

Pharyngitis

Purpose: The purpose of this course is to provide an overview of pharyngitis. It will focus on the diagnosis, treatment and complications of group A beta-hemolytic streptococcal pharyngitis. The course will discuss reasons and treatment options for other causes of sore throat.

Objectives

- List three common causes of sore throat
- Discuss three complications of group A beta-hemolytic streptococcal pharyngitis (GABHS)
- List four diagnostic signs or symptoms related GABHS
- Discuss the recommended treatment options for GABHS
- List four comfort measure that can be recommended to those with pharyngitis

Steven L, a nine year-old white male, presents with his mother to his pediatrician's office with a complaint of a sore throat. He has no chronic medical conditions, is on no medications and denies any medication allergies.

The sore throat started yesterday and was accompanied by a fever of 102.2 degrees Fahrenheit. The history revealed no myalgias, no rhinorrhea and no cough. He did report some mild nausea and a headache.

The physical exam showed a temperature of 99.7 degrees Fahrenheit and a heart rate of 102 beats per minute. His checks were flushed but he was in no acute distress. The eyes, ears, and nose exam were unremarkable. His throat was red with white exudate on the 2+ tonsils. Petechiae were noted on the soft palate. His anterior cervical nodes were swollen and tender, but his posterior cervical nodes were normal. His lungs were clear to auscultation.

Introduction

About ten percent of pediatric office visits are related to pharyngitis¹. When sore throat presents to the office the most important job of the provider is to rule out group A beta-hemolytic streptococcal pharyngitis (GABHS). Bacteria, with GABHS being the most common bacteria, are present in about 5-30 percent of cases of sore throat^{2, 3, 4, 5}.

GABHS is most common in children between the ages of 5-12 years old³. It is rare in the child under two years of age. There is no sex or racial disparity in the incidence of GABHS¹.

Most infections have a short incubation period of 1 to 5 days and are seen in the late winter and early spring. Infections of the throat are most commonly caused by viruses or bacteria from contact of nasal secretions via the hand.

Complications

Complications of GABHS are one of the main reasons to treat it, but complications rates are not as high as typically thought. Rheumatic fever – although rare, with a reported incidence of 1 case per 1 million population³ - is of great concern as a sequela of GABHS. Rheumatic fever presents after an untreated GABHS infection with joint pain and swelling, erythema marginatum, heart murmur or subcutaneous nodules. Labs will indicate an elevated antistreptolysin-O titer and erythrocyte sedimentation rate. Anyone with a history of rheumatic fever is at high risk for reoccurrence if GABHS is contracted again. Even those who are treated properly can develop rheumatic fever.

Peritonsillar abscess arises in less than one percent of those with GABHS treated with antibiotics⁵. Those with peritonsillar abscesses present acutely ill with a worsening sore throat, fever, ear pain, trismus (inability or difficulty opening the mouth), peritonsillar mass, deviation of the uvula and a hot potato voice. Intraoral ultrasound or computed axial tomography (CAT) scan will help to diagnosis the disease. Needle aspiration is the best diagnostic tool for peritonsillar abscess.

Scarlet fever presents as a blanchable, erythematous, sandpaper-like rash in the groin, axillae and/or neck. The rash may appear like a case of sunburn. Those with scarlet fever may have high fever and a strawberry-like look to the tongue. The rash typically lasts greater than 7 days and the skin often peels as the rash fades.

Post streptococcal glomerulonephritis – which is rare - presents with hematuria, edema (especially periorbital) and an elevated antistreptolysin O (ASO) titer. The patient may also be afflicted with generalized weakness, anorexia and nausea/vomiting. This disease affects the small blood vessels of the kidney and occurs 10-14 days after the sore throat. Antibiotics do not prevent it⁶.

Other complications of GABHS include: cervical lymphadenitis, otitis media, pneumonia, meningitis, sinusitis, mastoiditis and bacteremia³.

Causes of sore throat

Differentiating between the common causes of sore throat is best accomplished by a good history, physical exam and laboratory evaluation. The most common cause of a sore throat is a virus, but bacterial infection - especially GABHS - is critical to rule out. GABHS accounts for 15-30 percent of cases in kids 5-15 years old; and 5-15 percent of adults⁵.

Viral pharyngitis should be suspected when the sore throat is accompanied by cough, hoarseness, low grade fever, fatigue, and conjunctivitis. Pediatric patients may present with atypical symptoms including nausea, vomiting, abdominal pain, diarrhea or mouth breathing. Coxsackie virus, also known as hand-foot and mouth disease, presents with lesions in the mouth, sore throat and lesions on the hands and feet. It is one specific virus that causes sore throat.

Pharyngitis caused by bacteria typically is not associated with upper respiratory tract infection signs and symptoms such as runny nose, conjunctivitis, or cough.

Streptococcal throat infections tend to reoccur. When the patient is examined a red throat with exudate is common. Palatine petechiae may be present. The anterior cervical lymph nodes are swollen and at times the uvula appears swollen.

Infectious mononucleosis (IM) is another potential cause of sore throat and is also associated with fever and malaise. The throat will look red with exudate. One distinguishing factor on exam is the presences of posterior cervical lymphadenopathy. An enlarged liver and spleen is occasionally present. IM is sometimes mistaken as GABHS and treated with penicillin. Ninety percent of those treated with penicillin develop a maculopapular rash.

Sore throats can be caused by allergic rhinitis. Allergic rhinitis may cause chronic postnasal discharge leading to irritation of the throat causing sore throat. Lymphoid tissue may be noted in the throat which is referred to as "cobblestoning". The tonsils may be enlarged as well.

Candida infections can cause sore throats. The tongue, throat, cheeks and hard palate are covered with a cottage cheese like exudate. When the exudate is scraped, bleeding may occur.

Other bacterial causes of sore throat include: *Neisseria gonorrhoeae*, mixed anaerobes, group C & G *Streptococci*. *Neisseria gonorrhoeae* presents in sexual active individuals with fever, dysuria, and a greenish exudate.

Diphtheria presents with fever, sore throat, tender cervical adenopathy, serosanguineous nasal discharge and adherent grayish membranes with an erythematous throat. It is most common when people live in crowded conditions with poor cleanliness. It is a rare due to immunizations but can be fatal. The toxin formed by diphtheria can lead to heart or respiratory failure.

Kawasaki disease is a rare cause of sore throat that typically affects those under five. Bilateral non-purulent conjunctivitis, red oral mucosa, anterior cervical adenopathy, fever, strawberry tongue, cracked red lips, erythematous rash with edema of the hands and feet, followed by peeling of the palms characterize this disease⁵.

Other conditions that can cause sore throat include gastroesophageal reflux, smoking, persistent cough, postnasal drip secondary to rhinitis, foreign body, and thyroiditis.

Work up

Getting a good history followed by a physical exam is the first step to accurately determining the cause of sore throat. Key steps include determining when the sore throat started, its duration, how it has progressed, severity and associated symptoms such as runny nose, fever or cough.

The physical exam should not only look at the throat but, evaluate other signs that suggest the diagnosis. It should be noted if the throat is erythematous, has exudate, masses or petechiae on the palate. Enlargement of the tonsils should be noted. Lymph nodes should be checked for enlargement and tenderness. Tender, enlarged anterior cervical nodes are often present in sore throats from both bacterial and viral etiology. Posterior cervical adenopathy may suggest infectious mononucleosis. The nose should be looked into for any evidence of sinus inflammation or allergic symptoms which may suggest a virus or post-nasal drip as a cause of the sore throat. The heart should be listened to for murmurs. The liver and spleen should be checked for enlargement which may indicate IM. The skin should be assessed for any rash.

When should GABHS be suspected? Recent exposure to streptococcus and exudate in the throat or on the tonsils are the two most useful clinical features to predict strep throat. Absence of exudate on the tonsils, absence of enlarged tonsils and the absence of tender cervical adenopathy are the best criteria to rule out streptococcus⁵.

Clinical criteria have been developed to determine risk for streptococcus disease and are based on four key signs and symptoms and age⁷.

1. Sore throat without cough
2. Fever more 100.4 degrees Fahrenheit in past 24 hours
3. Tender anterior cervical lymph nodes
4. Tonsillar swelling or exudate

Table 1: Points based on age

Age	Points
3-14	+1
15-44	0
Over 45	-1

One point is given for points one to four and points are given for age based on table 1. The points are totaled and the score will range from -1 to 5. Those with a score of 0 or -1 have a 1% chance of having GABHS. Those with a score of one have a 10% chance. Those with a score of 2 have a 17% chance. There is a thirty-five percent chance of having GABHS for those with a score of 3; and a 51% chance of having GABHS in those with a score of 4 or 5⁷.

A score of four or more the clinician may choose to treat empirically or perform a culture⁷. Others have suggested that if 3 or 4 of the 4 criteria are present empiric treatment is a reasonable option in adults⁶.

Sore throats that last longer than 5 days are less likely to be GABHS. When sore throat persists other diagnoses to consider include: infectious mononucleosis, virus, sinusitis, or post-nasal drip⁹.

Laboratory Evaluation

Laboratory tests should be performed as an adjunct to the history and physical exam. Throat culture is the most commonly used diagnostic test for pharyngitis. A rapid test with a back up culture is the standard. To assure accurate results collection method is critical.

- Wear gloves to avoid contact with respiratory secretion.
- Look at the oropharynx with a light to identify the areas of redness and or exudate.
- While utilizing a tongue depressor the swab should touch the posterior pharyngeal wall and both tonsillar pillars.
- The tongue and cheeks should be avoided if possible.

The rapid antigen test should be performed first and if the test is positive no further diagnostic testing is necessary. If the test is negative, than a back up culture should be performed.

When is testing indicated? Clinicians vary in their approach to the use of diagnostic testing. One approach is to only test adults with 2 or more of the four hallmark symptoms of GABHS. For children between the ages of 3 and 15, testing should happen if there is at least one factor present⁴.

Rapid Antigen Detection Test

Rapid antigen detection test returns results in five to ten minutes. While its specificity approaches 100 percent the sensitivity is between 58-96 percent⁶. This means that if the results are positive the clinician can be fairly certain that the test is positive. Although if the test is negative, it does not necessarily mean that the patient does not have GABHS. The rapid test should not be done if the patient has had a positive GABHS test within the last 30 days.

Some attention has been given to the use of mouth swabs to replace throat swabs. Mouth swabs would be more comfortable and not induce the gag reflex. Unfortunately, they are not effective for the detection of GABHS⁸.

Throat Culture

The throat culture is an accurate method for confirming the presence of GABHS. The same principles that apply to the collection of the rapid test apply to the throat culture. It typically takes 24 to 48 hours for results to grow out. The sensitivity is about 97 percent with a specificity of 99%⁶.

A newer method to detect GABHS has been developed and its use has been suggested for stand-alone use. The LightCycler PCR can yield results in one hour⁹. Another test is the Gen-Probe GAS Direct Test for group A Streptococcus. It is a DNA probe assay and is indicated for use as a back up to a negative rapid antigen test or as a stand alone test for GABHS¹⁰.

When IM is suspected on clinical grounds lab work to assess for its presences includes a complete blood count with differential, a monospot test (heterophil antibody test) and possibly blood work to look for IgM antibodies to the viral capsid antigen⁵. IM diagnosis is supported when the complete blood count shows at least 10 percent atypical lymphocytes. The monospot test looks for the Epstein-Barr virus. The test misses about 31 percent of the cases the first week of illness but sensitivity improves to 81 percent in the second week⁵. Although often not done unless there is uncertainty about the diagnosis, IgM antibodies will help confirm the diagnosis.

Treatment

The goal of therapy is to prevent acute rheumatic fever and other complications, improve clinical signs and symptoms, reduce transmission, and minimize potential adverse effects of antibiotics¹¹.

As soon as the diagnosis is made treatment should be initiated. While it is safe to delay antibiotic treatment for nine days after the onset of symptoms when it comes to preventing acute rheumatic fever¹, earlier treatment results in an earlier resolution of signs, symptoms and period of infectivity.

Antimicrobial treatment is not a magic cure. While sore throats caused by GABHS last 3-7 days untreated; antibiotics typically resolves symptoms in 2 to 5 days which is only a decrease of 1 or 2 days of symptoms compared with no treatment^{4, 5}. For treatment to improve symptoms it must be started within 48-72 hours of symptom onset.

If the clinician is highly suspicious of GABHS and the rapid test is negative, treatment can be started with the understanding that if the confirmatory test (throat culture) comes back negative the antibiotics will be stopped.

Many antibiotics have proven efficacy against GABHS, but penicillin is the drug of choice. Penicillin V is the oral drug of choice while an injection with penicillin G benzathine is an alternative, especially in those who are likely to be non-compliant with therapy. It is safe, cheap, effective and has a narrow spectrum of activity. Amoxicillin is often used in place of penicillin V in children as it is equally effective and has a better tasting suspension.

Erythromycin is recommended for those who have a penicillin allergy. Erythromycin is not tolerated by many patients because of gastrointestinal side effects. Consequently, the use of the azithromycin or clarithromycin are often substituted.

First and second-generation cephalosporins can also be used in those who do not have a type I immediate hypersensitivity type allergy to penicillin. Cephalosporins have a wider spectrum of activity than penicillin V with the second-generation medications having a wider spectrum than the first. Patients who have a type I immediate hypersensitive reaction to penicillin should not be treated with cephalosporins.

Amoxicillin-clavulanate (Augmentin) can be used to treat recurrent pharyngitis. Although gastrointestinal side effects such as diarrhea and cost often limit its use.

Generally the length of treatment is for ten days, but some antibiotics have shorter indications. Azithromycin (Zithromax), cefpodoxime (Vantin) and cefdinir (Omnicef) are approved for 5 days courses.

Table 2: Generic Antibiotics for Treatment of GABHS

Name	Adult dose	Kid dose	Duration in days
*Penicillin G benzathine	1,200,000 units	600,000 units	1 dose
Penicillin V	500 mg tid/qid	25-50 mg/kg/d divided q 6 hrs	10
Amoxicillin	500 mg tid	40 mg/kg/d divided tid	10
Cephalexin	500 mg bid	25-50 mg/kg/d divided bid	10
Cefdinir	300 mg bid	7 mg/kg bid	5-10
Cefpodoxime	100 mg bid	5 mg/kg bid	5-10
Erythromycin ethylsuccinate	400 mg qid	40 mg/kg/d divided bid-qid	10
Clarithromycin	250 mg bid	15 mg/kg/d divided bid	10
Azithromycin	250 mg* qd	12 mg/kg/d qd	5
Clindamycin	150 mg qid	20 mg/kg/d divided tid	10
	Bid – 2 times a day, tid – three times a day; qid – four times a day	d – day q - every	

- Penicillin G benzathine is an intramuscular injection for one dose
- Azithromycin 250 mg is given as two pills the first day, followed by one pill every day for four more days.

Symptomatic treatment

Sore throats hurt. Both GABHS and other causes of pharyngitis warrant the use of measures to comfort the throat. This may be especially important in those with a non-bacterial source of sore throat, not because they hurt more, but because patients who are not given a prescription for an antibiotic often feel entitled to some type of treatment. Symptoms resolve 1 to 2 days sooner when comfort measures including antipyretics are used⁶. Options for pain management include:

- Two percent viscous lidocaine - 15 cc as a gargle or mouthwash every three hours as needed
- Warm salt water gargles

- Throat lozenges
- Phenol sprays
- Ibuprofen or acetaminophen
- Throat moisturization: drink cool or warm liquids, nasal saline, humidification, popsicles or hard candy

Follow up

Improvement should be noted within 48-72 hours. The patients should follow up if there is no improvement by 72 hours. Cellulitis or abscess may be present in the throat contributing to the persistent symptoms. Another organism may be causing the infection, possibly a virus or another bacterial pathogen such as *Group C or G streptococcus*. The patient may be a carrier of GABHS. The carrier will have positive cultures but the cause of the sore throat is possibly not GABHS. Infectious mononucleosis is another consideration if symptoms persist, especially if the patient develops a rash from penicillin. Sore throats that do not resolve may require laryngoscope for evaluation of neoplasm, foreign body, gastroesophageal reflux or another cause.

While reoccurrence does occur patients should not have repeat testing after therapy as long as they are symptom free. Similarly, asymptomatic household contact should not be tested. Those who are symptomatic and have a positive culture after treatment should be treated again.

Recurrent Strep Pharyngitis

If the patient returns a positive culture between 7 days and 4 weeks of finishing antibiotic therapy than recurrent strep throat is diagnosed. It is important to look at the patient clinically as some patients are colonized with GABHS. Colonization may be suggested by those who have positive cultures when they do not appear to have GABHS clinically.

If strep throat returns within seven days of completing the antibiotic, than the patient is said to have treatment failure. Causes of treatment failure can be resistant strains of bacteria, repeat exposure, or non-compliance with therapy. In patients with compliance issues, treatment with intramuscular penicillin should be considered. Switching antibiotics to one less likely to be resistant (stable against beta-lactamase) is an option for someone with a treatment failure who is compliant with medication. This includes amoxicillin-clavulanate, cephalosporins, clindamycin, ceftriaxone and macrolides^{3, 12}.

Repeat cases of GABHS should have family members checked for asymptomatic carriers. If they are found they should be treated.

Carriers

The carrier state describes someone who is chronically colonized with GABHS and affects between 10-25% of the population. They rarely develop complication or spread infection. Typically the carrier state is not treated. There are situations where the carrier state should be treated including¹²:

- Personal or family history of rheumatic fever
- Recurrent transmission within a family or close community
- When there is significant anxiety about GABHS

Clindamycin for 10 days is the treatment of choice or penicillin and rifampin will eliminate the carrier state¹².

Teaching points

- Do not return to work or school for 24 hours after starting therapy
- Use a new tooth brush after 24 hours of therapy
- Rinse removable orthodontic appliances thoroughly
- Teach about comfort measures: Ibuprofen or acetaminophen, warm salt-water gargles, popsicles, phenol sprays and throat lozenges
- Follow up with the health care provider if symptoms last longer than 5-7 days or they do not improve within 72 hours
- Complete a full course of antibiotics to reduce the risk of recurrent infection
- Do not take "left over" antibiotics for a sore throat. More than two doses of an antibiotic can invalidate the laboratory evaluation of GABHS¹²

Steven was given a likely diagnosis of GABHS based on clinical grounds. A positive rapid antigen test to GABHS confirmed the diagnosis. This was quite predictable since he met four key criteria for GABHS (fever, cervical adenopathy, absence of cough and tonsillar exudates) in addition to being in the most likely age category. He was treated with amoxicillin and had an unremarkable recovery.

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