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Pharyngitis

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KEYWORDS

• Pharyngitis • Throat • Infectious • Noninfectious

KEY POINTS

- Most infectious pharyngitis has a viral cause, which includes influenza, coronavirus, rhinovirus, adenovirus, enterovirus, human immunodeficiency virus, Epstein-Barr virus, cytomegalovirus, and herpes simplex virus.
- The clinician must quickly rule out parapharyngeal space infections, peritonsillar abscess, submandibular abscess (Ludwig angina), and epiglottitis. These conditions require emergency care.
- The Infectious Diseases Society of America advises the use of aspirin or nonsteroidal anti-inflammatory agents (NSAIDs) in adults and NSAIDs in children for the treatment of pain. There are several studies that show that NSAIDs relieve pharyngitis pain better than acetaminophen.
- Penicillin remains the antibiotic of choice of group A beta-hemolytic streptococcal (GAS) pharyngitis. Resistance has not developed to penicillin.
- Patients with GAS pharyngitis should have improvement in 3 to 4 days. If not better at that time, the patient should be seen for diagnostic reconsideration or the development of a suppurative complication.

INTRODUCTION

Sore throat is common and has substantial medical and societal costs. There were more than 15 million outpatient visits for pharyngitis in 2007 in the United States.¹ Overtreatment of non-group A beta-hemolytic streptococcal (GAS) infections is one of the major causes of inappropriate use of antibiotics. Patient's expectations are not for antibiotics, but for pain relief, reassurance, and information. When questioned, those who hoped for an antibiotic did so with the belief that an antibiotic would give pain relief. Therefore, it behooves the medical provider to have a rational, practical, and evidence-based approach to the treatment of pharyngitis.

CAUSES/EPIDEMIOLOGY OF PHARYNGITIS

The causes of pharyngitis may be categorized as infectious versus noninfectious. Infectious causes are shown in **Table 1**. Noninfectious causes include allergy, postnasal

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Bacteria	Viruses	Atypical Bacteria
Group A beta-hemolytic streptococci	Adenovirus	<i>Mycoplasma pneumoniae</i>
Group C streptococci	Herpes simplex virus 1 and 2	<i>Chlamydophila pneumoniae</i>
<i>Neisseria gonorrhoeae</i>	Coxsackievirus	<i>Chlamydophila psittaci</i>
<i>Corynebacterium diphtheriae</i>	Rhinovirus	—
<i>Fusobacterium necrophorum</i>	Coronavirus	—
<i>Francisella tularensis</i>	Influenza A and B	—
<i>Yersinia pestis</i>	Parainfluenza	—
<i>Treponema pallidum</i>	Respiratory syncytial virus	—
Mixed anaerobes	Human herpes virus 4 (Epstein-Barr virus)	—
—	Human herpes virus 5 (Cytomegalovirus)	—
—	HIV	—

Abbreviation: HIV, human immunodeficiency virus.

Data from Kociolek L, Shulman S. Pharyngitis. Ann Intern Med 2013;157(5):ITC3-1.

drainage, irritation (ie, smoke exposure, poorly humidified air), gastrointestinal reflux disease, foreign body, acute thyroiditis, and referred pain (ie, dental).² Infectious causes include viral and bacterial.² In the immune-compromised patient, fungal causes should be considered.² The most important of these infections is GAS because of the possible complications.

Most infectious pharyngitis has a viral cause, which includes influenza, coronavirus, rhinovirus, adenovirus, enterovirus, human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), cytomegalovirus, and herpes simplex virus.²

The major risk factors for GAS are age and exposure. Up to 30% of childhood pharyngitis is caused by GAS. Outbreaks occur during winter and early spring in the 5-year-old to 15-year-old age group, and spread by close contact (school and home). GAS is uncommon in preschool-aged children and adults. Group C and G beta-hemolytic *Streptococcus* causes pharyngitis in older children and adults.³ The infection is similar but less severe and does not lead to the significant complications of GAS infection. Consider mycoplasma and chlamydia infections when young adults present with pharyngitis and bronchitis.⁴

Fusobacterium necrophorum (Fn), an obligate anaerobic gram-negative bacillus, has been reported as causing pharyngitis in adolescents in the United Kingdom and Denmark.³ Although not a conclusive pathogen for pharyngitis, it has been suggested as a causative agent in Lemierre syndrome (septic thrombophlebitis of the internal jugular vein with septic emboli to the lungs).

HISTORY AND PHYSICAL EXAMINATION

The physical examination of the patient is focused on the head/neck/chest and skin. On initial examination, the provider should assess for signs of life-threatening disease, especially in children who have difficulty in localizing pain. Red flags for impending life-threatening deterioration include difficulty with handling secretions, drooling, hot-potato voice, toxic appearance, and unilateral neck swelling.¹ The

clinician must quickly rule out parapharyngeal space infections, peritonsillar abscess, submandibular abscess (Ludwig angina), and epiglottitis. These conditions require emergency care.¹

Viral Pharyngitis

Patients complain of sore throat, nasal congestion, coryza, hoarseness, sinus discomfort, ear pain, cough, conjunctivitis, diarrhea, and discrete ulcerative stomatitis. Herpangina (Coxsackie virus) manifests with fever and painful vesicular lesions in the posterior oropharynx. Hand, foot, and mouth disease (Coxsackie A-16) has painful vesicles and ulcers in the mouth, palms, and soles.

Infectious Mononucleosis

Patients present with a classic triad of severe sore throat, diffuse lymphadenopathy, and fever (up to 40°C [104°F]). Up to 90% of cases are caused by infection with human herpesvirus 4, more commonly known as EBV. The remaining 10% of cases are caused by cytomegalovirus (herpes virus 5) and herpes virus 6. There is a prodrome of chills, sweats, fever, and malaise. One-third of patients present with exudates and palatal petechiae that may mimic GAS infection. Approximately 15% of patients present with jaundice and 5% with a rash. Up to one-third of adults and adolescents have significant illness, whereas most children have subclinical infection. Patients with mononucleosis who ingest a β -lactam antibiotic often develop a pruritic maculopapular rash.

Acute Retroviral Syndrome

Primary HIV infection can mimic EBV infection. Patients present with fever, nonexudative pharyngitis, weight loss, and diffuse adenopathy. Between 40% and 80% of patients develop a rash 2 weeks after infection.

GAS Pharyngitis

GAS pharyngitis classically presents with sudden onset of severe sore throat, pain on swallowing, and fever without cough or rhinorrhea. Clinical signs include tonsillar erythema with or without exudate, anterior cervical adenitis, soft palate petechiae, red swollen uvula, and scarlatiniform rash. Patients with GAS may have milder symptoms and clinical signs after tonsillectomy.

Streptococcosis

Children less than 3 years of age with group B streptococcal infection may present with atypical symptoms. They have low-grade fever, tender anterior adenopathy, and nasal congestion/discharge. Nonsuppurative complications are rare and the only benefit to treating these children is to decrease transmission. The Infectious Diseases Society of America (IDSA) and the American Pediatric Academy (APA) do not recommend testing these children unless other risk factors are present.⁵

Scarlet Fever

Scarlet fever is GAS pharyngitis infection with a bacterial strain that produces erythrotoxic toxins. There is a characteristic fine, goose-pimple red rash that blanches with pressure. The rash begins on the neck and spreads to the trunk and extremities, sparing the face. It is more pronounced in creases. The rash fades in 3 to 4 days and the skin may have subsequent desquamation.

DIAGNOSIS

Expert clinicians cannot reliably identify patients infected with GAS, therefore microbiologic confirmation is necessary to diagnose GAS pharyngitis. Several prediction tools for determining the probability of GAS infection have been proposed. The IDSA recommends the use of a clinical scoring system to reduce unnecessary testing and treatment.⁵ The Centor Criteria (for adults) was modified by McIssac and colleagues⁶ to include an age criterion, and has expanded the applicability of the tool to all ages (Table 2).⁷

Those with 0 to 1 criterion are considered low risk and do not require additional evaluation or antibiotic treatment.⁷ Those with 2 to 3 criteria should be assessed for GAS and treated only if positive.⁷ Guidelines for management of patients with 4 criteria differ. Although the American College of Physicians (ACP) recommends empiric treatment of individuals with 4 positive criteria, the IDSA and the American Heart Association (AHA) do not.⁵ Routine empiric treatment of GAS in patients with 4 criteria increases unnecessary use of antibiotics by up to 50%.⁷

If the clinical symptoms suggest GAS infection, throat culture, rapid antigen detection testing (RADT), or DNA probe testing is indicated.⁸⁻¹⁰ The specimen should be obtained before the initiation of antibiotics, because even 1 dose can cause the test to be negative. Both tonsils and the posterior pharynx should be aggressively swabbed. Other areas of the mouth should be avoided with the swab.

In children, a throat culture should be performed if the RADT is negative in order to identify patients who have a false-negative result. In adults, the throat culture is not necessary after a negative RADT because of the low incidence of GAS and low risk of acute rheumatic fever (RF).⁸ Some laboratories are replacing throat culture confirmation with DNA probe testing. The turnaround time is 24 hours, compared with 48 hours with throat culture. There is no value in obtaining streptococcal antibody testing (antistreptolysin O [ASO]) and antideoxyribonuclease B during acute GAS infection. This testing is only needed to diagnose acute RF.

Acute Mononucleosis

With acute mononucleosis, a complete blood count shows an absolute lymphocytosis with greater than 10% atypical lymphocytes. Within 2 to 3 weeks the heterophile antibody test becomes positive. Because of a higher false-negative rate in children, an EBV-specific antibody may be necessary for diagnosis.

Acute Retroviral Syndrome

A presumptive diagnosis of acute retroviral syndrome is made with HIV antigen detection (HIV antibodies may be negative). An HIV viral load assay of more than 10,000 copies/mL confirms the diagnosis.

Fever	1 point
Absence of cough	1 point
Anterior cervical adenitis	1 point
Tonsillar exudate	1 point
Age (y)	
2-14	1 point
15-44	0 point
45 or older	-1 point

Group C and G Streptococci

Consider group C and G streptococcal infection when an RADT/culture is negative and the patient continues to have severe symptoms. Diagnosis requires throat culture with special notice to the laboratory of specific strains of interest because many laboratories ignore them in culture.

Fn

Fn is confirmed by growth of *Fn* bacteria in an anaerobic blood culture.

Treatment

Symptom relief, especially of pain, is the goal of treatment. Patients with confirmed GAS infection should be given antibiotics.

Topical treatment

Salt-water gargles, phenol throat sprays, and herbal remedies are often recommended, but there are no studies to recommend or discourage the practice. Sipping warm or cold beverages has been advocated, but honey should be avoided in those less than 1 year of age because of the concern regarding botulism. Both ambroxol and lidocaine lozenges are significantly better than placebo in providing pain relief without adverse effects.¹¹ Benzocaine lozenges also provide pain relief; however, the US Food and Drug Administration has published concerns about the risk of methemoglobinemia with their use.¹¹ Oral rinse with equal parts lidocaine, diphenhydramine, and Maalox may be helpful in patients with stomatitis, gingivitis, and ulcers.¹¹ It is important for the patient to swish and expectorate to avoid overdose of lidocaine.¹¹

Systemic analgesics

The IDSA advises the use of aspirin or nonsteroidal antiinflammatory agents (NSAIA) in adults and NSAIA in children for the treatment of pain.⁵ There are several studies that show that NSAIA relieve pharyngitis pain better than acetaminophen.

The use of glucocorticoids for the treatment of pharyngitis is controversial. The IDSA recommends against the use of glucocorticoids for decreasing the duration of pain.⁵ Glucocorticoids should be restricted to the exceptional patient with severe sore throat or inability to swallow.^{12,13} A single dose of oral dexamethasone of 0.6 mg/kg, maximum of 10 mg is recommended.¹⁴ In adults, a single dose of prednisone 60 mg for 1 to 2 days is acceptable.¹²

Antibiotics

GAS Penicillin remains the antibiotic of choice of GAS pharyngitis (**Table 3**). Resistance has not developed to penicillin. There are strains of GAS that have developed tolerance with minimal inhibitory concentration greater than 32. The clinical significance of this is unknown. Amoxicillin can replace penicillin for treatment, because it has a better taste than penicillin in the oral form. In patients allergic to penicillin, a first-generation cephalosporin or macrolide may be substituted. There are high rates of resistance to macrolides. Antibiotics should be given for 10 days to eradicate GAS from the pharynx.¹⁵ At this time, short-course treatment cannot be recommended except for cefpodoxime, cefdinir, or azithromycin.¹⁵

In most European guidelines, treatment of GAS is with symptomatic treatment alone.¹⁶ It is considered a self-limiting disease and antibiotics are not commonly recommended because they provide only moderate clinical benefits in a disease with low complication rates. Antibiotics are only prescribed for severe cases. There is a growing body of evidence that treating all patients with GAS pharyngitis to prevent a rare case of RF is not clinically prudent.⁸ Penicillin anaphylaxis occurs in approximately

Medication	Dosage	Frequency	Duration
Penicillin VK	40 mg/kg/d up to adult dose of 1000 mg/d	Two to 3 times a day	10 d
Amoxicillin	50 mg/kg/d up to adult dose of 1000 mg/d	Twice daily	10 d
Moxatag	750 mg/d (more than 12 y of age)	Daily	10 d
Penicillin G Benzathine	Weight <27 kg, 600,000 units Weight >27 kg, 1.2 million units	Intramuscular once	—
Use for patients who are unlikely to complete a full course of oral medications and for those with a personal or family history of RF			
First-generation cephalosporin	25–50 mg/kg/d up to adult dose of 1000 mg/d	Twice daily	10 d
Erythromycin	20–40 mg/kg/d up to adult dose of 1000 mg/d	Three to 4 times daily	10 d
Azithromycin	Day 1: 10 mg/kg up to adult dose of 500 mg Days 2–5: 5 mg/kg up to adult dose of 250 mg/d	Daily	Days
Dosage is not established for infants younger than 6 mo.			

0.015% of patients, with a fatality rate from shock of 0.002%. Overall morbidity from 10 days of antibiotics may be as high as 10%.

Group C or G beta-hemolytic *Streptococcus* Use the same doses as for GAS but treat for 5 days.

Fn Treatment of pharyngitis is controversial. Some clinicians recommend consideration of treating patients between 15 and 30 years of age with 3 or more Centor Criteria with penicillin or a cephalosporin. It is uncertain whether this treatment is effective for prevention of Lemierre syndrome.

FOLLOW-UP

Patients with GAS pharyngitis should have improvement in 3 to 4 days. If not better at that time, the patient should be seen for diagnostic reconsideration or the development of a suppurative complication.

A test of cure (either RADT or throat culture) is only indicated if the patient has a personal history of RF, develops GAS during RF or after streptococcal glomerulonephritis outbreak, or there is recurrent spread among family members.¹⁷

RECURRENT GAS PHARYNGITIS

Patients who have repeated symptomatic episodes of GAS are either carriers of GAS with recurrent viral infections, have nonadherence to antibiotic therapy, have new GAS infection, or are (rarely) a treatment failure. When a patient experiences a second episode of GAS after a short interval, the practitioner should repeat the course of therapy with an antibiotic with greater β -lactamase stability or treat with intramuscular penicillin. It is not recommended to obtain RADT or throat culture after the second course of antibiotics. If there is a concern that GAS is being spread among close

contacts, all close contacts should be tested for GAS and those who are positive should be treated. Family pets are not reservoirs and do not spread GAS.

The IDSA does not recommend tonsillectomy solely to reduce the frequency of GAS pharyngitis.⁵ Tonsillectomy provides a short-lived benefit for a small fraction of patients.¹⁸ However, many clinicians consider tonsillectomy if a child is severely affected by GAS pharyngitis (ie, 7 or more documented GAS infections within 1 year, 5 or more within 2 years, or 3 or more within 3 years).¹⁸ Other indications for tonsillectomy include tonsillar obstruction, recurrent peritonsillar abscess, and chronic GAS carrier in close contact with a patient who has had RF.¹⁸

GAS Carrier

Up to 20% of children are GAS carriers. The clinician should suspect a GAS carrier when the clinical picture is of viral pharyngitis but patients have positive RADT or throat culture when both symptomatic and asymptomatic. They have no serologic response to ASO and anti-DNase B and have very low risk for complications. They do not need to be identified or treated. There is no need to attempt to eradicate GAS from the pharynx and they do not spread disease to others.

COMPLICATIONS

Complications from GAS pharyngitis are classified as suppurative and nonsuppurative. Nonsuppurative complications include acute RF, acute poststreptococcal glomerulonephritis (poststrep GN) and poststreptococcal reactive arthritis. RF is rare in developed countries. In the United States, the last RF epidemic was in 1985. It occurs 2 to 3 weeks after GAS pharyngitis and is not seen after skin infection. RF is diagnosed using the Revised Jones Criteria for acute RF. Starting antibiotics within 9 days of symptoms can prevent acute RF. Acute poststrep GN occurs approximately 10 days after pharyngeal infection and up to 21 days after skin infection. Antibiotics do not alter the attack rate. Poststreptococcal reactive arthritis is similar to other reactive arthritis and is not altered by antibiotics.

Suppurative complications include peritonsillar abscess, retropharyngeal abscess, sinusitis, otitis media, and mastoiditis. Appropriate treatment of GAS pharyngitis may decrease these complications.

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Group A Streptococci

Pediatric autoimmune neuropsychiatric disorder associated with Group A streptococci (PANDAS) is a controversial diagnosis of children whose obsessive-compulsive disorder or tic disorder is worsened by GAS infection.

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