



**Pharyngitis Guideline
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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.

Pharyngitis

Patient population. Patients 3 years old through adulthood.

Objectives.

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

Key points

General principles.

- 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 [IB]. The endemic incidence of acute rheumatic fever is around 0.23-1.88/100,000 children of school age.
- Early treatment of GAS pharyngitis can decrease the time a patient is symptomatic by 1-2 days from the typical 3-7 days [IB] and can decrease the period of contagiousness [IB].

Diagnosis.

- Signs and symptoms of severe sore throat, fever, tender anterior cervical lymphadenopathy, red pharynx with tonsillar swelling with or without exudate, and no cough indicate a higher probability of GAS pharyngitis for both adults and children. Algorithms using epidemiologic and clinical factors can help identify patients with a low risk of GAS infection [C].
- Laboratory confirmation:
 - Neither on-site rapid antigen testing nor tests in the laboratory (PCR or culture) can 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 nasal congestion, 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].
- Rapid streptococcal antigen tests identify GAS quickly, but have variable sensitivity. Tests in the laboratory (PCR or culture) are considered the “gold standard” for diagnosis. [B].
 - Reserve rapid antigen tests for patients with a reasonable probability of having GAS.
 - Confirm negative GAS rapid antigen results in patients < 16 years old using PCR, due to their higher risk of acute rheumatic fever [IIC].
 - Consider testing the parents and siblings of affected school-age children.

Treatment.

- Penicillin V is the drug of choice in patients who can swallow pills.
- If using suspension, amoxicillin is better tolerated (tastes better) than penicillin V.
- 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 improves adherence but is painful.
- If the patient is allergic to penicillin (but has no history of type I hypersensitivity to penicillin), a 10-day course of a first-generation cephalosporin is indicated. 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 treated again 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 (or 5 days for azithromycin) to eradicate GAS from the upper respiratory tract and prevent acute rheumatic fever [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 testing 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 testing [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 lymph 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 nasal congestion
- Conjunctival inflammation ("pink eye")
- Hoarseness
- Pharyngeal ulcerations
- Diarrhea
- Characteristic viral rash

Table 3. Advantages and Disadvantages of GAS Rapid Antigen Test and Laboratory Tests

Rapid Antigen Test

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, and may shorten clinical symptoms

Disadvantage

- Less sensitive

Laboratory Test – PCR (or culture)

Advantage

- High sensitivity and specificity
- Result within 24 hours

Disadvantage

- Higher average total lab charges

Figure 1. An Approach to the Patient with Pharyngitis

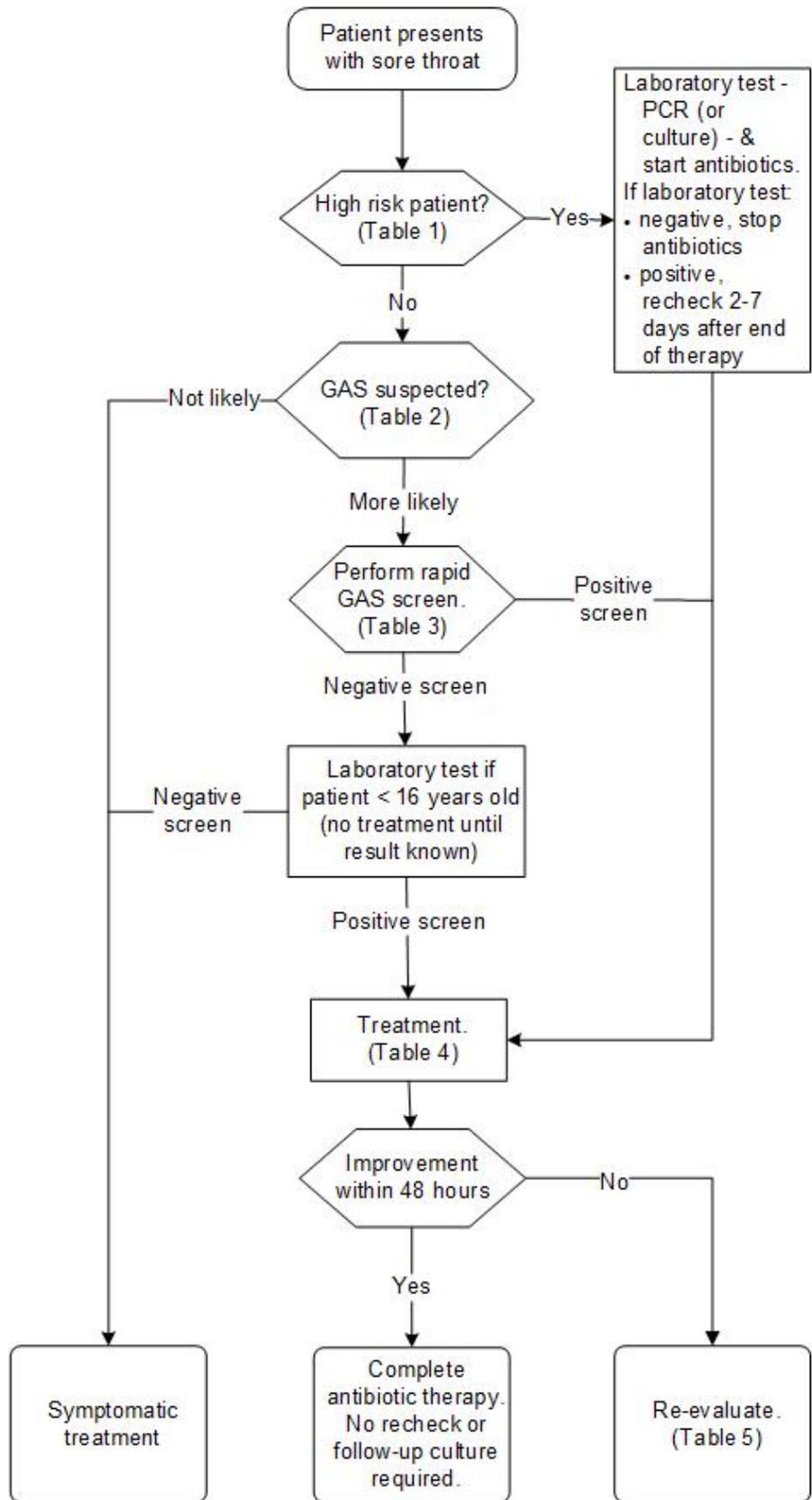


Table 4. Examples of Antibiotic Treatment for Group A Streptococcal Pharyngitis

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. 1 g/d)	\$10	\$10
Penicillin V	250 mg 2-3 times day	\$8	\$32
Penicillin G benzathine ^c	600,000 units IM one dose	NA	\$107
In penicillin-allergic			
Cephalexin ^{d, e}	25–50 mg/kg/d divided 2 times daily	\$16	\$141
Clindamycin ^f	20 mg/kg/d divided three times daily (max 1.8 g/day)	\$65	\$65
Azithromycin ^{d, g, h}	12 mg/kg/d once daily x 5 days (max 500 mg)	\$33	\$70
Adolescents and Adults (> 60 lbs/ 27 kg)			
Penicillin V	500 mg 2-3 times daily	\$10	\$55
Amoxicillin	1 g daily x 10 days (max. 1g/d)	\$5	\$10
Penicillin G benzathine ^c	1.2 million units IM one dose	NA	\$85
In penicillin-allergic			
Cephalexin ^{d, e}	500 mg twice daily	\$6	\$35
Clindamycin	300 mg three times daily for most adults, or 20 mg/kg/d divided 3 times daily (max 1.8 g/day)	\$13	\$101
Azithromycin ^{d, g, h}	12 mg/kg/d once daily x 5 days (max 500 mg/d)	\$11	\$70

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

^a Cost = Average Wholesale Price minus 10%. AWP from Lexicomp Online 01/2020. For generic drugs, Maximum Allowable Cost plus \$3 from BCBS of Michigan MAC List, 01/2020.

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

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

^d Cephalexin and azithromycin have better compliance than erythromycin due to high incidence of GI side effects from erythromycin.

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

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

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

^h Macrolide usage has been associated with prolonged QT effect. 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

Peritonsillar or retropharyngeal abscess (REQUIRES a prompt otolaryngology consultation)
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 2 times daily	\$12	\$44
Clindamycin	20 mg/kg/d divided three times daily (max 1.8 g/day)	\$23	\$20
Penicillin V plus rifampin ^c	Penicillin V: 250 mg 2-3 times daily + rifampin 20 mg/kg/d divided 2 times daily, max 600 mg/day during last 4 days of therapy	\$5	\$32
Penicillin G benzathine plus rifampin ^c	Penicillin G benzathine: 600,000 units IM one dose; rifampin 20 mg/kg/d divided 2 times daily, max 600 mg/day during last 4 days of therapy	NA	\$107
Adolescents and Adults			
Amoxicillin–clavulanic acid ^b	500 mg amoxicillin with 125 mg clavulanate twice daily or 875 mg amoxicillin with 125 mg clavulanate twice daily	\$14	\$68
Clindamycin	300 mg three times daily for most adults, or 20 mg/kg/d divided 3 times/day (max 1.8 g/day)	\$13	\$100
Penicillin V plus rifampin ^c	Penicillin V: 500 mg 2-3 times daily; rifampin: 300 mg/dose 2 times daily during last 4 days of therapy	\$12	\$42
Penicillin G benzathine plus rifampin ^c	Penicillin G benzathine: 1.2 million units IM one dose; rifampin: 300 mg/dose 2 times daily during last 4 days of therapy	NA	\$93

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 minus 10%. AWP from Lexicomp Online 01/2020. For generic drugs, Maximum Allowable Cost plus \$3 from BCBS of Michigan MAC List, 01/2020.

^b Other proportions of amoxicillin/clavulanate exist that do not provide the clavulanate dose recommended for this purpose (eg, 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 rapid antigen testing vs. laboratory testing. No clear strategy has been proposed for the cost-effective use of antigen testing and laboratory testing (polymerase chain reaction [PCR] testing, if PCR not available, then culture). For many years, culture for GAS had been the gold standard test, but it introduced a delay of 24 to 72 hours in reporting a diagnosis. As of 2019, PCR testing for GAS DNA has replaced culture for throat samples. PCR testing is faster but more expensive than culture.

The current GAS antigen detection tests (often called a “rapid strep test”) 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 increased laboratory costs for the majority of patients whose rapid GAS tests are negative and require a follow-up laboratory (PCR/culture) test. The benefit of follow-up laboratory testing 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 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, which is an autoimmune disease that can affect the heart and other organs. The endemic incidence of acute rheumatic fever is around 0.23-1.88/100,000 people (1980's data). In epidemics due to rheumatologic strains of GAS, acute rheumatic fever has occurred in up to 3% of patients with untreated GAS pharyngitis. It generally develops 10–14 days after onset of acute pharyngitis. Early treatment of GAS also shortens the clinical course of the pharyngitis, can reduce the risk of transmission, and may decrease the risk of other suppurative sequelae (including otitis media, sinusitis, peritonsillar or retropharyngeal abscesses, and mastoiditis). Post-streptococcal glomerulonephritis is another sequela of GAS infection, but it usually occurs after a streptococcal skin infection. Treating GAS pharyngitis does not appear to diminish the risk of post-streptococcal glomerulonephritis.

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. Acute rheumatic fever can occur more rapidly in someone who has had a previous episode of acute rheumatic fever, especially if there was prior valvular involvement. A high-risk patient presenting with a sore throat should be prescribed immediate

antibiotic treatment while awaiting PCR or culture test results. Discontinuation of antibiotics is appropriate if the PCR test or culture is negative for GAS.

Diagnosis

Symptoms. The diagnosis of GAS pharyngitis should be suspected based 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 testing to establish the diagnosis of GAS pharyngitis.

The constellation of sudden severe sore throat (especially with pain upon swallowing), fever, tender anterior cervical lymphadenopathy, red pharynx with tonsillar swelling +/- exudate, and no cough indicates 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, palatal 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, nasal congestion, conjunctival inflammation (“pink eye”), hoarseness, pharyngeal ulcerations, diarrhea, and/or a classic viral exanthem (such as vesicles or maculopapular rashes).

Diagnosis by testing on-site and in the laboratory. Testing to diagnose GAS pharyngitis is important because of lower sensitivity and specificity of clinical impressions. When the diagnosis of GAS pharyngitis is not ruled out by a viral clinical presentation, decisions regarding testing for GAS must consider the added value of the information given the prior probability that GAS is present.

For all testing, correct swabbing of the oropharynx is of paramount importance. Both tonsillar fauces and the posterior oropharynx must be vigorously swabbed. False negative rapid antigen and false negative PCR test / culture results may occur due to inadequate specimen collection.

The initial test is typically a rapid GAS antigen test performed on-site during the visit. For patients less than 16 years old, negative results are confirmed in the laboratory using a PCR or culture test for GAS DNA. The PCR test / culture may be used without a rapid antigen test, but a practical limitation is that PCR/culture results are typically not available until at least a day later. Explained below are the properties of these tests, their costs, and strategy in selecting them.

GAS rapid antigen test on-site. Most GAS antigen tests 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%. Because of this very high specificity, a positive test does not require PCR/ throat culture confirmation.

Sensitivity of the GAS antigen test ranges from 67% to 84%, when compared to blood agar plate culture. The lower sensitivity support the recommendation that in patients less than 16 years old, a negative antigen test should be confirmed with a laboratory PCR test. In adults the incidence of GAS infection is low and the risk of developing acute rheumatic fever is extremely low. Therefore, in adults making a diagnosis of GAS pharyngitis on the basis of a GAS antigen test alone, without confirmation by laboratory testing, is reasonable.

Testing in the laboratory: PCR test or culture. Historically, the gold standard for diagnosis of GAS pharyngitis was a throat culture (~95% sensitivity). Results were available in 1-3 days. However, PCR testing for GAS DNA is now widely available. Its specificity is 95% and sensitivity is 97%. The sensitivity is slightly higher than culture, and results are usually available in one day, compared to two days for culture.

The advantages of PCR testing over culture have resulted in some laboratories providing only PCR testing. Depending on the testing available locally and their costs, either may be used.

A positive PCR test (or culture) may reflect chronic colonization by GAS, and 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.

Laboratory charges. Laboratory charges can contribute significantly to the total cost of treatment for a patient with pharyngitis. For example, at the University of Michigan Health System as of 1/2020, the laboratory charge for a GAS antigen test is \$76 and the charge for a GAS PCR test alone is \$197. (Throat cultures are no longer performed.) If the antigen test is negative and a follow-up PCR test is performed, the total charge would be \$273 for both. (Other laboratories may structure charges for GAS antigen tests and cultures in other ways.)

Choosing between antigen test or laboratory test. When a clinician has decided to test for GAS pharyngitis, the choice between starting with an antigen test on site or simply ordering a laboratory test (PCR, if PCR or, if not available, 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 test can reduce the period of infectivity and morbidity and may allow the patient to return to normal activity sooner. Patients are

considered no longer infectious to others after receiving appropriate antibiotic therapy for at least 24 hours. However, for patients less than 16 years old, 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 non-GAS pharyngitis cases that require a confirmatory testing in the laboratory.

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 a rapid antigen diagnostic test PCR or throat culture. In patients with a 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 acute rheumatic fever, antibiotics may be initiated within 9 days of onset of symptoms and still be effective at preventing acute rheumatic fever.

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 recommended 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 [IB].

First-generation cephalosporins (such as cephalexin) are now recommended for those who cannot be safely prescribed a penicillin [IB]. (However, the cephalosporins should not be used for those who 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 [IB]. The extremely bitter taste of clindamycin solution may lead to nonadherence to the prescribed course.

Azithromycin may be used for penicillin-allergic patients [IB]. 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. Azithromycin 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 penicillin G benzathine has been shown to be slightly more efficacious than oral penicillin V and ensures adherence [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 for 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.

Treatments not recommended. Sulfonamides, fluoroquinolones (eg, 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 or retropharyngeal abscess. These complications require immediate consultation with otolaryngology as they may need surgical drainage and can pose a serious threat to the patient’s airway.

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

- GAS is present as a colonizer and does not pose a threat to cause acute rheumatic fever (ie, a coexisting viral infection is the cause of the acute symptoms). These GAS carriers are defined as individuals with positive tests of the throat 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 treated.
- Patient nonadherent with antibiotic course. The decision may be made to opt for intramuscular penicillin G benzathine in order to ensure adequate treatment. Also, the use of a better tolerated oral antibiotic, the use of a once

daily 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 [IIID].

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 penicillin G benzathine [IIC].

For frequent recurrences, expert opinions differ about the most appropriate course of action. One may consider using a non-beta-lactam (such as clindamycin) or a beta-lactam combined with a beta-lactamase inhibitor (amoxicillin-clavulanic acid) or adding rifampin to injectable penicillin G benzathine. 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 [IIC]. 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 testing. The majority of patients with GAS pharyngitis respond clinically to antibiotics, with GAS eradication from the pharynx. Repeat testing (with PCR or throat culture) after completion of therapy is 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 tests 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 a patient who has acute pharyngitis and any evidence of GAS (by rapid antigen test, PCR or throat culture) [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 beta-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. Clinicians need to be aware that PCR testing is specific for GAS and will not detect group C or group G strep infections. Unless specified by the ordering physician, most labs will not identify or report out these organisms on “routine” throat cultures.

Controversial Areas

Treatment over the phone based on symptoms. This approach is problematic because most cases of sore throat are due to 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 influenza season. An option may be to have a trained staff member triage symptoms over the phone. If the patient has symptoms consistent with GAS pharyngitis, consider bringing the patient into the office for a nurse visit and rapid GAS antigen test. If the rapid 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 PCR test or 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-test 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 test when empiric treatment may not be easily administered (eg, 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. 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, salt water gargles, and lozenges may be helpful. Also, avoid acidic drinks or spicy food. Non-steroidal anti-inflammatory drugs (NSAIDs) may also be helpful, but avoid use in patients with heart disease or its risk factors as NSAID use increases overall risk of heart attack or stroke.

PCR / throat culture testing for group A strep. Most results are available 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 can 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 the 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 (eg, 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 randomized controlled trials 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 UMHHC 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:

- Merit-Based Incentive Payment System (MIPS) Program
- Marketplace Quality Rating System (QRS)

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

Blue Cross Blue Shield of Michigan (BCBSM) and 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 (eg, method of data collection, population inclusions and exclusions), the general measures are summarized below.

Testing for children with pharyngitis. The percentage of children 3–18 years of age who were diagnosed with

pharyngitis, dispensed an antibiotic and received a group A streptococcus strep test for the episode. (MIPS, QRS, BCN, BCBSM)

Avoidance of antibiotic treatment for acute bronchitis/bronchiolitis. The percentage of episodes for members ages 3 months and older with a diagnosis of acute bronchitis/ bronchiolitis that did not result in an antibiotic dispensing event. (MIPS, QRS, BCN, BCBSM)

More general measures of clinical performance (eg, 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; R. Van Harrison, PhD; Michele Rea, RN; Barbara Reed, MD; Thomas Shope, MD; Connie Standiford, MD.

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

2006: Terrance P. Murphy, MD; Annissa J. Hammoud, 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).

These 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 testing in a university operated pediatric outpatient clinic.