxoviridae* family, is another common cause of pharyngotonsillitis and tends to be seasonal with outbreaks occurring in the late fall through spring in temperate climates. RSV is spread via respiratory secretions [8, 9]. Rapid antigen assays or polymerase chain reaction of nasopharyngeal swabs can make the diagnosis. Treatment of pharyngitis caused by RSV is supportive.

Enterovirus

Members of the *Enterovirus* family have been implicated in causing pharyngitis, specifically herpangina and hand-foot-mouth disease, which are more common in children than adults. These viruses spread either from gastrointestinal or respiratory shedding. Herpangina, most commonly caused by members of the group A Coxsackievirus family, refers to the clinical syndrome of fever and a painful vesiculo-ulcerative enanthem of the soft palate, posterior pharynx, and tonsils. Hand-foot-mouth disease is most commonly caused by Coxsackievirus A16 and enterovirus A71, although outbreaks attributed to Coxsackie A6 have been described [13, 14]. Hand-foot-mouth disease manifests clinically as herpangina in conjunction with a vesicular rash on the hands, feet, and buttocks [15, 16] (Fig. 17.3). Outbreaks are common in daycare settings. Diagnosis is usually clinical, and treatment is supportive.

Infectious Mononucleosis

Infectious mononucleosis (IM), characterized by fever, sore throat, adenopathy, and malaise, is classically caused by the herpesvirus EBV, although the differential diagnosis includes cytomegalovirus (CMV), human herpes virus 6, and HIV. Epstein Barr Virus is most common among those 5–25 years of age and spreads via contact with virus shed in oral secretions [17]. Clinical signs that point toward a diagnosis of EBV IM

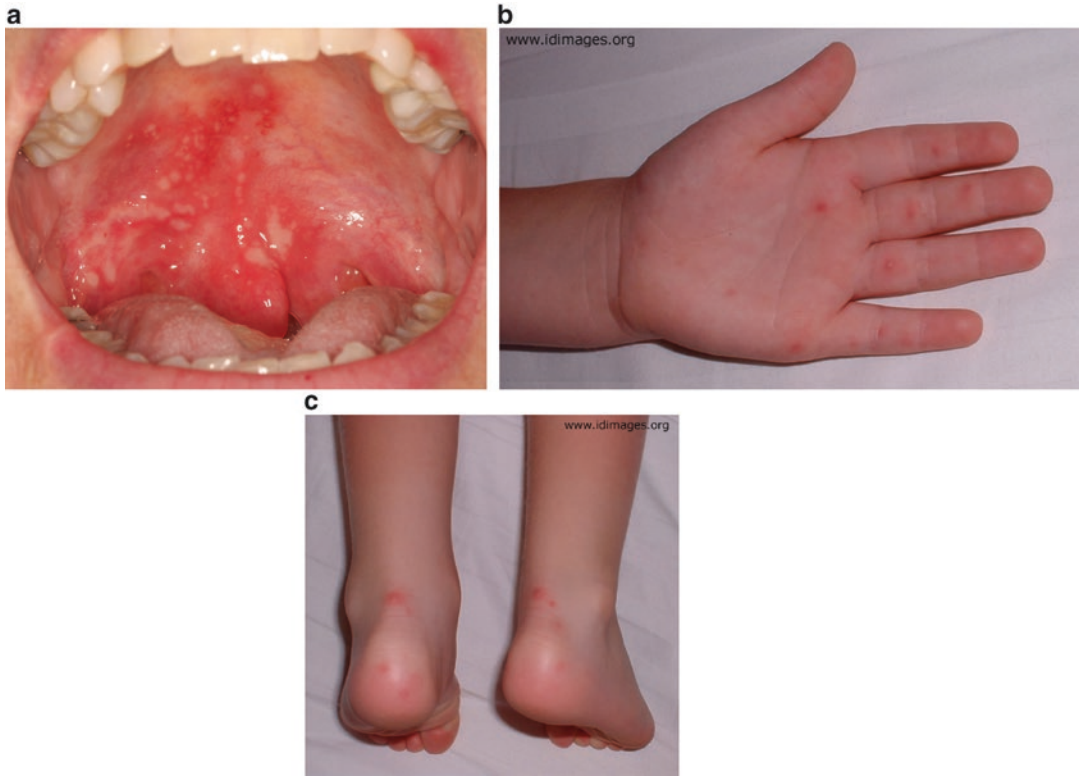

Fig. 17.3 Hand-foot-mouth disease. (**a**) Shallow lesions in the posterior oropharynx (Reproduced from Bruch and Treister [16] with permission from Springer), (**b**) Vesicular rash on the hands and (**c**) feet. (Reprinted with permission from Partners ID Images. Copyright Partners Healthcare System, Inc. All rights reserved) [15]

are palatal petechiae, seen in up to 25% of affected patients, and adenopathy in the posterior cervical, axillary, and inguinal chains [18, 19]. Other exam findings include tonsillar enlargement with or without exudates, splenomegaly, and jaundice. A diffuse maculopapular rash often develops in EBV IM after treatment with amoxicillin, ampicillin, or antibiotics containing these antibiotics such as amoxicillin-clavulanate. The incidence is approximately 30% in children with EBV IM treated with amoxicillin [20]. A rash in EBV IM has been described after treatment with other antibiotics, such as cephalexin [21], azithromycin [22], and quinolones [23], although this is rare—only three cases of azithromycin-related rash have been described, for example. The etiology of the amoxicillin-related rash in mononucleosis is unknown, but may represent a true allergy in some cases [24]. A rash may also accompany the EBV IM infection itself. In a study from Israel of 238 children hospitalized with EBV IM, a rash developed in 33% of children treated with antibiotics versus 23% of untreated children [20].

Lymphocytosis and atypical lymphocytes are also features of EBV IM, although these may also occur in IM due to CMV. A heterophile antibody test, also called monospot, is a latex agglutination assay that may be useful in confirming the diagnosis of EBV-associated IM [25, 26]. There are important limitations for this test. Children <5 years of age do not reliably produce heterophile antibody during acute infection [27]. A false positive heterophile antibody may occur in patients with other conditions such as lymphoma, acute HIV, and systemic lupus erythematosis. False negative heterophile testing is commonly seen when the test is sent early in the course of infection; the sensitivity of heterophile testing for IM reaches 95% sensitivity only after 2 weeks of

EBV infection. If the heterophile antibody is negative, but IM due to EBV is still suspected, then one option is to repeat the heterophile test later in the course of illness, and another is to send EBV-specific serologies. Notably, in Europe, EBV-specific antibodies are routinely used as the primary laboratory test for IM due to EBV whereas in the U.S., the heterophile is most often used, although this test is not recommended by the Centers for Disease Control and Prevention (CDC) for general use [28]. Epstein Barr Virus viral capsid antigen (VCA) IgM and IgG antibodies are sensitive and specific. In acute IM from EBV, the VCA IgM is elevated. Early in the course of infection, the VCA IgG is negative, but later in the course the VCA IgG level rises. VCA IgM levels tend to wane after 3 months, while VCA IgG antibodies persist for life. Nuclear antigen IgG antibodies (EBNA) are detectable 6–12 weeks after infection and persist for life. Early antigen (EA) IgG antibodies are variably expressed in acute illness (Table 17.2). Epstein Barr Virus polymerase chain reaction (PCR) testing should not be used to diagnose IM. Treatment for EBV IM is supportive, and patients should be counseled that they may continue to experience fatigue for months. The authors of a Cochrane review on the use of steroids for symptom control in IM concluded that based on the seven trials, there was insufficient evidence on the efficacy of steroids in this setting [29]. If splenomegaly is present, then contact sports should be avoided to decrease the risk of splenic rupture.

When a patient presents with an IM-like syndrome, acute retroviral syndrome due to HIV should be considered. Risk factors include, but are not limited to, high risk sexual behaviors (men who have sex with men, sex with sex workers, multiple partners), intravenous drug use, or intranasal cocaine use. In a prospective cohort study that identified 40 subjects with primary/early HIV infections, the symptoms most strongly associated with primary HIV infection were fever and rash [30]. In this population, the sensitivity of pharyngitis occurring in primary HIV infection was 44% and specificity 77%. Other symptoms associated with acute HIV infection include oral ulcers, weight loss, arthralgias, and anorexia. When acute HIV is suspected, typically a combination of HIV antigen/antibody immunoassay and an HIV viral load is obtained [31]. In acute infection, the antibody test is often negative, and the viral load is often very high. Patients with acute HIV should be referred urgently to providers with clinical experience in treating HIV.

Table 17.2 Epstein Barr virus serology interpretation

EBV status	VCA IgM	VCA IgG	EBNA	EA IgG
No exposure	–	–	–	–
Acute infection	+	+/–	–	+/–
Remote infection	+/–	+	+	+
Indeterminate	–	+	–	+

EA early antigen, *EBNA* nuclear antigen IgG, *VCA* viral capsid antigen

Herpes Simplex Virus

Herpes simplex virus (HSV) is another cause of pharyngitis and/or tonsillitis, especially in adolescents and young adults. In a study of college students presenting with "upper respiratory symptoms" who underwent a throat swab, 5.7% had cultures positive for HSV, with 17% of those having concomitant infections with GAS, *Mycoplasma pneumonia*, and EBV [32]. In this study 94% of the isolates were HSV type 1, although HSV type 2 causing pharyngotonsillitis has been described in sexually active patients [32, 33]. Symptoms of HSV pharyngotonsillitis include fever, pharyngeal erythema, tonsillar exudates, and enlarged, tender, cervical adenopathy. In the college campus study, only 17% of those with HSV had ulcerative lesions present on physical exam, highlighting the need to maintain a high clinical suspicion for this viral etiology as the culprit for pharyngotonsillitis [32]. Another possible explanation for the findings of this study is that HSV can reactivate in the setting of inflammation due to another etiology. Herpes simplex virus is diagnosed by viral culture of a throat swab, although a special type of swab (calcium alginate) and viral transport media are required. Valacyclovir, acyclovir, or famciclovir can be used for the treatment of HSV pharyngotonsillitis (Table 17.3).

Table 17.3 Recommended targeted therapy in older adolescents and adults for specific pathogens causing pharyngitis or tonsillitis

Pathogen	Recommended treatment for tonsillopharyngitis	Alternative treatment	Comments
Arcanobacterium haemolyticum	Macrolide (e.g., azithromycin, erythromycin)	Amoxicillin, cefuroxime, doxycycline, clindamycin	Trimethoprim-sulfamethoxazole resistance is common. Penicillin treatment failures have been reported
Chlamydia pneumoniae	Treatment is generally recommended only if there is concurrent pneumonia (see the text)	See adjacent comment	See adjacent comment
Chlamydia trachomatis	Azithromycin 1 g PO × 1	Doxycycline[a] 100 mg PO twice daily × 10 days	
Fusobacterium necrophorum	Penicillin VK 500 mg PO four times daily or Penicillin plus metronidazole 500 mg PO three times daily or Amoxicillin-clavulanate 875 mg PO twice daily[b]	Clindamycin 300–450 mg PO four times daily[c]	Macrolides lack activity against *Fusobacterium* spp. Parenteral therapy recommended for serious infections Metronidazole is drug of choice for *Fusobacterium* infections but does not cover GAS so should be combined with a GAS-active agent
Group A *Streptococcus* (GAS)	Penicillin V 250 mg PO four times daily or 500 mg PO twice daily × 10 days or Amoxicillin 1000 mg PO daily or 500 mg PO twice daily × 10 days Or Benzathine penicillin G 1,200,000 U ×1 IM Doses are for usual adult weight patients (at least 27 kg). See footnote for pediatric dosing information[c]	Cephalosporins Or Clindamycin 300 mg PO three times daily Or Clarithromycin 250 mg PO twice daily × 10 days Or Azithromycin 500 mg PO day 1 followed by 250 mg PO days 2 through 5 (use pediatric dosing for weights less than 40kg)[c]	Alternative therapy should be reserved for those truly penicillin allergic; because macrolides do not cover *Fusobacterium,* empiric macrolide treatment of pharyngitis is not recommended especially in the adolescent/young adult population
Group C/G *Streptococcus* (GCS/GGS)	Same as GAS		Treatment is controversial as GCS/GGS have not been linked to rheumatic fever
Herpes simplex virus (HSV)	Valacyclovir 1 g PO twice daily × 7–10 days	Famciclovir 250 mg PO three times daily × 7–10 days or Acyclovir 400 mg PO three times daily × 7-10 days	Treatment of first episode of HSV pharyngitis
Mycoplasma pneumoniae	Treatment is generally recommended only if there is concurrent pneumonia (see text)	See adjacent comment	See adjacent comment
Neisseria gonorrhoeae	Ceftriaxone 250 mg IM ×1 *and* Azithromycin 1 g	Gentamicin 240 mg IM and azithromycin 2 g PO ×1	Dual therapy (same day) is required for *N. gonorrhoeae*

IM intramuscular, *kg* kilogram, *mg* milligram, *PO* oral

[a]Off label use

[b]*Fusobacterium necrophorum* isolates may be resistant to penicillins (up to 10% of isolates) and clindamycin (up to 10% of isolates). Nearly all are susceptible to metronidazole and to a beta-lactam/beta-lactamase inhibitor combination such as amoxicillin-clavulanate

[c]Pediatric dosing for GAS is given in reference 34. Summary:Penicillin non-allergic: Penicillin 250 mg twice daily or three times daily x10 days, or amoxicillin 50 mg/kg daily (maximum 1000 mg) or 25 mg/kg PO twice daily (maximum 500 mg per dose) or penicillin G 600,000 units IM for patients weighing less than 27 kg, use adult dose for weight ≥ 27 kg. Penicillin-allergic: cephalosporins (if not allergic), clindamycin, azithromycin, clarithromycin (see reference [34] for dosing).

Bacterial Etiologies of Pharyngitis

Group A *Streptococcus* (*Streptococcus pyogenes*)

Group A *Streptococcus* (GAS), or *Streptococcus pyogenes*, is a leading bacterial cause of pharyngotonsillitis in children and adults and predominates in school-aged children [34, 35]. Typical symptoms include the sudden onset of sore throat, odynophagia, fever, headache, nausea with or without vomiting and abdominal pain. On exam, erythema with or without exudates on the pharynx and tonsillar pillars is generally present (Fig. 17.4a) and there may be petechiae on the soft palate, anterior cervical adenopathy, or a scarlatiniform rash. The rash is often described as a confluent, sandpaper rash that starts on the trunk and spreads to the extremities, sparing the palms and soles [35–37] (Fig. 17.4b). These symptoms/signs may be less sensitive and specific in younger children [35, 36]. Several prediction rules, based on clinical features and epidemiology, have been developed to aid the clinician in determining the likelihood of GAS pharyngitis (Table 17.4). The best-known prediction criteria are the Centor Criteria, derived from clinical and culture data obtained from 286 adults at a single emergency department [38]. This scoring system gives a point for each of the following: tonsillar exudates, cervical adenopathy, fever and absence of a cough. In a validation study, 7% of patients with one Centor criterion, 21% of patients with two Centor criteria, 38% of patients with three Centor criteria, and 57% of patients with four Centor criteria were confirmed to have GAS with either a rapid antigen detection test (RADT) or throat culture if the RADT was negative [39] (Table 17.5). These results highlight the fact that the Centor Criteria are more helpful for their negative predictive value than for positive predictive value. Specifically, the presence of three or four criteria has a positive predictive value of 40–60%, while the presence of two or fewer criteria has a negative predictive value of 80% for GAS infection. The McIsaac score, more

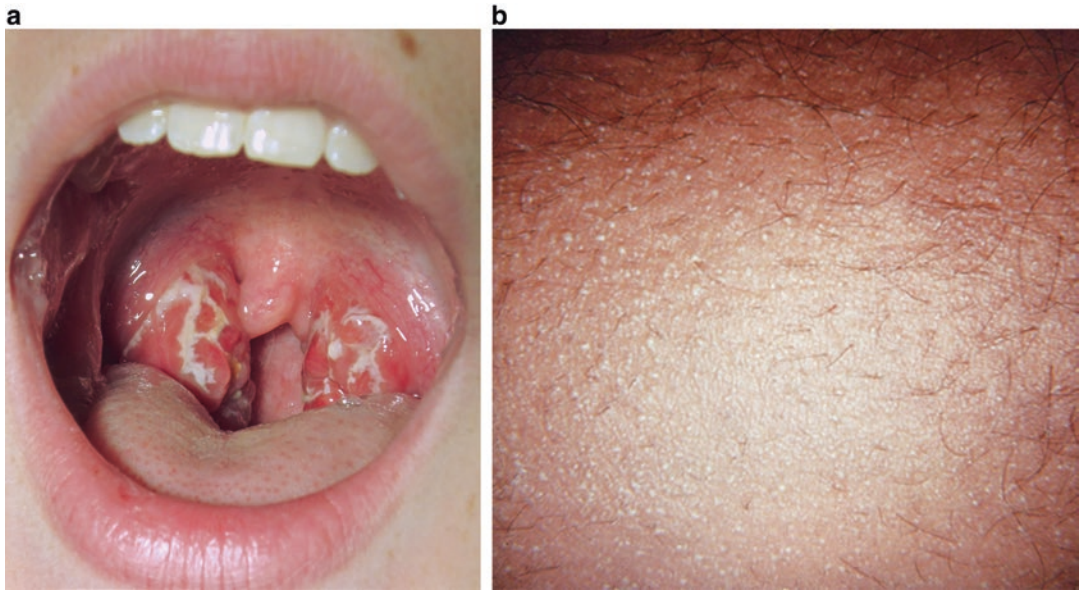

Fig. 17.4 (**a**) Erythema with exudates on the tonsillar pillars in a patient with culture positive Group A *Streptococcus* (Published under a Creative Commons Atrribution-Share Alike 3.0 Unported License. By James Heilman, MD—Own work, CC BY-SA 3.0 and GNU Free Documentation License, Version 2.1 https://commons.wikimedia.org/w/index.php?curid=11596322). (**b**) Sandpaper rash in a patient with scarlet fever secondary to Group A *Streptococcus*. (Reprinted with permission from Partners ID Images Copyright Partners Healthcare System, Inc. All rights reserved.) [37]

Table 17.4 Centor and McIsaac scores

Clinical criteria	Point
Centor score [30]	
Fever	1
Tonsillar exudates	1
Tender anterior cervical adenopathy	1
Absence of cough	1
McIsaac Score [32]	
Fever >38 °C	1
No cough	1
Tender anterior cervical adenopathy	1
Tonsillar swelling or exudate	1
Age 3–14 years	1
Age 15–44 years	0
Age ≥ 45 years	-1

C Celsius, *GAS* Group A *Streptococcus*

Table 17.5 Predictive value of Centor and McIsaac scores for pharyngitis due to group A *Streptococcus*

Score	Percent of patients testing GAS positive by Centor score, %	Percent of patients testing GAS positive by McIsaac score, %
0	3	3
1	7	5
2	17	11
3	34	28
≥4	56	53

commonly used for pediatric patients, adjusts the Centor score based on the patient's age, as children ages 3–14 are more likely to have GAS compared to adults over the age of 45, who are unlikely to have GAS pharyngitis [40]. More specifically, the likelihood of GAS as the etiology of pharyngitis in an adult patient is about 10% [41].

The Infectious Diseases Society of America (IDSA) has published guidelines on the diagnosis and management of GAS pharyngitis. When a patient presents with pharyngotonsillitis, unless rhinorrhea, cough, oral ulcers, and/or hoarseness are present to support a viral etiology, obtaining a throat swab for RADT and/or culture is recommended [34]. To obtain a throat swab, the tongue should be pressed down, and the swab should be rubbed over both tonsils and the posterior pharyngeal wall with caution to avoid touching any other intraoral mucosa or saliva [42]. Rapid antigen detection tests are either optic immunoassays, enzyme-linked immunoadsorbent assay (ELISA), or latex agglutination based on the Lancefield streptococcal group antigen A and have a sensitivity range of 65–96% and specificity of 68–99% [42]. Notably, the group C and G streptococcal antigens are not detected by RADTs. The IDSA guidelines recommend that for children and adolescents a negative RADT should be followed up by a throat culture, but a positive RADT does not require confirmatory testing [34]. For adults, the IDSA guidelines state that a negative RADT does not usually require a confirmatory culture. Anti-streptococcal antibody titers are not recommended in the diagnosis of acute pharyngitis. Post-treatment RADT or throat cultures are also not routinely recommended [34].

Group A *Streptococcus* remains 100% susceptible to penicillin, although some isolates are resistant to clindamycin, doxycycline, or macrolides [43]. A ten-day course of penicillin or amoxicillin is recommended as first-line treatment for GAS pharyngotonsillitis (Table 17.3). An alternative for patients who may have difficulty adhering to 10 days of treatment is to administer one dose of benzathine penicillin intramuscularly (1.2 million units). For those with true but non-life-threatening allergies to penicillins, alternatives include first-generation cephalosporins (for those not allergic) for 10 days, clindamycin or clarithromycin for 10 days, or azithromycin for 5 days. It is worth noting that there is significant resistance to macrolides among GAS in some areas of the world and that macrolides do not cover *Fusobacterium* species, which are important pathogens to consider especially in adolescents and young adults, as discussed later. For this and other reasons, it is worth exploring the penicillin allergy history thoroughly. If patients who report penicillin allergy say they have subsequently tolerated amoxicillin, amoxicillin-clavulanate, cephalexin, or other cephalosporin drugs, those agents are preferred over non-beta lactams for treating GAS pharyngitis.

The goals of GAS pharyngitis treatment are to prevent complications, shorten the duration of illness, and decrease infectivity [35]. Complications or infections that may accompany GAS pharyngitis include peritonsillar abscess (discussed

later), retropharyngeal abscess (Chap. 27), sinusitis (Chap. 11), otitis media (Chap. 4), mastoiditis (Chap. 6), and cervical lymphadenitis (Chap. 26) [35]. Streptococcal toxic shock syndrome is another potential complication of GAS pharyngitis and is associated with shock and organ failure. Nonsuppurative complications include acute rheumatic fever, which is thought to be driven at least in part by molecular mimicry leading to tissue injury, and acute glomerulonephritis. Patients with acute rheumatic fever present with varied clinical manifestations, including arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules. Late manifestations of acute rheumatic fever include rheumatic heart disease with severe calcification of the mitral valve leading to mitral stenosis. Acute rheumatic fever is rare in the U.S. but remains common in other areas of the world such as Africa and in aboriginal populations in Australia and New Zealand, perhaps due to differences among commonly circulating GAS strains in those areas. Acute glomerulonephritis is a delayed complication of GAS infection with clinical presentations ranging from asymptomatic hematuria to acute nephritic syndrome.

Groups C and G *Streptococcus*

While they can be normal colonizers of the oropharynx, both group C and group G *Streptococcus* have been identified as causes of acute pharyngotonsillitis. In a study of college students presenting with acute sore throat, group C or G *Streptococcus* was detected in 9% [41]. Group C *Streptococcus* has been linked to endemic cases of pharyngitis. In a cohort study evaluating throat swabs from college students presenting with exudative pharyngitis compared to controls, symptomatic subjects were more likely than controls to have group C *Streptococcus* cultured from their swabs [44]. Patients with group C *Streptococcus* pharyngitis tend to present like GAS with fevers and exudative tonsillitis [45]. Group G *Streptococcus* has been implicated as the causative agent of several epidemics of pharyngitis in the community and has been linked to ingesting contaminated foods, particularly dairy and egg products [46, 47]. There is no known association between pharyngitis with group C or G streptococci and acute rheumatic fever.

Fusobacterium necrophorum

Fusobacterium necrophorum, an obligate anaerobic Gram-negative bacillus, is another common cause of pharyngitis, particularly in adolescents and young adults [48, 49]. In a recent study of 312 college students presenting to a student health clinic, *F. necrophorum* was detected in 20.5% of symptomatic cases, whereas GAS was detected in only 10.3% of cases [41]. Co-infection with beta-hemolytic streptococci has been implicated in recurrent episodes of pharyngitis as well [41, 50]. *Fusobacterium necrophorum* is a primary cause of peritonsillar abscess and Lemierre's syndrome, a suppurative internal jugular thrombophlebitis that can cause septic pulmonary emboli. Numerous virulence factors, including leucotoxin, proteolytic enzymes, and haemagluttinin, are felt to contribute to invasive disease [48, 51]. *Fusobacterium necrophorum* is not detected on rapid streptococcal testing methods or on routine throat cultures. *Fusobacterium necrophorum* is usually susceptible to penicillins but some strains are resistant due to the presence of a beta-lactamase; these are susceptible to beta-lactam/beta-lactamase inhibitor combinations such as amoxicillin-clavulanate. Fusobacteria are also susceptible to clindamycin or metronidazole, although metronidazole does not treat group A streptococci. Robert Centor recently reviewed the data for *F. necrophorum* and group A streptococcal pharyngitis and noted that in patients ages 15–24, each of these organisms causes approximately 10% of pharyngitis cases, but that one in 400 cases due to *Fusobacterium* would likely result in Lemierre's syndrome if not treated appropriately [52]. Given the severity of illness associated with this pathogen, consideration should be given for treating of adolescents and young adults who have streptococcus-negative pharyngitis with penicillin plus metronidazole, amoxicillin-clavulanate, or clindamycin. Macrolides lack activity against *F. necrophorum* so should not be used unless combined with

metronidazole, if *Fusobacterium* infection is a consideration [52]. The diagnosis and management of Lemierre syndrome is reviewed in Chap.18.

Arcanobacterium haemolyticum

Arcanobacterium haemolyticum is isolated most commonly in adolescents and young adults. It is a facultative anaerobic Gram-positive bacillus that grows slowly; cultures discarded early may miss isolating the bacteria. Clinically it presents similarly to GAS pharyngitis, although a rash develops in up to 50% approximately 1–4 days after the sore throat begins and may be the predominant clinical manifestation [53]. The rash is a scarlatiniform, maculopapular rash that starts on the extremities and progresses to the trunk, sparing the palms, soles, and face [54]. Macrolides are considered drugs of choice for pharyngitis caused by *A. haemolyticum* [55, 56] (Table 17.3). The optimal dosing and duration, however, is unknown as no prospective clinical trials have been performed. In vitro studies demonstrate susceptibility to beta-lactams, although treatment failures with penicillin have been reported. The organism is also susceptible to clindamycin and doxycycline.

Mycoplasma and *Chlamydia pneumoniae*

"Atypical" bacteria including *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* can cause pharyngitis [8, 9]. These are often associated with a cough which may be prolonged (weeks). Diagnosis is difficult due to limited testing options and the fact that the organisms will not grow on routine culture. Some labs may be able to perform PCR, whereas others rely on serologic testing. A review of the laboratory diagnosis of *C. pneumoniae* infections highlights that throat swabs are suitable for specimen testing [57]. In this review, the sensitivity of the various PCR protocols was comparable and PCR had a sensitivity of 10–100 elementary bodies. Based on seroprevalence studies demonstrating that 50–70% of adults have *C. pneumoniae* IgG antibodies, it is thought that reinfection is common and this may limit the ability of serologic testing to make conclusive diagnoses in the setting of acute pharyngitis [57]. Patients with pharyngitis due to *Mycoplasma* or *C. pneumoniae* generally are not treated unless there is concurrent pneumonia. Pneumonia due to these organisms is treated with a macrolide, fluoroquinolone, or doxycycline.

Sexually Transmitted Infections: *Gonorrhea* and *Chlamydia trachomatis*

Neisseria gonorrhoeae and *Chlamydia trachomatis*, both classically sexually transmitted urogenital organisms, are increasingly being isolated from the oropharynx due to oral sex. Pharyngeal infections are generally asymptomatic, but tonsillar exudates have been described. Fever and adenopathy are often absent. In a report from Japan, 225 heterosexual patients with acute tonsillitis, acute pharyngitis, or abnormal pharyngeal sensation underwent a throat swab. Five cases (2.2%) of *N. gonorrhoeae* and two cases (0.9%) of *C. trachomatis* were identified; none of the seven cases had genitourinary symptoms [58]. In a German study of men who have sex with men, the authors found on pharyngeal testing a prevalence of 1.5% for *C. trachomatis* and 5.5% for *N. gonorrhoeae,* but pharyngeal symptoms were reported in only 5% of the cases where one of the two pathogens was detected, highlighting the importance of screening high risk individuals as a public health intervention [59]. Nucleic acid amplification tests (NAATs) are recommended for the detection of *N. gonorrhoeae* in urogenital but not extragenital sites, because NAAT is not approved by the Food and Drug Administration (FDA) for testing oropharyngeal or conjunctival sites [60, 61]. Culture should be performed for pharyngeal infections. Treatment for *N. gonorrhoeae* pharyngitis consists of a single intramuscular dose of ceftriaxone 250 mg, combined with a single dose oral dose of azithromycin 1 g [62]. Treatment of *C. trachomatis* pharyngitis consists of either a single dose of 1 g azithromycin or a course of doxycycline for 7 days [62] (Table 17.3).

Diphtheria

Diphtheria, caused by *Corynebacterium diphtheriae,* is rare in developed countries due to vaccination but is a cause of severe pharyngitis in non-immune persons and can be spread person to person. Diphtheria is discussed in Chap. 19.

Recurrent Tonsillitis and Tonsillectomy

Experts recommend defining "recurrent acute tonsillitis" as >2 distinct episodes in 12 months and chronic tonsillitis as symptoms persisting for >3 months [63]. It is important to consider viral infection with concurrent GAS colonization in patients who present with recurrent tonsillitis complaints and have repeatedly positive swab studies for GAS, since about 15% of the population is colonized with GAS. These colonized patients lack elevated antistreptococcal antibody titers or other evidence of inflammatory response to GAS, and are not thought to be suffering ill consequences from GAS carriage or to be contagious.

Surgical management of recurrent bacterial tonsillitis has historically included tonsillectomy, although this is not performed during an episode of tonsillitis or peritonsillar abscess (the latter sometimes called a "quinsy" tonsillectomy). Both extracapsular (removal of the entire palatine tonsils) and intracapsular (reducing the volume of tonsils without exposing the tonsillar capsule) tonsillectomy have been performed. The effect of tonsillectomy in children is most clearly seen in the reduction of sore throat episodes, particularly in the first year after the procedure [63]. The long-term effect of tonsillectomy in adults is not clear [63, 64]. European guidelines recommend consideration of tonsillectomy only if more than six episodes of tonsillitis have occurred [64]. Clinical practice guidelines in the U.S. from the American Academy of Otolaryngology-Head and Neck Surgery include the following statement regarding tonsillectomy in children ages 1–18 years old: "The panel offered *options* to recommend tonsillectomy for recurrent sore throat infection with a frequency of at least 7 episodes in the past year or at least 5 episodes per year in the past 2 years or at least 3 episodes per year in the past 3 years with documentation in the medical record of each episode of sore throat and 1 or more of the following: temperature >38.3°C, cervical adenopathy, tonsillar exudate, or positive test for group A beta-hemolytic streptococcus" [65].

Peritonsillar Abscess

Peritonsillar abscess, a complication of tonsillitis, occurs when pus collects between the capsule of the palatine tonsil and the pharyngeal muscle [66] (Fig. 17.1b). It has been described as an extreme end of the spectrum of tonsillitis—ranging from tonsillitis to peritonsillar cellulitis to peritonsillar abscess [67].

Clinical Presentation and Epidemiology

Patients present with fever, severe often unilateral sore throat, a muffled "hot potato" voice, drooling, trismus, and ipsilateral ear pain. A course of antibiotics for pharyngitis does not preclude progression to a peritonsillar abscess in some cases. In a large series from Denmark, 73% of cases occurred in patients who were 8–30 years old, and the median duration of symptoms was 5 days [68]. Nearly 40% of patients had taken antibiotics prior to admission, and this was a penicillin-type antibiotic in 94%. On examination, there may be unilateral peritonsillar swelling with displacement of the tonsil (Fig. 17.4).

Peritonsillar abscess is the most common deep neck space infection in children and adults and may be life threatening as it can cause septic shock, airway compromise, necrosis leading to carotid sheath hemorrhage or extension into the deep neck space of the posterior mediastinum [67, 69, 70]. The peak incidence occurs in the teen years, although studies have shown that *F. necrophorum* peritonsillar abscess is more age-dependent than GAS peritonsillar abscess [71].

Studies have also shown an association with smoking in young adults. A retrospective Danish cohort study, with enrolled subjects having a median age of 21, found an odds ratio of 2.5 for the development of peritonsillar abscess in smokers [72].

Microbiology

Group A *Streptococcus* is commonly regarded as the primary peritonsillar abscess pathogen, but normal oral flora are the only organisms cultured in nearly half of peritonsillar abscess cases and *F. necrophorum* appears to be more common than GAS in series that culture for *Fusobacterium* species [66–68]. In a study of 760 patients cultured for peritonsillar abscess in Denmark 2001–2006, 47% of cultures grew only mixed oral flora, 25% grew *F. necrophorum*, and 19% grew GAS [68]. Most of the *Fusobacterium* cases (87%) and group A streptococcal cases (90%) grew in pure culture, although mixtures of these two organisms or other pathogens occurred. Other specific etiologies were uncommon: group C/G streptococci (5%), *Staphylococcus aureus* (2%), and *Haemophilus influenzae* (1%) [68]. Patients with *Fusobacterium* peritonsillar abscess were younger than patients with group A streptococcal peritonsillar abscess, although not by much (median age 18 versus 23, respectively).

Evaluation and Treatment

Patients with uncomplicated peritonsillar abscess may be managed as an outpatient, but many providers recommend an inpatient stay. In the United Kingdom for a first episode of uncomplicated peritonsillar abscess in an immunocompetent host, imaging and cultures are not generally recommended [67]. Intraoral ultrasound can be used to confirm the diagnosis and assist in determining drainage strategies. Computerized axial tomography scan or magnetic resonance imaging can be reserved for cases where there is concern for spread of infection beyond the peritonsillar space [67].

Treatment strategies range from medical management to abscess tonsillectomy. In a retrospective cohort study of patients with a peritonsillar abscess in the U.S., 33% received initial medical management, which included antibiotics in all cases and corticosteroids in 78% [69]. The remaining 67% of patients who received initial surgical management also all received antibiotics but additionally underwent incision and drainage (77%), needle aspiration (22%), or tonsillectomy (2%). Those with larger abscess size, muffled voice, drooling, peritonsillar bulge, trismus, and dysphagia were more likely to receive initial surgical therapy. Patients managed surgically were more likely to receive corticosteroids. Patients treated medically were more likely to be admitted to the hospital, but there was no difference in complication rates, return visits, or failure rates. While there were limitations to the study, including a lack of randomization and limited statistical power due to low failure rates in both groups, the authors argue that for smaller, less advanced abscesses, initial medical therapy may be considered. Medical management includes analgesia, rehydration, and antibiotic therapy—often with empiric penicillin based therapy targeting GAS and broader anaerobic coverage with metronidazole. In a meta-analysis that included 153 combined subjects, steroids were associated with improvement in trismus, reduction in fever and length of stay and percent of patients swallowing water sooner, but there was no difference in eating a normal diet at 7 days [73]. Guidelines suggest that steroids may be useful, but more evidence is needed to make a recommendation [67, 70].

Surgical interventions include aspiration, incision and drainage (I&D), and abscess tonsillectomy. Treatment should be individualized. Aspiration and I&D have a similar failure rate of approximately 10%. Although I&D may relieve pain faster and will drain most of the accumulated pus in one setting, it is a more painful procedure. Needle aspiration management requires the use of a large bore needle to adequately aspirate thick material and often employs three aspirations to achieve acceptable decompression. Similarly, repeat aspiration may be required. In a

review of the literature comparing needle aspiration to I&D, Johnson et al. found that I&D had an initial success rate of 93.7% versus 91.6% for needle aspiration, but this would mean that 48 patients would need to undergo I&D to save one patient an initial treatment failure using aspiration [70]. Unfortunately, the management protocols for both aspiration treatment patients and I&D treatment were variable among the reviewed studies, so there was not uniformity in the post-procedure care including the plans for inpatient versus outpatient treatment, intravenous vs. oral antibiotics, etc. Both needle aspiration and I&D require patient cooperation to be successfully completed in the non-operating room setting. If managed as an outpatient, patients should be seen again within 24–48 h to assure appropriate treatment response. In some cases, I&D is completed under general anesthesia.

Abscess tonsillectomy, which is removal of the tonsil with a peritonsillar abscess ("quinsy tonsillectomy"), has traditionally been preferred if there are complications or if alternative therapy has failed [42]. The tonsillectomy is usually only performed on the abscessed site, because surgery of the inflamed contralateral tonsil can lead to increased complications such as bleeding. Intubation for tonsillectomy may be more challenging in the setting of peritonsillar abscess but may be required for children who may not be able to cooperate with an awake procedure [42]. The procedure itself is done in the fashion of standard extracapsular tonsillectomy, with the bulk of the dissection work already having been accomplished by the accumulation of pus between the tonsil and the superior constrictor. Care must be taken not to dissect through the constrictor muscles into the parapharyngeal space and associated neurovascular structures. Interval tonsillectomy, performed after the peritonsillar abscess has resolved with the goal of preventing recurrence, may be more challenging than abscess tonsillectomy given scarring/fibrosis that develops after the infection. Interval tonsillectomy generally is reserved for those at high risk for recurrence (prior peritonsillar abscess, age <40) [67]. It is important to consider that abscess tonsillectomy has been shown to be as safe as interval tonsillectomy and only one recovery period is necessary for abscess tonsillectomy compared to two with interval tonsillectomy [70]. Yet, with interval tonsillectomy, both tonsils may safely be removed.

Summary

Pharyngitis and tonsillitis are common in both adults and children. Most infectious pharyngitis is viral, especially in adults, but distinguishing viral from bacterial infections clinically is challenging. Guidelines currently recommend using a combination of clinical features to guide the decision to test for GAS, which is more common in children than in adults. Patients who are very likely to have viral pharyngitis based on clinical criteria such as the Centor or McIsaac Criteria should not undergo testing or treatment for GAS. Eliciting a social history is important in patients with pharyngitis, as sexually transmitted infections including HIV, HSV, gonorrhea, and *Chlamydia* are rare but important causes of pharyngitis in patients with epidemiologic risk factors. *Fusobacterium necrophorum* is an important cause of pharyngitis, especially in adolescents and young adults where it may be a more common etiology than GAS. *Fusobacterium* is not treated by macrolides, which are often prescribed for penicillin-allergic patients with pharyngitis, but is susceptible to amoxicillin-clavulanate, penicillin plus metronidazole, or clindamycin. Most isolates are susceptible to penicillin but some strains have a beta-lactamase. Pharyngeal colonization with GAS must be considered in patients who frequently have GAS in throat samples. Peritonsillar abscess may complicate *Fusobacterium* or GAS pharyngitis, but in many cases, cultures grow only oral flora. Treatment usually includes drainage of the abscess plus antibiotic therapy. Antibiotics should be broad-spectrum and include coverage of GAS, oral anaerobes including *Fusobacterium*, *S. aureus*, and *H. influenzae.*

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