



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.

1. Utilize signs and symptoms to determine pretest probability of Group A beta hemolytic streptococcal (GABHS) pharyngitis.
2. In patients where GABHS pharyngitis is suspected and a rapid strep screen is performed, confirm all negative results with culture in patients <16 years old.
3. Reduce indiscriminate use of antibiotics to minimize potential adverse effects.
4. Assure appropriate course of antibiotic treatment to prevent rheumatic fever and suppurative complications (e.g., otitis media, sinusitis, peritonsillar/ retropharyngeal abscesses or mastoiditis).
5. Hastening illness resolution and reduction in transmission of GABHS pharyngitis to others.

Key points

General principals.

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

Diagnosis.

- Signs/symptoms of recent fever, tender anterior cervical lymphadenopathy, red pharynx +/- tonsillar swelling or exudate, and no cough indicate a higher probability of GABHS for both adults and children. Algorithms incorporating epidemiologic and clinical factors improve diagnostic accuracy primarily by identifying patients with an exceedingly low risk of streptococcal infection [C*].
- Laboratory confirmation: Test when diagnosis is not ruled out by viral symptoms (Tables 2 & 7).
 - For adults: confirmation is most useful when GABHS is suspected; however, only test those with at least 2 or more signs/ symptoms mentioned above. [C*].
 - For patients between 3-15 years of age: confirmation is most useful when GABHS cannot be excluded. Nevertheless, only test those with at least 1 or more signs/ symptoms mentioned above [C*]. The threshold for testing is lower for children because their risk of developing acute rheumatic fever is higher.
- Throat culture is the presumed “gold standard” for diagnosis [C*]. Rapid streptococcal antigen tests identify GABHS more rapidly, but have variable sensitivity [C*].
 - Reserve rapid strep tests for patients with a reasonable probability of having GABHS. In patients screened with a rapid strep test, a negative result should be confirmed by culture in patients < 16 years old (and considered in parents or siblings of school age children) due to their higher incidence of developing acute rheumatic fever [C*].
 - If screening for GABHS in very low risk patients is desired, culture alone is cost effective.

Treatment.

- Penicillin is the treatment of choice for secondary prophylaxis in patients who've had rheumatic fever. Penicillin is the drug of choice in patients who can swallow pills. If suspension must be prescribed, amoxicillin is better tolerated due to the extremely bitter taste of penicillin.
 - Erythromycin is preferred for patients allergic to penicillin.
 - For patients expected to be intolerant or non-compliant with an erythromycin product (e.g., younger patients), consider azithromycin or a narrow spectrum oral cephalosporin like cephalexin.
- Antibiotic treatment must be started within 9 days after onset of the acute illness and continued for 10 days (or 5 days for azithromycin) to eradicate GABHS from the upper respiratory tract and prevent acute rheumatic fever [D*].

Controversial areas:

- Based on a description over the phone, a clinician may decide to screen or treat for GABHS [D*]:
- When clinic access is a problem (e.g., during flu season), one may elect to have a staff member triage symptoms for GABHS screening.
 - When a symptomatic patient is ≥ 3 years old and has a family member recently documented by lab testing to have GABHS pharyngitis, one may elect to treat without screening.

* Levels of evidence for the most significant recommendations:

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

Table 1. High Risk Patients

- Past history of rheumatic fever, especially carditis/valvular disease
- Household contact with someone having a history of rheumatic fever

Table 2. Signs and Symptoms

Suggestive for GABHS (need 2 or more)

- Fever > 38° C (100.4° F) in past 24 hours
- Tender anterior cervical nodes
- Enlarged, red tonsils or purulent exudate or red pharynx
- No cough

Suggestive for viral etiology

- Cough and coryza
- Scleral conjunctival inflammation
- Hoarseness
- Pharyngeal ulcerations
- Diarrhea

Table 3. Advantages / Disadvantages of Strep Screens and Cultures

Screen

Advantage

- Rapid positive result
- High specificity
- On site diagnosis may aid in arranging day care, school, or work absence
- Prompt treatment may lower risk of spread to others & may shorten clinical symptoms by 1-2 days

Disadvantage

- Less sensitive
- Higher average lab cost – screen is \$51
- Majority are neg., requiring \$41 backup culture

Culture

Advantage

- High sensitivity & specificity.
- Lower average lab cost, \$41 for culture alone

Disadvantage

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

Table 4. Preferred Treatment Regimens

Adolescents and adults: Penicillin VK 500 mg bid-tid for 10 days

Amoxicillin 750 mg (250 mg 3 tabs) as a single daily dose for 10 days is adequate if compliance is a concern

See Table 11 for alternatives & costs

Figure 1. Adult Pharyngitis (Patients ≥ 16 years old)

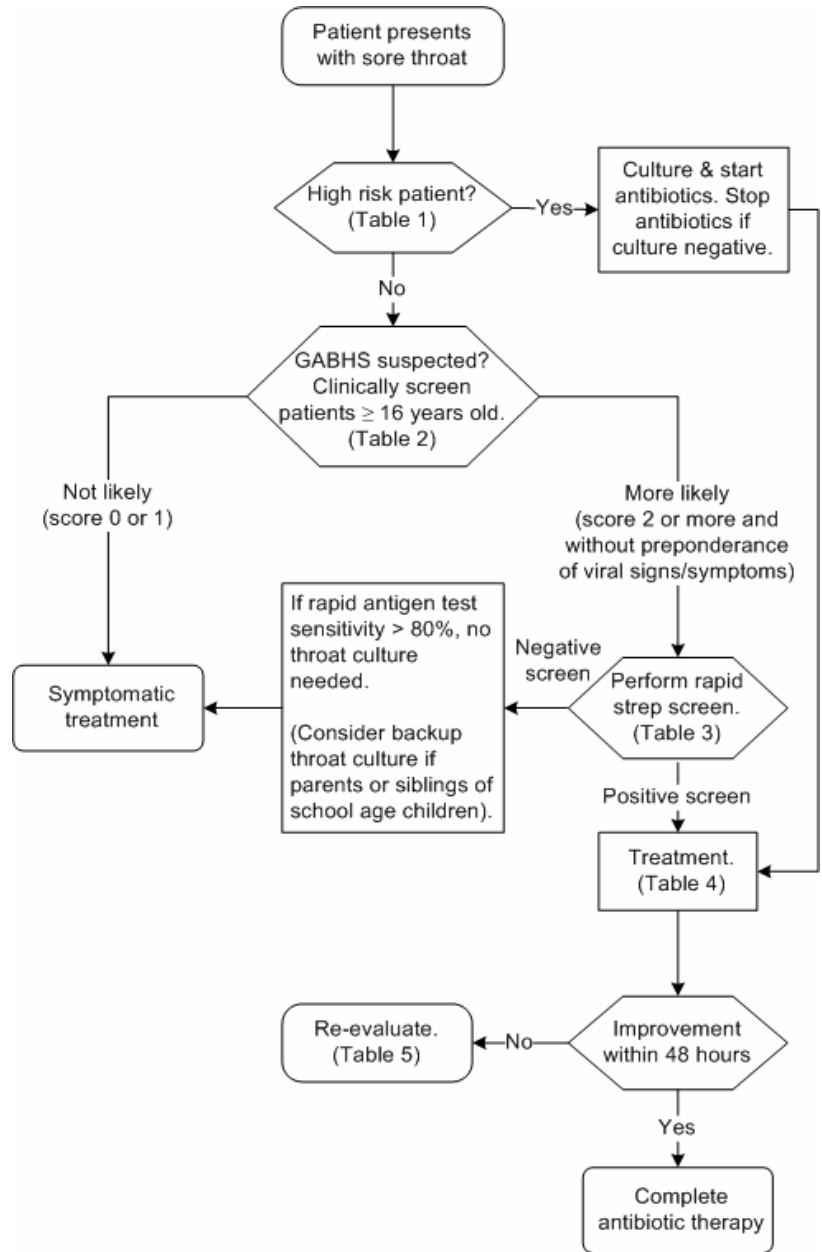


Table 5. Reasons for Failure of Response

- Peritonsillar or retropharyngeal abscess REQUIRES a prompt ENT evaluation
- Strep carrier with acute pharyngitis actually due to a virus or other bacteria
- Compliance problem with medication
- Failure of antibiotic to eradicate Strep (such as macrolide resistance, theories of co-habitation with Staph, etc.)

Table 6. High Risk Patients

- Past history of rheumatic fever, especially carditis/valvular disease
- Household contact with someone having a history of rheumatic fever

Table 7. Signs and Symptoms

Suggestive for GABHS (need 1 or more)

- Fever > 38° C (100.4° F) in past 24 hours
- Tender anterior cervical nodes
- Enlarged, red tonsils or purulent exudate or red pharynx
- No cough

Suggestive for viral etiology

- Cough and coryza
- Scleral conjunctival inflammation
- Hoarseness
- Pharyngeal ulcerations
- Diarrhea

Table 8. Advantages / Disadvantages of Strep Screens and Cultures

Screen

Advantage

- Rapid positive result
- High specificity
- On site diagnosis may aid in arranging day care, school, or work absence
- Prompt treatment may lower risk of spread to others & may shorten clinical symptoms by 1-2 days

Disadvantage

- Less sensitive
- Higher average lab cost – screen is \$51
- Majority are neg., requiring \$41 backup culture

Culture

Advantage

- High sensitivity & specificity
- Lower average lab cost, \$41 for culture alone

Disadvantage

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

Table 9. Preferred Treatment Regimens

Pen VK 250 mg bid-tid (for < 60 lbs or 27 kg) and 500 mg bid-tid (for heavier kids & adolescents) for 10 days

Amoxicillin 40 mg/kg/24 hr bid-tid or 750 mg (250 mg 3 tabs) as a single daily dose for 10 days is adequate if compliance is a concern

See Table 11 for alternatives and costs

Figure 2. Pediatric Pharyngitis (Patients 3-15 years old)

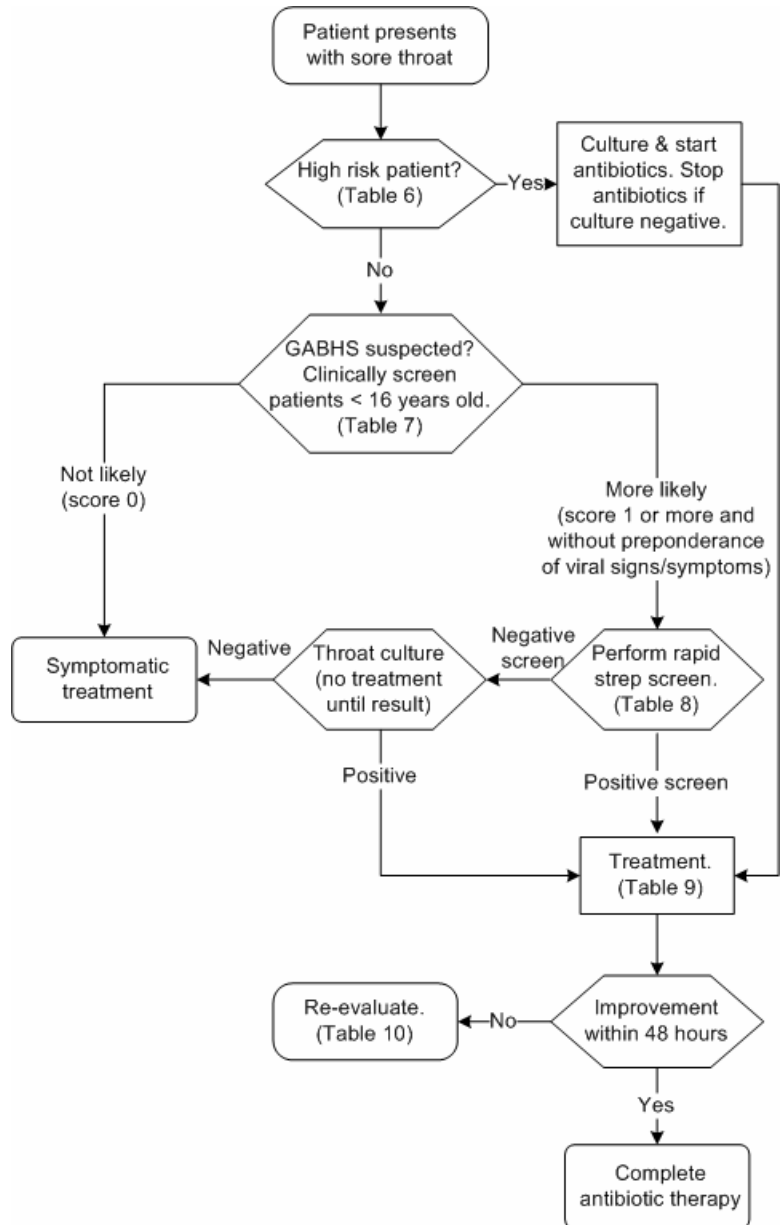


Table 10. Reasons for Failure of Response

- Peritonsillar or retropharyngeal abscess: REQUIRES a prompt ENT evaluation.
- Strep carrier with acute pharyngitis actually due to virus or other bacteria
- Compliance problem with medication
- Failure of antibiotic to eradicate Strep (such as macrolide resistance, theories of co-habitation with Staph, etc.).

Table 11. Examples of Antibiotic Treatment for Group A Streptococcal Pharyngitis

DRUG	DOSE	COST ^a	
		Generic	Brand
Preferred Treatment			
Pediatrics (child < 60 lbs/ 27 kg)			
<u>Amoxicillin suspension or chewable</u> ^b	40 mg/kg/d divided BID–TID	\$5	\$5
	750 mg (250 mg 3 tabs) daily	\$5	\$5
Penicillin VK	250 mg/dose BID–TID	\$9	\$9
Benzathine penicillin G ^c	600,000 U IM one dose	NA	\$19
In penicillin-allergic			
<u>Erythromycin</u>			
Ethyl succinate (EES)	40 mg/kg/d divided TID–QID (max 1 g/d)	\$6	\$15
Estolate (tastes better than EES)	20-30 mg/kg/d divided BID–TID (max 1 g/d)	NA	\$9
Azithromycin ^{d,e}	12 mg/kg/d once daily x 5 days (max 500 mg) ^f	NA	\$23
Cephalexin ^{d,f}	25–50 mg/kg/d divided BID–QID	\$13	NA
Adolescents and Adults (> 60 lbs/ 27 kg)			
<u>Penicillin VK</u>	500 mg/ dose BID–TID	\$9-11	NA
Amoxicillin	750 mg (250 mg 3 tabs) daily	\$5	\$5
Benzathine penicillin G ^c	1.2 million IM one dose	NA	\$33
In penicillin-allergic			
<u>Erythromycin</u>			
Erythromycin base			
• Ery-tab (enteric-coated)	250 mg QID; 333 mg TID; 500 mg BID	\$6; NA; \$7	\$10; \$11; \$8
• E-Mycin (enteric-coated)	250 mg QID; 333 mg TID	\$6; NA	NA
• PCE Dispartab (polymer-coated tabs)	333 mg TID	NA	\$58
• Eryc (delayed release caps with enteric-coated pellets)	250 mg QID	\$10	\$25
Ethyl succinate (EES)	400 mg/dose QID	NA	\$9
Azithromycin ^{d,e}	500 mg/day 1, then 250 mg daily x 4 days	\$16	\$52
Cephalexin ^{d,f}	250–500 mg/dose QID	\$9	\$72-162
Alternative for Initial Therapy or for Treatment Failure^c			
Pediatrics (40 kg child)			
Amoxicillin–clavulanic acid ^g	250 mg amoxicillin with 62.5 mg clavulanate at 40 mg/kg/d divided BID, max 500 mg/day of amoxicillin	\$33	\$88
Cefuroxime axetil	20 mg/kg/d divided BID	NA	\$63
Cephalexin	25–50 mg/kg/d divided BID–TID	\$11	NA
Clindamycin	20 mg/kg/day divided TID; max dose: 1.8 g/day	\$75	\$1475
Cefadroxil	30 mg/kg/d divided BID–QD	NA	\$26
Adolescents and Adults			
Amoxicillin–clavulanic acid ^g	500 mg amoxicillin with 125 mg clavulanate BID	\$46	\$97
Cefuroxime	250 mg/dose BID	\$41	\$142
Cephalexin	250–500 mg/dose QID	\$9	\$72-162
Clindamycin	20 mg/kg/day divided TID; max dose: 1.8 g/day	\$75	\$1475

Note: **Antibiotics not effective against GABHS:** tetracyclines, trimethoprim, sulfonamides, chloramphenicol & fluoroquinolones.

^a Cost = Average wholesale price based -10% for brand products and Maximum Allowable Cost (MAC) + \$3 for generics on 30-day supply, *Amerisource Bergen item Catalog 6/06 & Blue Cross Blue Shield of Michigan Mac List, 3/31/06.*

^b Amoxicillin suspension is generally preferred due to significantly higher compliance since penicillin suspension tastes extremely bitter. The potential for leading to broader resistance remains a concern, since amoxicillin has a somewhat broader coverage than penicillin, but not as broad as the alternative drug choices listed.

^c Benzathine penicillin G injection has somewhat better efficacy than orally. Ideal if compliance doubtful or if treatment failure is likely due to non-compliance in taking pills. Painful for 2–3 days at site of injection. Increased risk of anaphylaxis.

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

^e 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).

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

^g 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).

Table 12. Examples of Antibiotic Treatment for Recurrent Group A Streptococcal Pharyngitis

DRUG	DOSE	COST ^a	
		Generic	Brand
Pediatrics (40 kg child)			
Amoxicillin–clavulanic acid ^b	Use 250 mg amoxicillin with 62.5 mg clavulanate at 40 mg/kg/d divided BID, max 500 mg/day of amoxicillin	\$33	\$88
Clindamycin	20–30 mg/kg/d divided TID-QID	NA	\$55
Penicillin VK with rifampin ^c	Pen VK: 250 mg BID–TID; rifampin: last 4 days	\$10	\$24
Benzathine penicillin G with rifampin ^c	20 mg/kg/d divided BID, max 600 mg/day Benzathine penicillin G: 600,000 U IM one dose; rifampin: 4 days 20 mg/kg/d divided BID, max 600 mg/day	NA	\$31
Adolescents and Adults			
Amoxicillin–clavulanic acid ^b	Use 500 mg amoxicillin with 125 mg clavulanate BID	\$46	\$97
Clindamycin	600 mg/d divided BID-QID	\$38-73	\$116
Penicillin VK with rifampin ^c	Pen VK: 500 mg/ dose BID–TID; rifampin: last 4 days 300 mg/dose BID	\$11	NA
Benzathine penicillin G with rifampin ^c	Benzathine penicillin G: 1.2 million U IM one dose; rifampin: 4 days 300 mg/dose BID	NA	\$45

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 30-day supply, *Amerisource Bergen item Catalog 6/06 & Blue Cross Blue Shield of Michigan Mac List, 3/31/06*.

^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 *Streptococcus* infection (GABHS), is one of the most common presenting complaints for which patients present to primary care offices.

GABHS 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 GABHS and non-GABHS pharyngitis overlap quite a bit. The usefulness of laboratory tests for GABHS depends on the prior 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 screens vs. culture. No clear strategy has been proposed for the cost effective use of

antigen screens and cultures. Culture is the presumed "gold standard" but involves a delay of 24 to 72 hours in reporting a diagnosis. The current GABHS 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 strep screens are negative and require a follow-up culture.

Overuse of antibiotics. Despite the low incidence of GABHS pharyngitis, numerous studies reveal that approximately 75% of adult patients with acute pharyngitis are prescribed antibiotics. Also worrisome, a recent study revealed that a strep 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 since the development of a rash was due to a viral exanthum (not the antibiotic) and increase the emergence of resistant strains of GABHS or other pathogenic bacteria.

Rationale for Recommendations

Treatment Goal

The most important goal in treating GABHS infection is to decrease the occurrence of acute rheumatic fever (ARF). The endemic incidence is somewhere around 0.23-1.88/100,000 (1980's data). In epidemics with rheumatologic strains of strep, ARF has occurred in up to 1%-3% of patients with untreated GABHS pharyngitis. It generally occurs 10–14 days post acute pharyngitis onset. Early treatment of GABHS shortens the clinical course, may reduce the risk of transmission, and may decrease the risk of other suppurative sequela (e.g., otitis media, sinusitis, peritonsillar/retropharyngeal abscesses or mastoiditis). Post-streptococcal glomerulonephritis (PSGN) is another sequela of GABHS infection, but usually occurs after a streptococcal skin infection. Treating GABHS 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 (ARF); specifically, those who have had rheumatic carditis or valvular disease. These patients are at high risk for complications of GABHS pharyngitis (see Table 1 or 6). 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. Discontinue antibiotics if the culture returns negative.

Diagnosis

Symptoms. The diagnosis of GABHS pharyngitis should be suspected on epidemiological and clinical factors and then supported by performance of a lab test. 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 streptococcal infection. With increasing national concern about overuse of antibiotics, symptoms can only provide reliable guidance on which patients to screen with a laboratory test to establish diagnosis of GABHS (see below). Using symptoms alone to initiate empirical treatment will result in appreciable unnecessary utilization of antibiotics.

In adults. In adults, the three findings of history of fever, tender anterior cervical nodes, and swollen exudative red tonsils have been demonstrated to have a positive correlation with GABHS. Cough lowers the pretest probability of GABHS pharyngitis.

Patients at least 16 years old with none or only 1 of the 4 criteria in Table 2 have a very low probability of GABHS (2.5%-4%). Patients at least 16 years old with 3-4 criteria from Table 2 comprise the highest probability group (28%-

56%). Empirically treating the higher probability group has been suggested by some, but it is problematic. Bisno, Peter and Kaplan (2002) note that in the Centor (1981) study only 10% of patients at least 16 years old with pharyngitis who presented to an urban emergency department manifested all 4 predictive factors. In this group, the probability that a patient would have a throat culture positive for GABHS was 56%, a finding almost similar to a subsequent study by McIsaac, et al (1998). In the 20% of subjects exhibiting 3 predictive factors, the probability of a positive throat culture result was only 30%-34%. Therefore, of the 30% of adults with 3 or 4 symptoms, approximately 60% would have negative lab tests (rapid screen +/- throat culture). If these “higher probability” patients were treated empirically, the majority would be prescribed antibiotics unnecessarily.

Initial assessment of the probability of GABHS based on symptoms can be modified by an adult's likelihood of environmental exposure. The probability of GABHS pharyngitis is apt to be higher for parents or siblings of school age children and for adults whose occupation brings them into close contact with children.

In children. In patients < 16 years old, a similar clinical evaluation is required before deciding whether the patient is at risk for GABHS. Findings that exclude GABHS from consideration include scleral conjunctival inflammation, hoarseness, pharyngeal ulcerations, or diarrhea. Findings more likely to indicate the presence of GABHS include the same 4 criteria used for adults which are no cough, presence of fever > 38 C in past 24 hours, tender anterior cervical nodes (lymphadenitis), and beefy red, enlarged tonsils or tonsillar exudate or red pharynx.

As for adults, symptoms are of limited predictive value in children. When all four of the symptoms suggestive for GABHS (see Table 7) are present, an experienced clinician will guess correctly between 40%-65% in a community with the usual levels of infection. Empirical treatment with antibiotics based on symptoms alone will result in substantial over treatment.

However, the incidence of acute rheumatic fever is higher in patients less than 16 years old. Therefore, the presence of one symptom in children suggestive for GABHS should be followed up with laboratory diagnosis when diagnosis is not ruled out by classic viral symptoms (see Table 7).

Laboratory diagnosis. Laboratory diagnosis of GABHS pharyngitis can be 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.

GABHS culture. The gold standard of diagnosis for GABHS 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.)

GABHS antigen screen. Most current GABHS antigen screens use a rapid immunoassay method (usually EIA technique) for determining the presence of GABHS in a throat swab. Results should be available within a few minutes in the office. The 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 screen should be confirmed by a culture in patients less than 16 years old.

A new 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 throat culture backup even in children.

Laboratory charges. The UMHS laboratory charge for a GABHS throat culture alone is \$41. The charge for a GABHS antigen screen is \$51. If a screen is negative and a follow-up culture is performed, the total cost is \$92 for both a screen and culture. (Other laboratories may structure charges for GABHS screens and cultures in other ways.)

Choosing between a screen or culture. When a clinician has decided to order a laboratory test to diagnose GABHS, 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 strep screen may reduce the period of infectivity and morbidity and may allow the patient to return to normal activity sooner. However, the value of early diagnosis in the minority of cases when strep is present and identified must be weighed against the higher total laboratory charges for the majority of cases screened. Most screens are negative and additional charges will be incurred for a subsequent culture.

When should strep testing be done? When diagnosis is not ruled out by viral symptoms, decisions regarding any testing for GABHS must consider the added value of the information given the prior probability that GABHS is present based on symptoms.

For adults. For adults, consideration of the prior probabilities provided by symptom scores and of the costs associated with laboratory tests suggests that diagnostic testing is generally not worthwhile for low probability groups, but is worthwhile for intermediate or high probability groups not ruled out by classic viral symptoms.

- Test all intermediate and high probability adults – i.e. adults with 2 or more symptoms (Table 2). The substantial minority with GABHS will then be appropriately treated and the majority will not be over treated with antibiotics. The results of a highly sensitive

rapid antigen screen with > 80% sensitivity, as we use in the UMHS, may be used as a basis for diagnosis without confirmatory culture results in patients at least 16 years old. This strategy considers the relatively low incidence of GABHS pharyngitis in adults, the extremely low risk of a first attack of acute rheumatic fever in adults in the U.S. at the present time, and the rarity of serious suppurative sequelae.

- If all low probability adults are not tested and not treated, about 1% of the population would have GABHS and would not be treated. However, expensive testing would be avoided in the 35% of the population with pharyngitis that falls into this low risk group.

For children. In patients 3-15 years of age, the higher risk of rheumatic fever associated with GABHS infection increases the need for laboratory testing to assure appropriate treatment. If no symptoms suggesting GABHS (Table 7) are present, laboratory testing is not likely worthwhile. If the symptoms are uncertain or suggest GABHS exists (i.e. 1 or more suggestive symptoms without classic viral symptoms), a laboratory test should be performed to assure that treatment is appropriate. If a rapid strep screen is chosen and is negative, the result should be confirmed by culture.

Laboratory confirmation may not be necessary for a patient with clinical findings indicative of scarlet fever or for a symptomatic household contact older than 3 years old of an index case with recently lab confirmed GABHS (remember the incubation period for GABHS pharyngitis is only 2-5 days).

Treatment of GABHS pharyngitis. Examples of preferred and alternative treatments are presented in Table 11. In a patient with no prior history of ARF, antibiotics may be given up to nine days after onset of symptoms and still be effective at preventing ARF.

Preferred treatment. Penicillin is the treatment of choice for secondary prophylaxis in patients who've had rheumatic fever. GABHS still demonstrates susceptibility to penicillin in North America, thus penicillin is the drug of choice in those not allergic to penicillin. If suspension is required, although Amoxicillin has broader spectrum of action, children tolerate the taste of Amoxicillin suspension better than penicillin suspension, increasing likelihood of compliance. At least a couple of well designed studies indicate that Amoxicillin 750 mg (250 mg 3 tabs) taken once daily for 10 days is as effective as penicillin TID for 10 days.

A single intramuscular injection of benzathine penicillin has been shown to be slightly more efficacious than oral penicillin VK and ensures compliance. Also, this route can be very useful in children who present with severe abdominal pain and vomiting along with their GABHS pharyngitis. It does, however, produce a significant amount of pain at the injection site that may last a number of days.

Treatment if penicillin allergic. Erythromycin has traditionally been the preferred drug for patients allergic to penicillin. However, if patient intolerance or non-compliance with an erythromycin product is a concern, consider azithromycin or a narrow spectrum (first generation) oral cephalosporin like cephalexin (if the patient does not exhibit immediate hypersensitivity to cephalosporins). Erythromycin or a narrow spectrum (first generation) oral cephalosporin needs to be taken for a full ten days in order to adequately treat GABHS and thus decrease the risk of ARF. If one chooses azithromycin, note that the dose is 12 mg/kg/day for 5 full days, which is a higher dose than that used to treat otitis media.

Alternative primary treatments. Other antibiotics can offer more convenient dosing schedules and sometimes better tolerability, which may increase compliance. However, these antibiotics are broader spectrum and may cause drug resistance to other organisms. Also, they are significantly more expensive than penicillin. Examples of effective alternative antibiotics are: amoxicillin-clavulanic acid, cephalexin, cefuroxime, cefprozil, and clindamycin. Sulfonamides, fluoroquinolones and tetracyclines are not acceptable for the treatment of GABHS pharyngitis.

Failure to improve with treatment. Any patient with documented GABHS infection 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 necessitate surgical drainage and pose a serious threat to the patient's well being.

No local complications. The persistence of GABHS despite adequate therapy suggests a number of 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). Colonization occurs often after a primary GABHS pharyngitis and it may persist for many months. Throat culture surveys of asymptomatic children during school outbreaks of pharyngitis have yielded GABHS prevalence rates as high as 15-50%. However, in an individual with symptoms compatible with acute GABHS, it is not easy to decide whether the GABHS isolated from the oropharynx is the cause of symptoms or from carriage. Thus GABHS persisting in a symptomatic individual should be retreated.
- Organism was not killed by the antibiotic treatment. This could be due to "co-pathogenicity" with oral bacteria (such as Staph) secreting beta-lactamases into the oropharyngeal environment, thus passively protecting GABHS from the actions of penicillin. In this case, reasonable treatment would be clindamycin or possibly a penicillinase-resistant antibiotic.

- Patient not compliant with antibiotic course. The decision may be made to opt for intramuscular benzathine penicillin in order to ensure adequate treatment, use of a better tolerated oral antibiotic, or one of the easier to use once-a-day or short-course antibiotics (azithromycin).

Treatments for recurrence. Patients who have recurrence of GABHS 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 IM dose of benzathine pen G. For frequent recurrences, a non-beta-lactam (Clindamycin) or beta-lactam combined with a beta-lactamase inhibitor (amoxicillin-clavulanic acid) or the addition of rifampin to benzathine penicillin G may be beneficial for eradication of streptococci 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. Table 12 presents examples of treatments for recurrent GABHS 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 GABHS. The presence of GABHS in a symptomatic, or an asymptomatic, high risk patient should be retreated.

Controversial Areas

Treatment over the phone based on symptoms. This approach is problematic due to symptoms alone without lab testing not providing a high probability for predicting the presence of GABHS.

However, interactions by phone may have value in initiating testing and subsequent care. For example, clinic access can be an issue during flu season. An option may be to have a staff member triage symptoms over the phone. If the patient has symptoms compatible with GABHS, consider bringing the patient into the office for a nurse visit and rapid strep test. If the rapid strep 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 test is positive, one may elect to work the patient into the physician schedule to confirm risk of true GABHS (vs. carriage) or one may elect to write a prescription without seeing the patient per nursing protocol. This would help with patient access, cost and patient satisfaction.

Family member with GABHS pharyngitis. A patient at least 3 years old with symptoms compatible with GABHS who has a family member with a recently lab confirmed GABHS 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 GABHS, it is preferable to perform a lab screen when empiric treatment may not be easily performed (e.g., patients with multiple antibiotic allergies or patients on anticoagulants).

Zinc to reduce viral upper respiratory infection symptoms. Evidence is mixed regarding benefits of zinc, and practical issues lower compliance. Two small, randomized, controlled trials showed a decrease in symptoms with the use of zinc. Patients who used zinc acetate lozenges every two to three hours, while awake, noted significant benefit in terms of a decrease in symptoms. Side effects, mainly bad taste, were common. Follow up studies have not consistently demonstrated a benefit.

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. Patient education information about sore throats is available to provide more detail and reinforce instruction.

Sore throats. The majority of sore throats are not caused by GABHS and do not require antibiotic therapy.

Symptomatic treatment. Use of acetaminophen, salt water gargles and lozenges are helpful. Avoid acidic drinks or food.

Throat cultures. They may take up to 2-3 days, but the majority are positive within 24 hours.

Full antibiotic treatment. Except for 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 sooner.

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

Contagious. The incubation period for strep throat is 2-5 days. Patients are considered noncontagious 24 hours after starting therapy.

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

Follow up. Symptoms which require early follow-up include: persistent fever or throat pain lasting greater than 48 hours, 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 2000 version of this guideline. A search for literature published since that time was performed. The search on Medline was conducted prospectively for literature published from 7/1/00 to 5/30/05 using the major keywords of: *GABHS pharyngitis (streptococcal infections, streptococcus pyogenes, pharyngitis, pharynx), strep throat; human; English; guidelines; controlled trials.* Searches were performed separately for *children*, for *adults*, and for *age not specified* for the following specific topics: *history, physical exam, signs, symptoms, throat culture (strep culture), rapid strep screen, observation, antibiotics, other treatment/ management, and other references.* Specific search terms and strategy are available upon request.

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 clinical 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.

Disclosures

None of the members of the Pharyngitis guideline team have a relationship with commercial companies whose products are discussed in this guideline. The team members are listed on the front page of this guideline.

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.

Annotated References

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

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

Bisno AL, Peter GS, Kaplan EL. Diagnosis of Strep Throat in Adults: Are Clinical Criteria Really Good Enough? *Clinical Infectious Diseases*. 2002;35:126-129.

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 four preceding references address recommendations from the American Academy of Pediatrics (AAP), 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 and Bisno articles do not include selective empirical treatment as an option. The Red Book, the first Bisno article, and the Cooper article review the bases for antibiotic choices.

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 GABHS.

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.