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Pharyngitis

- Pharyngitis is an acute infection of the oropharynx or nasopharynx.
- While viral causes are most common, group A β-hemolytic Streptococcus, or S. pyogenes, is the primary bacterial cause.
- In the pediatric population, group A *Streptococcus*, or "strep throat," causes 15% to 30% of cases of pharyngitis.
- In adults, it is the cause of 5% to 15% of all symptomatic episodes of pharyngitis.

MICROBIOLOGY

- Viruses cause the majority of acute pharyngitis cases:
- Specific etiologic agents include:
- rhinovirus (20%)
- coronavirus ($\geq 5\%$)
- adenovirus (5%)
- herpes simplex (4%)
- influenza virus (2%)
- parainfluenza virus (2%)
- Epstein-Barr virus (<1%)

MICROBIOLOGY...

- Other, less-common causes of acute pharyngitis include:
- groups C and G Streptococcus
- Corynebacterium diphtheriae,
- Neisseria gonorrhoeae,
- Mycoplasma pneumoniae,
- Arcanobacterium haemolyticum,
- Yersinia enterocolitica,
- Chlamydia pneumoniae.

PATHOPHYSIOLOGY

- The mechanism by which group A *Streptococcus* causes pharyngitis is not well defined.
- Asymptomatic pharyngeal carriers of the organism may have an alteration in host immunity (e.g., a breach in the pharyngeal mucosa) and the bacteria of the oropharynx, allowing colonization to become infection.
- Pathogenic factors associated with the organism itself also may play a role.
- These include pyrogenic toxins, hemolysins, streptokinase, and proteinase.

CLINICAL PRESENTATION

- However, although all age groups are susceptible, epidemiologic data show that certain groups are at higher risk:
- Children ages 5 to 15 years old are most susceptible;
- Parents of school-age children
- Those who work with children are also at increased risk.

CLINICAL PRESENTATION...

- Seasonal outbreaks occur, and the occurrence of group A streptococcal pharyngitis is highest in winter and early spring.
- The incubation period is 2 to 5 days, and the illness often occurs in clusters.
- Spread occurs via direct contact (usually from hands) with droplets of saliva or nasal secretions, and transmission is thus worse in institutions, schools, families, and areas of crowding.
- Untreated, patients with streptococcal pharyngitis are infectious during the acute illness and for another week thereafter.
- Effective antimicrobial therapy reduces the infectious period to about 24 hours.



TABLE 112-10 Clinical Presentation and Diagnosis of Group A Streptococcal Pharyngitis

General

A sore throat of sudden onset that is mostly self-limited Fever and constitutional symptoms resolving in about 3 to 5 days Clinical signs and symptoms are similar for viral causes as well as nonstreptococcal bacterial causes

Signs and symptoms

Sore throat

Pain on swallowing

Fever

Headache, nausea, vomiting, and abdominal pain (especially children) Erythema/inflammation of the tonsils and pharynx with or without patchy exudates Enlarged, tender lymph nodes

Red swollen uvula, petechiae on the soft palate, and a scarlatiniform rash

Several symptoms that are not suggestive of group A Streptococcus are cough, conjunctivitis, coryza, and diarrhea

Laboratory tests

Throat swab and culture or rapid antigen detection testing

CLINICAL PRESENTATION...

- Nonsuppurative complications such as acute rheumatic fever, acute glomerulonephritis, and reactive arthritis may occur.
- Suppurative complications, such as peritonsillar abscess, retropharyngeal abscess, cervical lymphadenitis, mastoiditis, otitis media, sinusitis, and necrotizing fasciitis.

Diagnosis

- For a patient presenting with pharyngitis, the most important clinical decision that needs to be made is whether or not the pharyngitis is caused by group A *Streptococcus*.
- Group A streptococcal pharyngitis is difficult to differentiate from viral pharyngitis based on history and clinical findings.

Diagnosis...

 Clinical scoring systems such as the Centor criteria or modifications have been advocated for diagnosis in adults as a way:

- to overcome the lack of sensitivity and specificity of clinician judgment
- and to avoid laboratory testing of all patients.



Criteria	Points
Temperature >38°C (100.4°F)	1
Absence of cough	1
Swollen tender anterior cervical nodes	1
Tonsillar swelling or exudate	1
Age	
3–14 years	1
15–44 years	0
45 years or older	-1
Score	Risk of streptococcal infection
≤ 0	1%-2.5%
1	5%-10%
2	11%-17%
3	28%-35%
≥4	51%-53%

The original Centor score applies to adults only. This modified version allows for age. Data from McIsaac WJ, Kellner JD, Aufricht P, et al. JAMA 2004;291:1587–1595.

Diagnosis...

- However, concern exists that use of these criteria *alone* leads to overprescribing.
- Guidelines from the Infectious Disease Society of America, the American Academy
 of Pediatrics, and the American Heart Association suggest that testing be done in all
 patients with signs and symptoms of pharyngitis.
- Only those with a positive test for group A *Streptococcus* require antibiotic treatment.
- Recent studies suggest that limiting testing to patients who meet <u>two or more</u> <u>Centor criteria</u> will minimize overtesting.
- The simplest approach is likely bedside testing with culture confirmation in cases of negative results.
- This ensures those with disease are not missed.



There are several options to test for group A streptococcal pharyngitis:

- A throat swab can be sent for culture or used for the rapid antigen-detection test (RADT).
- Cultures are the "gold standard" but require 24 to 48 hours for results.
- The RADT is more practical in that it provides results quickly, it can be performed at the bedside, and it is less expensive than culture.
- Cultures are recommended for children, adolescents, parents, and schoolteachers with negative RADTs, as well as in situations of outbreak or to monitor resistance.
- Delaying therapy while awaiting culture results does not affect the risk of complications (although some argue that symptomatic benefit is postponed, and contagion remains)



TABLE 112-12 Evidence-Based Principles for Diagnosis of Group A Streptococcus

Recommendations Level Selective use of diagnostic testing in only those with clinical features A-II suggestive of group A Streptococcus will increase the proportion of positive tests as well as results of those truly infected, not carriers. Clinical diagnosis cannot be made with certainty even by the most A-II experienced clinician; bacteriologic confirmation is required. Throat culture remains the diagnostic standard with a sensitivity of A-II 90%–95% for detection of group A Streptococcus if done correctly. Rapid identification and treatment of patients with disease can reduce A-II transmission, allow patients to return to work or school earlier, and reduce the acute morbidity of the disease. The majority of rapid antigen-detection tests available have a specificity A-II >95% (minimizes overprescription to those without disease), and a sensitivity of 80%-90%, compared to culture. Early initiation of antimicrobial therapy results in faster resolution of A-L signs and symptoms. Delays in therapy (if awaiting cultures) can be made safely for up to 9 days after symptom onset and still prevent major complications such as rheumatic fever.

Diagnosis...

- It is important to note that laboratory testing should not be used without consideration of clinical criteria.
- This is because a positive test does not necessarily indicate disease.
- A positive test may indicate carriage (not active infection) with group A *Streptococcus*.



DESIRED OUTCOME The goals of treatment of pharyngitis are:

- Improve clinical signs and symptoms
- Prevent transmission to close contacts,
- Prevent acute rheumatic fever
- Prevent suppurative complications, such as peritonsillar abscess, cervical lymphadenitis, and mastoiditis

- Antimicrobial therapy should be limited to those who have clinical and epidemiologic features of group A streptococcal pharyngitis with a positive laboratory test.
- Empiric therapy is not recommended.
- Antimicrobial overuse in those without disease and underuse in those with disease is well documented.

- Because pain is often the primary reason for visiting a physician, emphasis on analgesics such as acetaminophen and NSAIDs to aid in pain relief is strongly recommended.
- However, acetaminophen is a better option
- because there is some concern that <u>NSAIDs may increase the</u> <u>risk for necrotizing fasciitis/toxic shock syndrome.</u>
- Toxic shock syndrome has been linked to group A streptococcal pharyngitis.

- Either systemic or topical analgesics can be used,
- as well as antipyretics and other supportive care, including rest, fluids, lozenges, and saltwater gargles.
- Symptoms may resolve 1 to 2 days sooner with such interventions.

Antimicrobial Therapy:

- Antimicrobial therapy decreases the duration of signs and symptoms by 1 to 2 days.
- Therapy also decreases the severity of symptoms when initiated within 2 to 3 days of onset in patients with proven group A *Streptococcus*.
- Microbiologic eradication will occur in 48 to 72 hours, which aids in decreasing transmission.



Penicillin is the drug of choice.

It has the narrowest spectrum of activity, and it is effective, safe, and inexpensive

- The only controlled studies that have demonstrated that antimicrobial therapy prevents rheumatic fever following group A streptococcal pharyngitis were done with procaine penicillin, which was later replaced with benzathine penicillin.
- Penicillin given by other routes is assumed to be equally efficacious.
- The ability of other antibiotics to eradicate group A *Streptococcus* has led to extrapolation that these agents also will prevent rheumatic fever.
- Amoxicillin can be used in children because the suspension has a better taste than that of penicillin.
- Gastrointestinal side effects and rash, however, are more common.

- In patients who are allergic to penicillin, a macrolide such as erythromycin or a first-generation cephalosporin such as cephalexin (if the reaction is non–IgE-mediated hypersensitivity) can be used.
- Newer macrolides such as azithromycin and clarithromycin are equally effective as erythromycin and cause fewer gastrointestinal adverse effects.
- Second-generation cephalosporins, such as cefuroxime and cefprozil, or thirdgeneration cephalosporins, such as cefpodoxime and cefdinir, which are βlactamase–stable, have been advocated for clinical failures with penicillin.

 Amoxicillin- clavulanate or clindamycin may be considered for recurrent episodes of pharyngitis to maximize bacterial eradication in potential carriers and to counter copathogens that produce lactamases.

TABLE 112-13 Dosing Guidelines for Pharyngitis

Drug	Adult Dosage	Pediatric Dosage	Duration
Penicillin VK	250 mg three or four times daily or 500 mg twice daily	50 mg/kg/day divided in three doses	10 days
Penicillin benzathine	1.2 million units intramuscularly	0.6 million units for weight <27 kg (50,000 units/kg)	One dose
Penicillin G procaine and benzathine mixture	Not recommended in adolescents and adults	 1.2 million units (benzathine 0.9 million units, procaine 0.3 million units) 	One dose
Amoxicillin	500 mg three times daily	40–50 mg/kg/day divided in three doses	10 days
Erythromycin			10 days
Estolate	20–40 mg/kg/day divided two to four times daily (max: 1 g/day)	Same as adults	
Stearate	1 g daily divided two to four times daily (adolescents, adults)	-	
Ethylsuccinate	40 mg/kg/day divided two to four times daily (max 1 g/day)	Same as adults	
Cephalexin	250–500 mg orally four times daily	25–50 mg/kg/day divided in four doses	10 days

TABLE 112-14 Antibiotics and Dosing for Recurrent Episodes of Pharyngitis				
	Drug	Adult Dosage	Pediatric Dosage	
	Clindamycin	600 mg orally divided in two to four doses	20 mg/kg/day in three divided doses (max: 1.8 g/day)	
	Amoxicillin-davulanate	500 mg twice daily	40 mg/kg/day in three divided doses	
	Penicillin benzathine	 1.2 million units intramuscu- larly for one dose 	0.6 million units for weight <27 kg (50,000 units/kg)	
	Penicillin benzathine with rifampin	As above Rifampin 20 mg/kg/day orally in two divided doses during last 4 days of treat- ment with penicillin	As above Rifampin dose same as adults	

- To date, no resistance of group A *Streptococcus* to penicillin has been reported in clinical isolates.
- Macrolide resistance is low (>5%) and is not widespread.
- Internationally, higher rates have also been reported, and as usage of macrolides increases, these rates will continue to rise.
- Group A Streptococcus resistance rates to <u>Tetracyclines</u> and <u>Sulfonamides</u> are high; consequently, use of these agents is no longer recommended.

- The duration of therapy for group A streptococcal pharyngitis is 10 days to maximize bacterial eradication.
- Short-course therapy has been advocated to help overcome compliance issues that lead to bacteriologic failure.
- A 6-day course of amoxicillin shows promising results;
- Recent studies with newer broad-spectrum agents (e.g., azithromycin, cefuroxime, cefprozil, cefdinir, cefixime, cefpodoxime, and telithromycin) have demonstrated durations of 5 days to be effective.

Evaluation of Therapeutic Outcomes/Contact Cases...

- Followup testing generally is not necessary for index cases or in asymptomatic contacts of the index patient.
- Symptomatic contacts may be treated without cultures.
- The incidence of invasive group A streptococcal infection in household contacts is rare, and routine chemoprophylaxis is not recommended by the CDC.
- 25% of household contacts are carriers, but treatment would only be required in persons with signs and symptoms of disease or contacts of severe or resistant disease.

