

Pharyngitis

Pharyngitis Guideline Team

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Patient population. Patients 3 years old through adulthood.

Objectives.

- Minimize the risk of developing rheumatic fever and suppurative complications.
- Utilize symptoms to determine probability of group A strep (GAS) pharyngitis before testing.
- Confirm all negative GAS rapid screen results with culture in patients <16 years old.
- Reduce indiscriminate use of antibiotics, minimizing adverse effects & bacterial drug resistance.

Key points

General principals.

- Viral pathogens cause most cases of pharyngitis: around 90% in adults and 70% in children [C*].
- The primary reason to identify and treat GAS pharyngitis is to decrease the risk of acute rheumatic fever (ARF) [IB*]. The endemic incidence of ARF is around 0.23-1.88 / 100,000.
- Early treatment of GAS can decrease the time a patient is symptomatic by 1-2 days from a typical 3-7 days [IB*] and can decrease the period of contagiousness [IB*].

Diagnosis.

- Signs/symptoms of severe sore throat, fever, tender anterior cervical lymphadenopathy, red pharynx with tonsillar swelling +/- exudate, and no cough indicate a higher probability of GAS pharyngitis for both adults and children. Algorithms of epidemiologic and clinical factors improve diagnosis by identifying patients with an exceedingly low risk of GAS infection [C*].
- Laboratory confirmation:
 - Neither culture nor rapid antigen screen differentiate individuals with GAS pharyngitis from GAS carriers with an intercurrent viral pharyngitis.
 - Consider clinical and epidemiological findings (Table 2) when deciding to perform a microbiological test. [IB*].
 - Patients with manifestations highly suggestive of a viral infection such as coryza, scleral conjunctival inflammation, hoarseness, cough, discrete ulcerative lesions, or diarrhea, are unlikely to have GAS infection and generally should NOT be tested for GAS infection [IIB*].
- Throat culture is the presumed “gold standard” for diagnosis. Rapid streptococcal antigen tests identify GAS more rapidly, but have variable sensitivity [B*].
 - Reserve rapid strep tests for patients with a reasonable probability of having GAS.
 - Confirm negative screen results by culture in patients < 16 years old (& consider in parents/siblings of school age children) due to their higher risk of acute rheumatic fever [IIC*].
 - If screening for GAS in very low risk patients is desired, culture alone is cost-effective [IIC*].

Treatment.

- Penicillin V is the drug of choice in patients who can swallow pills.
- If using suspension, amoxicillin is better tolerated than penicillin V due to the salty/bitter taste.
- Amoxicillin as a single daily dose (1 gram/day) for 10 days is as effective as penicillin V or amoxicillin given multiple times per day for 10 days.
- A single dose of intramuscular penicillin G benzathine avoids the problem of adherence, but is painful.
- If allergic to penicillin, a 10-day course of a first generation cephalosporin is indicated if no history of a type I hypersensitivity to penicillin. Oral clindamycin is an acceptable alternative, if one is unable to use a first generation cephalosporin.
- A macrolide is also acceptable for patients allergic to penicillins (resistant rates range 5-8%).
- Children with a recurrence of GAS pharyngitis shortly after completing a course of an oral antimicrobial agent can be retreated with the same agent, given an alternative oral drug, or given an intramuscular injection of penicillin G benzathine (expert opinions differ).
- Antibiotics must be started within 9 days after onset of acute illness and continued for 10 days (5 days for azithromycin) to eradicate GAS from the upper respiratory tract and prevent ARF [D*].

Controversial areas.

- Diagnosis over the telephone based on symptoms alone without lab testing is unreliable. [IIID*].
- Based on a phone description, a nurse triage algorithm may guide screening for GAS. [IID*].
- When an appropriately symptomatic patient is ≥ 3 years old and has a family member recently diagnosed with laboratory confirmed GAS pharyngitis, one may treat without screening [IID*].

*** Strength of recommendation:**

I = generally should be performed; II = may be reasonable to perform; III = generally should not be performed.

Levels of evidence reflect the best available literature in support of an intervention or test:

A=randomized controlled trials; B=controlled trials, no randomization; C=observational trials; D=opinion of expert panel.

Table 1. High Risk Patients

- Concurrent diagnosis of rheumatic fever or a past history of rheumatic fever, especially with carditis or valvular disease
- Household contact with someone having a history of rheumatic fever

Table 2. Signs and Symptoms

Suggestive for GAS

- Fever > 38° C (100.4° F)
- Tender anterior cervical nodes
- Enlarged, red tonsils +/- purulent exudate
- Palate petechiae
- Headache
- Abdominal pain, nausea and/or vomiting
- Scarlet fever rash
- Age 5-15 years
- Presents in late autumn, winter or spring
- History of recent exposure

Suggestive for viral etiology

- Cough and coryza
- Scleral conjunctival inflammation ("pink eye")
- Hoarseness
- Pharyngeal ulcerations
- Diarrhea
- Characteristic viral rash

Table 3. Advantages / Disadvantages of GAS Screens and Cultures

Screen

Advantage

- Rapid positive result
- May aid in arranging day care, school, or work absence
- High specificity
- Prompt treatment may lower risk of spread to others & may shorten clinical symptoms

Disadvantage

- Less sensitive

Higher average lab charges: initial charge for rapid screens (e.g., \$57 at UMHS) and, if negative and patient < 16 years, additional charge for backup culture (e.g., \$52 at UMHS)

Culture

Advantage

- High sensitivity & specificity
- Lower average lab charge for culture alone (e.g., \$52 at UMHS)

Disadvantage

- Up to 3 days delay for result
- Logistics of reporting back result
- Delay in treatment if test positive

Figure 1. An Approach to the Patient with Pharyngitis

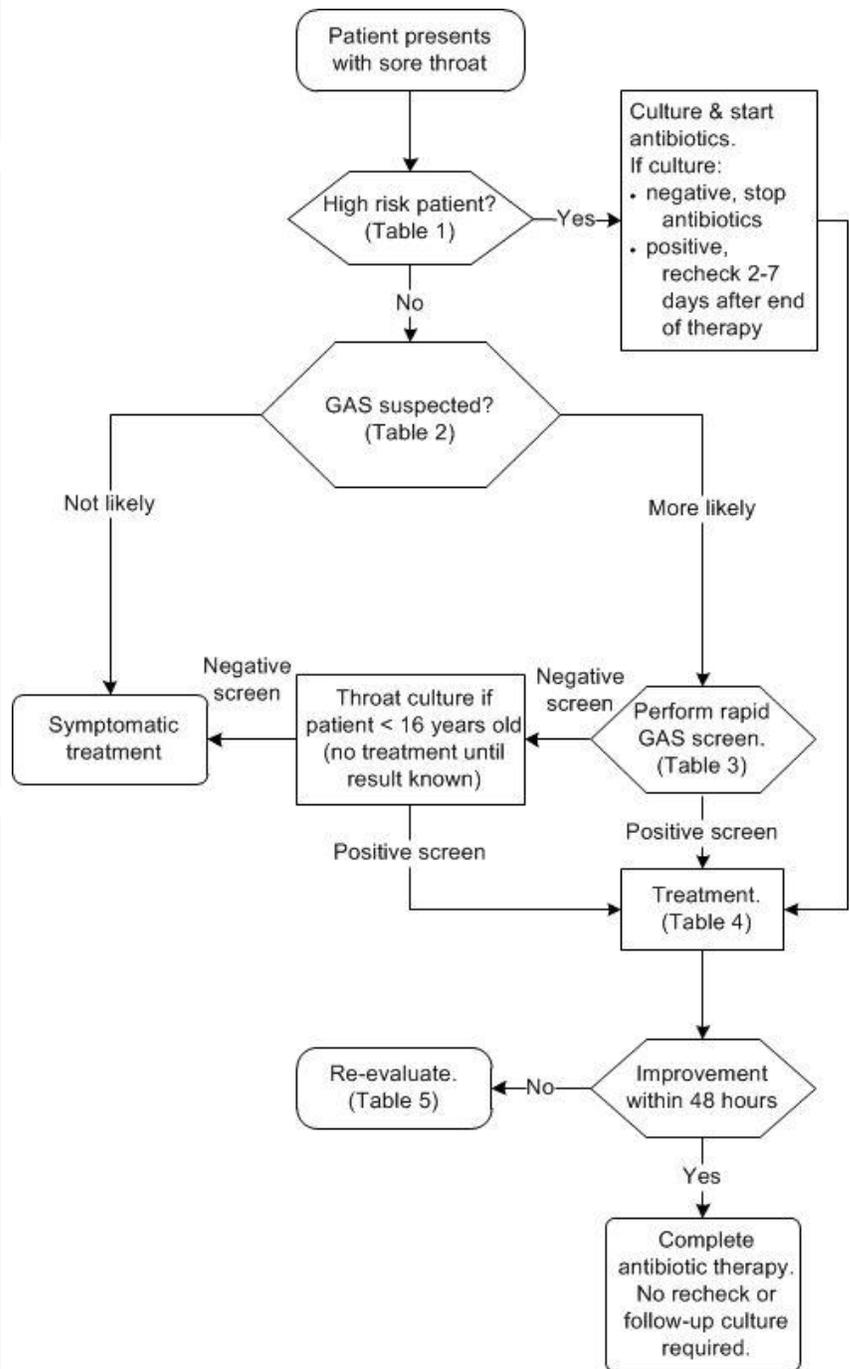


Table 4. Examples of Antibiotic Treatment for Group A Streptococcal Pharyngitis

DRUG	DOSE treatments are for 10 days unless otherwise stated	COST ^a	
		Generic	Brand
Preferred Treatment			
Pediatrics (child < 60 lbs/ 27 kg)			
Amoxicillin suspension or chewable ^b	50 mg/kg once daily (max. 1g/d)	\$10	
Penicillin V	250 mg/dose BID–TID	\$5	
Benzathine penicillin G ^c	600,000 U IM one dose	NA	\$35
In penicillin-allergic			
Cephalexin ^{d, e}	25–50 mg/kg/d divided BID	\$18	
Clindamycin ^f	20 mg/kg/d divided TID (max 1.8 g/day)	\$65	
Azithromycin ^{d, g, h}	12 mg/kg/d once daily x 5 days (max 500 mg)	\$27	
Adolescents and Adults (> 60 lbs/ 27 kg)			
Penicillin V	500 mg/ dose BID–TID	\$11	
Amoxicillin	1 gm/d x 10 days (max. 1g/d)	\$8	
Benzathine penicillin G ^c	1.2 million IM one dose		\$35
In penicillin-allergic			
Cephalexin ^{d, e}	500 mg/dose BID	\$6	
Clindamycin	300 TID for most adults, or 20 mg/kg/d divided TID (max 1.8 g/day)	\$23	
Azithromycin ^{d, g, h}	12 mg/kg/d once daily x 5 days (max 500 mg)	\$27	

Note: Antibiotics not effective against GAS: tetracyclines, trimethoprim, sulfonamides, chloramphenicol, and fluoroquinolones.

^a Cost = Average wholesale price based -10% for brand products and Maximum Allowable Cost (MAC) + \$3 for generics on 10-day supply, *Amerisource Bergen item Catalog 2/12 & Blue Cross Blue Shield of Michigan Mac List, 2/12.*

^b Amoxicillin suspension is generally preferred due to significantly higher compliance since penicillin suspension tastes salty/bitter.

^c Benzathine penicillin G injection has somewhat better efficacy than oral. It avoids the problem of adherence, but administration is painful for 2-3 days at injection site. Increased risk of anaphylaxis severity – can stop oral medication at first sign of reaction.

^d Better compliance due to high incidence of GI side effects from erythromycin.

^e Acceptable for patients who do not exhibit immediate-type I hypersensitivity to beta-lactam antibiotics.

^f Extremely bitter taste of suspension may lead to decreased completion of prescribed course.

^g This dose is higher than the usual dose for otitis media and requires 5 days (not 3 days as can be used when treating otitis). In recent years, macrolide resistant rates in most areas of the U.S. have been 5-8%. Macrolide usage has been associated with prolonged QT effect.

^h The FDA issued a warning that azithromycin could cause potentially fatal irregular heart rhythm in some patients. At-risk patients include those with a slower-than-normal heartbeat, with potassium or magnesium deficiencies, and those using medications to treat existing heart arrhythmia.

Table 5. Reasons for Failure of Response

- | |
|---|
| <ul style="list-style-type: none"> ▪ Peritonsillar or retropharyngeal abscess (which REQUIRES a prompt ENT evaluation) ▪ GAS carrier with acute pharyngitis due to an intercurrent virus or other bacteria ▪ Inability to comply with medication regimen ▪ Failure of antibiotic to eradicate GAS (such as macrolide resistance) |
|---|

Table 6. Examples of Antibiotic Treatment for Frequent Recurrent Group A Streptococcal Pharyngitis

DRUG	DOSE treatments are for 10 days unless otherwise stated	COST ^a	
		Generic	Brand
Preferred Treatment			
Pediatrics			
Amoxicillin–clavulanic acid ^b	Augmentin ES suspension (600 mg of amoxicillin with 42.9 mg of clavulanate/5 mL) at 90 mg/kg/day divided BID.	\$63	
Clindamycin	20mg/kg/d divided TID (max 1.8 g/day)	\$65	
Penicillin VK with rifampin ^c	Pen VK: 250 mg BID–TID + rifampin 20 mg/kg/d divided BID, max 600 mg/day during last 4 days of therapy	\$35	
Benzathine penicillin G with rifampin ^c	Benzathine penicillin G: 600,000 U IM one dose; rifampin 20 mg/kg/d divided BID, max 600 mg/day during last 4 days of therapy		\$62
Adolescents and Adults			
Amoxicillin–clavulanic acid ^b	Use 500 mg amoxicillin with 125 mg clavulanate BID	\$30	
Clindamycin	300 TID for most adults, or 20mg/kg/d divided TID (max 1.8 g/day)	\$23	
Penicillin VK with rifampin ^c	Pen VK: 500 mg/ dose BID–TID; rifampin: last 4 days 300 mg/dose BID	\$37	
Benzathine penicillin G with rifampin ^c	Benzathine penicillin G: 1.2 million U IM one dose; rifampin: 4 days 300 mg/dose BID		\$71

Note. All treatments are for 10 days unless otherwise stated. **Macrolides and cephalosporins are not included because data are insufficient regarding their efficacy for recurrent episodes.**

^a Cost = Average wholesale price based -10% for brand products and Maximum Allowable Cost (MAC) + \$3 for generics on 10-day supply, *Amerisource Bergen item Catalog 2/12 & Blue Cross Blue Shield of Michigan Mac List, 2/12.*

^b Other proportions of amoxicillin/clavulanate exist that do not provide the clavulanate dose recommended for this purpose (e.g., two tablets each with 250 mg amoxicillin can total twice as much clavulanate as one tablet with 500 mg amoxicillin).

^c Addition of rifampin may be beneficial for eradication of streptococci from the pharynx. Rifampin is relatively contraindicated for pregnant women.

Clinical Background

Clinical Problem

Epidemiology. Pharyngitis, either as a part of a viral upper respiratory tract infection or as a manifestation of group A beta hemolytic *Streptococcal* infection (GAS), is one of the most common complaints for which patients present to primary care offices.

GAS pharyngitis is much more common in children (15%–30%) than in adults (5%–10%). It is seasonal, with an increase seen in late autumn, winter, and spring in temperate climates. It occurs predominantly in school-age children, although it can occur in those living in close quarters such as child care centers, dormitories, or in the military.

Diagnostic difficulty. Unfortunately, the clinical manifestations of GAS and non-GAS pharyngitis overlap quite a bit. The usefulness of laboratory tests for GAS pharyngitis depends on the probability of the disease. Laboratory testing and treatment may be under or over

utilized in the absence of a reasoned, cost-effective, diagnostic strategy.

Decisions about antigen screening vs. culture. No clear strategy has been proposed for the cost effective use of antigen screening and/or culture. Culture is the presumed "gold standard" but involves a delay of 24 to 72 hours in reporting a diagnosis. The current GAS antigen detection tests (rapid strep screens) using EIA techniques have a high degree of specificity, but their sensitivity can still be variable. The benefit of a more rapid positive diagnosis for a minority of patients must be weighed against the doubling of laboratory costs for the majority of patients whose rapid GAS screens are negative and require a follow-up culture. The benefit of follow-up cultures differs by age, resulting in different follow-up recommendations for children and adults.

Overuse of antibiotics. Despite the low incidence of GAS pharyngitis, numerous studies reveal that approximately 75% of adult patients with acute pharyngitis are prescribed antibiotics. Also worrisome, a previous study revealed that

a GAS test was performed on only 15-36% of children with sore throats even though 53% of them received antibiotics. Indiscriminate antibiotic use may increase the incidence of allergic reactions to antibiotics, increase the incidence of mislabeling patients as allergic to antibiotics when a simultaneous rash develops due to a viral exanthem (not the antibiotic), and increase the emergence of resistant strains of other pathogenic bacteria, especially Gram-negative rod enteric organisms.

Rationale for Recommendations

Treatment Goal

The most important goal in treating GAS infection is to decrease the occurrence of acute rheumatic fever (ARF). The endemic incidence is around 0.23-1.88/100,000 people (1980's data). In epidemics with rheumatologic strains of GAS, ARF has occurred in up to 3% of patients with untreated GAS pharyngitis. It generally occurs 10–14 days after onset of acute pharyngitis. Early treatment of GAS also shortens the clinical course, can reduce the risk of transmission, and may decrease the risk of other suppurative sequelae (e.g., otitis media, sinusitis, peritonsillar/retropharyngeal abscesses or mastoiditis). Post-streptococcal glomerulonephritis (PSGN) is another sequela of GAS infection, but usually occurs after a streptococcal skin infection. Treating GAS pharyngitis does not appear to diminish the risk of PSGN.

Identify High Risk Patients

It is important to identify patients who have a personal history or family member with a history of acute rheumatic fever (see Table 1); specifically, those who have had rheumatic carditis or valvular disease. These patients are at high risk for complications of GAS pharyngitis. ARF can occur more rapidly in someone who has had a previous episode of ARF, especially if there was prior valvular involvement. A high-risk patient presenting with a sore throat should be prescribed immediate antibiotic treatment while awaiting culture results. Discontinuation of antibiotics is appropriate if the throat culture yields no growth.

Diagnosis

Symptoms. The diagnosis of GAS pharyngitis should be suspected on epidemiological and clinical factors and then supported by performance of a lab test. Using epidemiological and clinical factors alone to initiate empirical treatment will result in many people being treated unnecessarily. A number of algorithms incorporating epidemiologic and clinical factors have been devised. These algorithms improve diagnostic accuracy primarily by identifying patients with an exceedingly low risk of GAS infection. Signs and symptoms can only provide guidance to determine which patients should have laboratory screening to establish the diagnosis of GAS pharyngitis.

The constellation of severe sudden sore throat (especially with pain upon swallowing), fever, tender anterior cervical lymphadenopathy, red pharynx with tonsillar swelling +/- exudate, and no cough indicate a higher probability of GAS for both adults and children. Other associated clinical findings suggestive of GAS as the cause of an episode of acute pharyngitis include headache, abdominal pain, nausea, vomiting, palate petechiae, and a scarlatiniform rash. Important historical factors include a high prevalence of GAS infections in the community; patient presentation in late autumn, winter, or spring seasons; or exposure to individuals confirmed to have had GAS pharyngitis.

Findings that clearly suggest more of a viral etiology include cough, coryza, scleral conjunctival inflammation ("pink eye"), hoarseness, pharyngeal ulcerations, diarrhea, and/or a classic viral exanthema (such as vesicles or maculopapular rashes).

Laboratory diagnosis. Laboratory diagnosis of GAS pharyngitis is important because of lower sensitivity and specificity of clinical impressions. Correct swabbing of the oropharynx is of paramount importance. Both tonsillar fauci and the posterior oropharynx must be vigorously swabbed. False negative cultures may result from an inadequate specimen collection process.

GAS culture. The gold standard for diagnosis of GAS pharyngitis is a throat culture (~95% sensitivity). Results are available in 1-3 days. (The blood agar plate should be held for 48 hours prior to discarding.) However, a positive throat culture may reflect chronic colonization by GAS; another pathogen may be the actual cause of the acute illness. Quantitation of GAS from the throat swab cannot be used to differentiate carriage from infection because sparse growth may be associated with true infection.

GAS antigen screen. Most current GAS antigen screens use a rapid immunoassay method (usually EIA technique) for determining the presence of GAS in a throat swab. Results should be available within minutes. Depending upon the test used, antigen testing is reported to have a specificity of >95% and a sensitivity ranging from 67% to 84%, compared to blood agar plate culture. Because of the very high specificity of these rapid tests, a positive test generally does not require throat culture confirmation. Because of the sensitivity, a common recommendation is that a negative antigen test should be confirmed by a culture in patients less than 16 years old.

Diagnosis of GAS pharyngitis in most adults on the basis of a GAS antigen screen alone, without confirmation by a negative throat culture, is reasonable [IIC*]. In adults the incidence of GAS infection is low and the risk of developing acute rheumatic fever is extremely low.

A newer generation of rapid diagnostic tests have been developed, although their use is not yet widespread. These tests use techniques such as optical immunoassay and chemiluminescent DNA probes. Published data suggest that these tests may be as sensitive as standard throat cultures. Some experts believe that the optical immunoassay may be

sufficiently sensitive to be used without a backup throat culture, even in children.

Laboratory charges. Local laboratory charges for GAS throat cultures and antigen screens can contribute significantly to the total cost of treatment for a child with pharyngitis. For example, at UMHS the current laboratory charge for a GAS throat culture alone is \$52 and for a GAS antigen screen is \$57. If a screen is negative and a follow-up culture is performed, the total charge is \$109 for both a screen and culture. (Other laboratories may structure charges for GAS screens and cultures in other ways.)

Choosing between a screen or culture. When a clinician has decided to order a laboratory test to diagnose GAS pharyngitis, the choice between starting with an antigen screen or simply obtaining a culture should consider the benefits and costs in the context of the individual patient. Early positive diagnosis and initiation of therapy with the use of the rapid GAS screen can reduce the period of infectivity and morbidity and may allow the patient to return to normal activity sooner. Patients are no longer considered infectious to others after receiving appropriate antibiotic therapy for at least 24 hours. However, the value of early diagnosis in the minority of cases when GAS is present and identified by antigen testing must be weighed against the higher total laboratory charges for the majority of non-GAS pharyngitis cases which require a confirmatory throat culture in patients less than 16 years old.

When should GAS testing be done? When the diagnosis of GAS pharyngitis is not ruled out by a viral clinical presentation, decisions regarding any testing for GAS must consider the added value of the information given the prior probability that GAS is present.

Treatment of GAS Pharyngitis

Antimicrobial therapy should be prescribed for individuals with symptomatic pharyngitis only after the presence of GAS in the throat has been confirmed by either throat culture or a rapid antigen diagnostic test. In situations such as concurrent diagnosis of rheumatic fever or a past history of rheumatic fever, antimicrobial therapy can be initiated while awaiting laboratory confirmation, provided that such therapy is discontinued if the diagnosis of GAS pharyngitis is not confirmed by a laboratory test.

Preferred treatment. Examples of preferred treatments are presented in Table 4. In a patient with no prior history of ARF, antibiotics may be initiated within 9 days of onset of symptoms and still be effective at preventing ARF.

Penicillin V administered orally two or three times daily is the treatment of choice for prevention of acute rheumatic fever [IB*]. GAS still demonstrates susceptibility to penicillin in North America, thus penicillin is the drug of choice in those not allergic to penicillin and who can swallow pills.

Oral Amoxicillin once daily is now given almost equal favor to oral penicillin V [IB*]. (Note that the 50 mg/kg dosing is not the same as dosing for otitis media.)

Erythromycin, which had been the preferred antibiotic for those allergic to penicillin in the past, has fallen out of favor with most health care professionals and experts. Erythromycin is associated with substantially higher rates of GI side effects compared to the other agents [IIB*].

Narrow spectrum cephalosporins (such as cephalexin) are now recommended for those who cannot be safely prescribed a penicillin [IB*]. The cephalosporins are recommended for those who do not have immediate type (type 1) hypersensitivity to beta-lactam antibiotics. They have the most activity against Gram-positive bacteria and little activity against Gram-negative enteric organisms, so they are less likely to encourage antibiotic resistance than the extended-spectrum cephalosporins.

Clindamycin is a reasonable choice for treating penicillin-allergic patients, especially if they have had immediate (type 1) hypersensitivity to beta-lactam antibiotics [IIB*]. The extremely bitter taste of clindamycin solution may lead to nonadherence to the prescribed course.

Newer macrolides or azalide (such as azithromycin) antibiotics may be used for penicillin-allergic patients [IIB*]. When prescribing azithromycin, note that the dose is 12 mg/kg/day for 5 full days, which is higher than the dose used to treat otitis media. These medications can cause prolongation of the QT interval in a dose-dependent manner. Because macrolides are metabolized extensively by cytochrome P-450, they should not be taken concurrently with inhibitors of cytochrome P-450, such as azole antifungal agents, HIV protease inhibitors, and some selective serotonin reuptake inhibitor antidepressants. In recent years, macrolide resistance rates among pharyngeal isolates in most area of the U.S. have been approximately 5-8%.

A single intramuscular injection of benzathine penicillin G has been shown to be slightly more efficacious than oral penicillin V and ensures compliance [IIB*]. Also, this route can be very useful in children who present with severe abdominal pain and vomiting along with their GAS pharyngitis. It does, however, produce a significant amount of pain at the injection site that may last a 2-3 days following injection.

Alternative primary treatments. Examples of effective alternative antibiotics are: amoxicillin-clavulanic acid, and cefuroxime. These antibiotics are broader spectrum and may select for antibiotic-resistant flora. Also, they are significantly more expensive than penicillin. Sulfonamides, fluoroquinolones (e.g., ciprofloxacin) and tetracyclines are not acceptable for the treatment of GAS pharyngitis.

Failure to improve with treatment. Any patient with documented GAS pharyngitis who fails to improve within 48 hours, despite an appropriate course of antibiotics, should be reevaluated.

Local complications. An exam should be performed to rule out occurrence of a local complication, such as peritonsillar abscess (Quinsy) or retropharyngeal abscess. These complications require immediate consultation with otolaryngology as they may necessitate surgical drainage and pose a serious threat to the patient's airway.

No local complications. Persistence of GAS pharyngitis despite adequate therapy suggests several possibilities:

- **Organism is present as a colonizer** and does not pose a threat to cause acute rheumatic fever (i.e., a coexisting viral infection is the cause of the acute symptoms). These GAS carriers are defined as individuals with positive throat cultures for GAS without an immunologic response to GAS. Colonization occurs often after a primary GAS pharyngitis and it may persist for many months. Throat culture surveys of asymptomatic children during school outbreaks of pharyngitis have yielded GAS prevalence rates as high as 15-50%. However, in an individual with symptoms compatible with an acute GAS infection, it is not easy to decide whether the GAS isolated from the oropharynx is the cause of symptoms or from GAS carriage. Thus GAS persisting in a symptomatic individual should be retreated.
- **Patient nonadherent** with antibiotic course. The decision may be made to opt for intramuscular benzathine penicillin G in order to ensure adequate treatment. Also, the use of a better tolerated oral antibiotic, the use of a once-a-day antibiotic, or the use of a short-course antibiotic may improve adherence.
- **Organism was not killed** by the antibiotic treatment. One theory that has yet to be convincingly documented is that this could be due to "co-pathogenicity" with oral bacteria (such as Staph) secreting beta-lactamases into the oropharyngeal environment, thus passively protecting GAS from the actions of penicillin. In this case, reasonable treatment would be clindamycin or possibly a penicillinase-resistant antibiotic, such as amoxicillin-clavulanic acid [IID*].

Treatments for recurrence. Patients who have a recurrence of GAS pharyngitis shortly after completing a 10 day course of oral penicillin can be retreated with the same agent, given an alternative oral drug, or given an injectable dose of benzathine penicillin G [IC*].

For frequent recurrences, expert opinions differ about the most appropriate course of action. One may consider using a non-beta-lactam (Clindamycin) or a beta-lactam combined with a beta-lactamase inhibitor (amoxicillin-clavulanic acid) or the addition of rifampin to injectable benzathine penicillin G. These options may be beneficial for eradication of GAS from the pharynx. It has also been reported that addition of rifampin during the final 4 days of a 10-day course of oral penicillin V may achieve high rates of eradication [IC*]. Table 6 presents examples of treatments for frequent recurrent GAS pharyngitis. Macrolides and cephalosporins are not included in this table because data

are insufficient regarding their efficacy for frequent recurrent episodes.

Special Circumstances

Reevaluate high risk patients. High risk patients (see Table 1 above) should be reevaluated 2 to 7 days after the end of treatment in order to ensure that an adequate response has been obtained. This means that symptomatic improvement should be noted and re-swabbing of the throat should be performed to ensure eradication of GAS. GAS should be treated in high risk patients whether they are symptomatic or not.

Follow up throat cultures. The majority of patients with GAS pharyngitis respond clinically to antibiotics, with GAS eradication from the pharynx. Throat cultures after completion of therapy are indicated only in patients who remain symptomatic, whose symptoms recur, or who are high risk patients as outlined above.

Carriers. Chronic GAS carriers (defined as individuals with positive throat cultures for GAS without clinical findings or immunologic response to GAS antigens) usually do not need to be identified or treated with antibiotics. Distinguishing carriers from infected individuals is often impossible. Therefore, a single course of antibiotic therapy should be administered to any patient with acute pharyngitis and any evidence of GAS via a throat culture or rapid antigen screen [IC*]. GAS carriers appear to be at little risk for development of rheumatic fever. In general, chronic carriers are thought not to be important in the spread of GAS to others.

Non-GAS pharyngitis. Both group C and group G β -hemolytic streptococci can cause acute pharyngitis with clinical features similar to those of GAS pharyngitis, especially among college students. Acute rheumatic fever has not been described as a complication of either group C and group G streptococcal pharyngitis. Unless specified by the ordering physician, most labs will not identify or report out these organisms on "routine" GAS throat cultures.

Controversial Areas

Treatment over the phone based on symptoms. This approach is problematic because most cases of sore throat are from causes other than GAS.

However, some health systems may consider implementing nurse triage algorithms for screening for GAS pharyngitis. For example, clinic access can be an issue during flu season. An option may be to have a trained staff member triage symptoms over the phone. If the patient has symptoms compatible with GAS pharyngitis, consider bringing the patient into the office for a nurse visit and rapid GAS test. If the rapid GAS test is negative, the nurse counsels the patient on symptomatic therapy and when to return to the office. If the patient is < 16 years old, a backup throat

culture is sent. If a rapid GAS test is positive, one may elect to work the patient into the physician schedule to confirm risk of true GAS (vs. carriage) or one may elect to write a prescription without a physician encounter using an approved nursing protocol. This would help with patient access, cost and patient satisfaction.

Family member with GAS pharyngitis. A patient at least 3 years old with symptoms compatible with GAS pharyngitis who has a family member with a recently lab confirmed GAS infection may be treated presumptively without evaluation in the office. This would help with patient access, cost and patient satisfaction. However, even if a family member has documented GAS, it is preferable to perform a lab screen when empiric treatment may not be easily administered (e.g., patients with multiple antibiotic allergies or patients on anticoagulants).

Adjunctive treatment. The discomfort of GAS pharyngitis may be considerable. Often insufficient attention is paid to symptomatic treatment, whether caused by GAS or other pathogens. Please see the patient education section below for suggestions.

In addition to the common symptomatic treatments mentioned below, some physicians have recommended oral corticosteroids for pain relief. However, the benefits (mean reported onset of pain relief was 6.3 hours earlier compared to controls) seem to be meager in comparison with the possible adverse effects of corticosteroids.

Patient Education

Educating patients helps assure appropriate care during the current episode and appropriate use of health care services in the future. Some points that may be relevant to communicate to patients are summarized below. Information for patients about sore throats is available to provide more detail and reinforce instruction.

Causes of sore throats. The majority of sore throats are not caused by GAS and do not benefit from antibiotic therapy.

Symptomatic treatment. Use of acetaminophen or Non-steroidal anti-inflammatory drugs (NSAIDs), salt water gargles and lozenges may be helpful. Also, avoid acidic drinks or spicy food.

Throat cultures. May take up to 2-3 days for results to be known, but the majority are positive within 24 hours.

Full antibiotic treatment. Except for a 5 day course of azithromycin, all antibiotics need to be taken for the entire 10 days to prevent the risk of acute rheumatic fever, even if you are feeling better before then.

Antibiotic side effects. These may include rash, nausea, abdominal pain, and/or diarrhea.

When no longer contagious. The incubation period for strep throat is several days. Patients are considered noncontagious 24 hours after starting therapy.

Preventing rheumatic fever. Therapy may be initiated as late as 9 days after onset of symptoms and still be effective in preventing rheumatic fever.

Reexamination. Symptoms which require early follow-up include: persistent fever or throat pain lasting greater than 48 hours after initiating therapy, increasing difficulty swallowing, or development of new symptoms.

Strategy for Literature Search

The literature search for this update began with the results of the literature search performed for the 2006 version of this guideline performed in June, 2005. A search for literature published since that time was performed. The search on Medline was conducted prospectively for literature published from 6/1/05 to 3/30/11. One set of searches used the major keywords of: *GAS pharyngitis (streptococcal infections, streptococcus pyogenes, pharyngitis, pharynx), strep throat; human; English; guidelines, controlled trials, cohort studies.* Within these major keywords, specific searches were performed for the following topics: *history; physical exam, signs, symptoms throat culture (strep culture); rapid strep screen; observation; antibiotics, other treatment/management, rheumatic fever or group A strep reactive arthritis; and other references found under the major search terms.* Specific search terms and strategy are available upon request. Another set of searches used the major keywords of viral pharyngitis/ viral sore throat with specific searches performed for: alternative and complimentary therapies (e.g., zinc, Vitamin C, Echinacea); other treatment.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle. Conclusions were based on prospective randomized controlled trials if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Related National Guidelines

The UMHC Clinical Guideline on pharyngitis is consistent with:

American Academy of Pediatrics: Red Book, 2012 Report of the Committee on Infectious Diseases

American Heart Association and American Academy of Pediatrics: Prevention of Rheumatic Fever and Diagnosis and Treatment of Acute Streptococcal Pharyngitis, 2009

Infectious Diseases Society of America: Practice Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis, 2002

Measures of Clinical Performance

National programs that have clinical performance measures for pharyngitis include the following.

Centers for Medicare & Medicaid Services:

- Clinical Quality Measures for financial incentives for Meaningful Use of certified Electronic Health Record technology (MU)

Regional programs that have clinical performance measures for pharyngitis include the following.

Blue Care Network [HMO]:

- Clinical performance measures (BCN)

These programs have clinical performance measures for pharyngitis addressed in this guideline. While specific measurement details vary (e.g., method of data collection, population inclusions and exclusions), the general measures are summarized below.

Testing for children with pharyngitis. Of children age 2–18 years with a diagnosis of pharyngitis who had an ambulatory or pediatric encounter and who were prescribed a pharyngitis medication less than three days after the encounter, the percentage who received a group A streptococcus (strep) test less than four days before or after being prescribed an antibiotic to treat pharyngitis. (MU, BCN)

More general measures of clinical performance (e.g., immunizations, tobacco use assessment in adults) can apply to all clinical visits, including those for pharyngitis.

Disclosures

Neither the members of the Pharyngitis guideline team nor the consultant have a relationship with commercial companies whose products are discussed in this guideline. The team members and consultant are listed on the front page of this guideline.

Review and Endorsement

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Family Medicine, General Internal Medicine, General Pediatrics, Pediatric Medical Surgical Joint Practice Committee, and Mott Executive Committee. The Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers endorsed the final version.

Acknowledgments

Listed on the first page are members of the team that reviewed the previous version of this guideline and produced this update. The following individuals developed earlier versions of this guideline:

1996: John Crump, MD, Van Harrison, PhD, Michele Rea, RN, Barbara Reed, MD, Thomas Shope, MD, Connie Standiford, MD

2000: John Crump, MD, Van Harrison, PhD, Thomas Shope, MD, Raymond Rion, MD.

2006: Terrance P. Murphy, MD, Annissa J. Hammound, MD., R. Van Harrison, PhD, Gary Yen, MD. Consultants, R. Alexander Blackwood, MD, PhD, John R. Crump, MD

Annotated References

American Academy of Pediatrics. Red Book: 2012 Report of the Committee on Infectious Diseases. Pickering LK, ed. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2009.

Summarizes current recommendations for diagnosis and treatment of over 200 childhood infectious diseases.

Baltimore RS. Re-evaluation of antibiotic treatment of streptococcal pharyngitis. *Curr Opin Pediatr.* 2010 Feb;22(1):77-82

Bisno AL, Gerber MA, Gwaltney JM, Kaplan EL, Schwartz. Practice Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis. *Clinical Infectious Diseases.* 2002;35:113-125

Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and treatment of acute streptococcal pharyngitis. (American Heart Association scientific statement endorsed by the American Academy of Pediatrics). *Circulation,* 2009; 119:1541-1551.

Cooper RJ, Hoffman JR, Bartlett JG, Besser RE, Gonzales R, Hickner JM, Sande MA. Principles of Appropriate Antibiotic Use for Acute Pharyngitis in Adults: Background. *Annals of Internal Medicine.* March 20, 2001;134:509-517.

The preceding references address recommendations from the American Academy of Pediatrics (AAP), the American Heart Association, the Infectious Diseases Society of America, the CDC collaborating with members of the American College of Physicians-American Society of Internal Medicine and endorsed by the American Academy of Family Physicians (AAFP), regarding prescribing antibiotics for adults and for children. The Cooper article includes selective empirical treatment as an option. The Red Book, Baltimore, Bisno and Gerber articles do not include selective empirical treatment as an option.

Centor RM, Witherspoon JM, Dalton HP, Brody CE, Link KL. The diagnosis of strep throat in adults in the emergency room. *Med Decision Making*. 1981;1:239-245

McIsaac WJ, White D, Tannenbaum D, Low DE. A Clinical Score to Reduce Unnecessary Antibiotic Use in Patients with Sore Throat. *Canadian Medical Association Journal*. January 13, 1998;158(1).

Here are 2 landmark studies that generated the symptom score for pharyngitis. They demonstrate a correlation between symptom score and probability of presence of GAS.

Linder JA, Bates DW, Lee GM, Finkelstein JA. Antibiotic treatment of children with sore throat. *JAMA*, 2005 Nov 9; 294(18):2315-22.

Park SY, Gerber MA, Tanz RR, Hickner JM, Galliher JM, Chuang I, Vesser RE. Clinicians' management of children and adolescents with acute pharyngitis. *Pediatrics*, 2006; 117(6):1871-78.

These two articles document the continued overuse of antibiotic treatment.

Edmonson MB, Farwell Kr. Relationship between the clinical likelihood of group A streptococcal pharyngitis and the sensitivity of a rapid antigen detection test in a pediatric practice. *Pediatrics*, 2005; 115(2): 280-285.

This article addresses the cost-effectiveness of rapid antigen detection screening in a University operated pediatric outpatient clinic.