

Diagnosis and Management of Group A Streptococcal Pharyngitis: A Practice Guideline

Alan L. Bisno, Chairman, Michael A. Gerber,
Jack M. Gwaltney, Jr., Edward L. Kaplan,
and Richard H. Schwartz

From the Acute Pharyngitis Guideline Panel, Infectious Diseases Society of America, Alexandria, Virginia

This is the second in a series of practice guidelines commissioned by the Infectious Diseases Society of America through its Practice Guidelines Committee. The purpose of these guidelines is to provide assistance to clinicians when making decisions on treating the conditions specified in each guideline. The targeted providers are pediatricians, family practitioners, and internists. The targeted patients and setting for the acute pharyngitis guideline are pediatric, adolescent, and adult outpatients with a complaint of sore throat. Funding was provided by the IDSA. Panel members represented experts in adult and pediatric infectious diseases. The guidelines are evidence-based. A standard ranking system was used for the strength of the recommendations and the quality of the evidence cited in the literature reviewed. The document has been subjected to external review by peer reviewers as well as by the Practice Guidelines Committee and was approved by the IDSA Council. An executive summary, algorithms, and tables highlight the major recommendations. Indicators of quality will assist in guideline implementation. The guideline will be listed on the IDSA home page at <http://www.idsociety.org>.

—Peter A. Gross, MD, for the IDSA Practice Guidelines Committee

Executive Summary

The objective of this practice guideline is to provide recommendations for the accurate diagnosis and optimal treatment of group A streptococcal pharyngitis. The desired outcomes are: (1) prevention of acute rheumatic fever; (2) prevention of suppurative complications; (3) abatement of clinical symptoms and signs; (4) reduction in transmission of group A β -hemolytic streptococci to close contacts; and (5) minimization of potential adverse effects of inappropriate antimicrobial therapy.

Diagnosis

Acute pharyngitis is one of the most frequent illnesses for which pediatricians and other primary care physicians are consulted. Although the group A streptococcus is the most common bacterial cause of acute pharyngitis, only a minority of patients with pharyngitis are infected by group A streptococci. Moreover, group A streptococcal pharyngitis is the only commonly occurring form of acute pharyngitis for which antibiotic therapy is definitely indicated. Therefore, when a physician treats a patient with acute pharyngitis, the clinical decision that usually needs to be made is whether the pharyngitis is attributable to group A streptococci.

The signs and symptoms of group A streptococcal pharyngitis and nonstreptococcal pharyngitis (most frequently viral) overlap broadly. Thus, unless the physician is able to confidently exclude the diagnosis of streptococcal pharyngitis on epidemiological and clinical grounds, a laboratory test should be performed to determine whether group A streptococci are present in the pharynx. This test may be either a throat culture or a rapid antigen detection test (RADT). The latter test detects the presence of group A streptococcal carbohydrate on a throat swab. For a patient with signs and symptoms of acute pharyngitis, a positive throat culture or RADT is considered, for clinical purposes, to establish the diagnosis of "strep throat." However, because the RADT is less sensitive than are throat cultures, a negative RADT should be confirmed with the results of a throat culture.

Therapy

Patients with acute streptococcal pharyngitis should receive therapy with an antimicrobial agent in a dosage and for a duration that is likely to eradicate the infecting organism from the pharynx. A number of antibiotics have been shown to be effective in therapy for group A streptococcal pharyngitis. These agents include penicillin and its congeners (such as ampicillin, amoxicillin, and the semisynthetic penicillins) as well as numerous cephalosporins, macrolides, and clindamycin. However, penicillin remains the treatment of choice because of its proven efficacy, safety, narrow spectrum, and low cost. Intramuscular benzathine penicillin G is preferred for patients who are unlikely to complete a full 10-day course of oral therapy. Erythromycin is a suitable alternative for patients who are allergic to penicillin. First- or second-generation cephalosporins are also acceptable for treating patients who do not exhibit immediate hypersensitivity to β -lactam antibiotics.

This guideline is part of a series of updated and new guidelines from the IDSA that will appear in *CID*.

Reprints or correspondence: Dr. Alan L. Bisno, Medical Service (111), Miami Veterans Affairs Medical Center, 1201 N.W. 16th Street, Miami, Florida 33125.

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Most oral antibiotics must be administered in the conventional 10-day course to achieve maximal pharyngeal eradication of group A streptococci, but the use of certain newer agents has been reported to achieve comparable bacteriologic and clinical cure rates among patients with streptococcal pharyngitis when these agents are given for ≤ 5 days. However, definitive results from comprehensive studies are not available; thus, final evaluation of these proposed shorter courses of oral antibiotic therapy is not possible, and they cannot be recommended at this time. Moreover, these antibiotics have much broader spectrums than penicillin, and most, even when administered for short courses, are more expensive.

Except under special circumstances, neither repeated bacteriologic testing (culture or RADT) of patients who have successfully completed a course of antimicrobial therapy nor routine testing of asymptomatic household contacts of patients with group A streptococcal pharyngitis is recommended.

A small percentage of patients will have recurrences of acute pharyngitis that are associated with throat cultures (or RADTs) positive for group A streptococci within a short period following completion of a course of antimicrobial therapy. Such episodes may be treated with one of the antimicrobial agents appropriate for treatment of the initial illness. If these episodes were previously treated with oral agents and compliance is in question, retreatment with intramuscular benzathine penicillin G should be considered. When multiple episodes occur over the course of months or years, it may be difficult to differentiate viral infections in a streptococcal carrier from true group A streptococcal infections. Certain antimicrobial agents, such as clindamycin and amoxicillin/clavulanate, may be beneficial because they have been shown to yield high rates of pharyngeal eradication of streptococci under these particular circumstances.

Definition

Group A streptococcal pharyngitis (pharyngotonsillitis) is an acute infection of the oropharynx and/or nasopharynx with *Streptococcus pyogenes*.

Objective

The objective of this practice guideline is to provide recommendations for the accurate diagnosis and optimal treatment of group A streptococcal pharyngitis.

Options

Physicians caring for patients with acute pharyngitis must formulate differential diagnoses and determine which, if any, confirmatory tests should be performed. If clinical and laboratory evaluations result in a diagnosis of group A β -hemolytic streptococcal pharyngitis, one of several antimicrobial agents and treatment schedules may be selected.

Outcomes

The desired outcomes are: (1) prevention of acute rheumatic fever; (2) prevention of suppurative complications (e.g., peritonsillar abscess, cervical lymphadenitis, or mastoiditis); (3) abatement of clinical symptoms and signs; (4) a rapid decrease in infectivity so as to reduce transmission of group A β -hemolytic streptococci to family members, classmates, and other close contacts and to allow the rapid resumption of usual activities; (5) minimization of potential adverse effects of inappropriate antimicrobial therapy.

Evidence

We reviewed a large number of clinical trials of diagnostic and treatment strategies for group A streptococcal pharyngitis. The reports were examined for indicators of quality. For example, studies of treatment were evaluated for randomization, blinding, use of streptococcal typing to differentiate treatment failures from new infections, duration and timing of follow-up examinations, and statistical power [1, 2].

Values

In evaluating diagnostic options, we placed a high value on selecting the diagnostic test that was most accurate for differentiating acute pharyngitis due to group A β -hemolytic streptococci from that due to other agents. For evaluation of treatment, particularly high values were assigned to proven clinical and bacteriologic efficacy, safety, spectrum of antimicrobial activity, and relative cost.

Benefits and Costs

The group A β -hemolytic streptococcus is the most common bacterial cause of acute pharyngitis [3]. Accurate diagnosis, followed by appropriate antimicrobial therapy, is important for the reasons previously stated (see the section on outcomes). Although acute pharyngitis is one of the most frequent illnesses for which pediatricians and other primary care physicians are consulted, less than half of patients with this condition are infected by group A streptococci. Moreover, the signs and symptoms of group A streptococcal and nonstreptococcal pharyngitis overlap so broadly that accurate diagnosis on clinical grounds alone is usually impossible [4].

With the exception of very rare infections by certain of the other pharyngeal bacterial pathogens listed in table 1 (e.g., *Corynebacterium diphtheriae* and *Neisseria gonorrhoeae*), antimicrobial therapy is of no proven benefit in the treatment of acute pharyngitis due to bacteria other than the group A streptococcus. It is therefore extremely important for physicians to be able to exclude the diagnosis of group A streptococcal pharyngitis to prevent inappropriate administration of antimicrobials to large numbers of patients with pharyngitis. The administration of such therapy unnecessarily exposes patients to the associated expense and hazards, and it may also contribute to the emergence of

Table 1. Microbial etiology of acute pharyngitis.

Microbe	Disorder
Bacteria	
Streptococcus, group A	Pharyngitis, tonsillitis, scarlet fever
Streptococcus, groups C and G	Pharyngitis, tonsillitis, scarlatiniform rash
Mixed anaerobes	Vincent's angina
<i>Neisseria gonorrhoeae</i>	Pharyngitis, tonsillitis
<i>Corynebacterium diphtheriae</i>	Diphtheria
<i>Arcanobacterium haemolyticum</i>	Pharyngitis, scarlatiniform rash
<i>Yersinia enterocolitica</i>	Pharyngitis, enterocolitis
<i>Yersinia pestis</i>	Plague
<i>Francisella tularensis</i>	Tularemia (oropharyngeal form)
Viruses	
Rhinovirus	Common cold
Coronavirus	Common cold
Adenovirus	Pharyngoconjunctival fever, acute respiratory disease
Herpes simplex virus 1 and 2	Pharyngitis, gingivostomatitis
Parainfluenza virus	Cold, croup
Coxsackievirus A	Herpangina, hand-foot-and-mouth disease
Epstein-Barr virus	Infectious mononucleosis
Cytomegalovirus	Cytomegalovirus mononucleosis
Human immunodeficiency virus	Primary HIV infection
Influenza virus A and B	Influenza
Mycoplasmas	
<i>Mycoplasma pneumoniae</i>	Pneumonia, bronchitis, pharyngitis (?)
Chlamydiae	
<i>Chlamydia psittaci</i>	Acute respiratory disease, pneumonia
<i>C. pneumoniae</i>	Pneumonia, pharyngitis (?)

NOTE. Modified from *Pediatrics* 1996;97:949–54 with permission [3].

antibiotic-resistant bacteria that is being reported with increasing frequency in the United States and elsewhere.

If a diagnosis of group A streptococcal pharyngitis is confirmed, the clinician must select the most appropriate antimicrobial agent known to be effective against the group A streptococcus. The cost of an effective course of antimicrobial therapy may vary as much as 20-fold, depending on the drug chosen. The regimens recommended herein are judged to be optimal in regard to specificity, safety, and cost.

Recommendations

A. Diagnosis

Differential diagnosis. Viruses are the most common non-bacterial causes of acute pharyngitis (table 1) [3]. Respiratory viruses such as adenovirus, parainfluenza virus, rhinovirus, and respiratory syncytial virus frequently cause acute pharyngitis. Other viral agents of acute pharyngitis include coxsackievirus and ECHO viruses as well as herpes simplex virus. Epstein-Barr virus is a frequent cause of acute pharyngitis that is often accompanied by the other clinical features of infectious mononucleosis (e.g., generalized lymphadenopathy and splenomegaly). Systemic infections with measles virus, cytomegalovirus,

rubella virus, influenza virus, and a number of other viral agents may be associated with acute pharyngitis. Other agents such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* are uncommon causes of acute pharyngitis.

The group A β -hemolytic streptococci are the most common cause of bacterial pharyngitis, but other bacteria are also capable of producing acute pharyngitis (table 1). These include groups C and G β -hemolytic streptococci and *C. diphtheriae* [5–8]. *Arcanobacterium haemolyticum* has been reported to be an important cause of acute pharyngitis in Scandinavia and the United Kingdom, but this organism is rarely recognized in the United States. Pharyngitis caused by *A. haemolyticum* is often associated with a scarlet fever–like rash and is particularly common among teenagers and young adults. *N. gonorrhoeae* can occasionally cause acute pharyngitis in sexually active individuals, and other bacteria such as *Francisella tularensis* and *Yersinia enterocolitica* and mixed anaerobic infections (i.e., Vincent's angina) are rare causes of acute pharyngitis.

As is evident from this list of potential etiologic agents, group A β -hemolytic streptococcal pharyngitis is the only commonly occurring form of acute pharyngitis for which antibiotic therapy is definitely indicated. Therefore, when a clinician is evaluating a patient with acute pharyngitis, the clinical decision that usually needs to be made is whether the pharyngitis is attributable to group A β -hemolytic streptococci.

Clinical diagnosis. There are certain characteristic epidemiological and clinical features of acute group A β -hemolytic streptococcal pharyngitis [9]. This disorder is primarily a disease of children between 5 years and 15 years of age, and in temperate climates, it usually occurs in the winter and early spring. Patients with group A β -hemolytic streptococcal pharyngitis commonly present with sore throats (generally of sudden onset), pain on swallowing, and fever. Headache, nausea, vomiting, and abdominal pain may also be present, especially in children. Physical examination reveals tonsillopharyngeal erythema with or without exudates and tender enlarged anterior cervical lymph nodes (lymphadenitis). Other findings may include a beefy red swollen uvula, petechiae on the palate, excoriated nares (especially in infants), and a scarlatiniform rash. However, none of these findings is specific for group A β -hemolytic streptococcal pharyngitis, and they may occur with other upper respiratory infections. Conversely, the absence of fever or the presence of clinical features such as conjunctivitis, cough, hoarseness, coryza, anterior stomatitis, discrete ulcerative lesions, viral exanthem, and diarrhea strongly suggests a viral rather than a streptococcal etiology.

Who Should Be Tested for Group A β -Hemolytic Streptococcal Pharyngitis?

When attempting to decide whether to perform a laboratory test for a patient who presents with acute pharyngitis, the clinical and epidemiological findings mentioned above should be considered before the test is performed. A history of close contact with a well-documented case of streptococcal pharyngi-

tis is helpful, as is an awareness of a high prevalence of group A β -hemolytic streptococcal infections in the community. Testing usually need not be performed for patients with acute pharyngitis whose clinical and epidemiological features do not suggest a group A streptococcal etiology. Selective use of diagnostic studies for group A β -hemolytic streptococci will result in an increase in both the proportion of positive test results and the percentage of patients with positive tests who are truly infected rather than merely streptococcal carriers (category A, grade II).

Efforts have been made to incorporate clinical and epidemiological features of acute pharyngitis into scoring systems that attempt to predict the probability that a particular illness is caused by group A β -hemolytic streptococci [10, 11]. However, at best these clinical scoring systems predict positive results of throat cultures or RADTs only $\leq 80\%$ of the time. Therefore, unless the diagnosis of group A streptococcal pharyngitis can be confidently excluded on clinical and epidemiologic grounds (see Clinical Diagnosis above), bacteriologic studies should be performed (category A, grade II).

Throat Cultures

Culture of a throat swab on a sheep blood agar plate remains the standard for the documentation of the presence of group A streptococci in the upper respiratory tract and for the confirmation of the clinical diagnosis of acute streptococcal pharyngitis [12] (category A, grade II). A single throat swab cultured correctly on a blood agar plate has a sensitivity of 90%–95% in detecting the presence of group A β -hemolytic streptococci in the pharynx [13] (category A, grade II).

Several variables impact on the accuracy of the throat culture results. For example, the manner in which the swab is obtained has an important impact on the yield of streptococci from the throat culture [14, 15]. Throat swab specimens should be obtained from the surface of both tonsils (or tonsillar fossae) and the posterior pharyngeal wall. Other areas of the oropharynx and mouth are not acceptable sites for sampling, and these sites should not be touched before or after the appropriate areas have been sampled. In addition, false-negative results may be obtained if the patient has received antibiotics shortly before or at the time the throat swab specimen is collected.

It has also been reported that the use of anaerobic incubation and selective culture media may increase the proportion of positive cultures [16, 17]. However, the data on the impact of the incubation atmosphere and the culture media are conflicting, and, in the absence of a definite benefit, the increased cost and effort associated with anaerobic incubation and selective culture media are difficult to justify, particularly for physicians who process throat cultures in their own offices [16, 18, 19] (category A, grade II).

Another variable that can impact on the yield of the throat culture is the duration of incubation. Once plated, cultures should be incubated at 35°–37°C for 18–24 hours before they are read. However, additional overnight incubation at room temperature allows identification of a considerable number of

positive throat cultures that would not otherwise be identified. Thus, while initial therapeutic decisions may be made on the basis of the results of an overnight culture, it is advisable to reexamine plates at 48 hours that are negative at 24 hours [20] (category A, grade II).

The clinical significance of the number of group A β -hemolytic streptococcal colonies present on the throat culture plate is problematic. While cultures are more likely to be strongly positive for patients with true acute group A streptococcal pharyngitis than for patients who are streptococcus carriers, there is so much overlap that the differentiation cannot be made accurately on the basis of the degree of positivity of the throat culture alone [19] (category A, grade II).

The most widely used test for differentiating group A streptococci from other β -hemolytic streptococci in physicians' offices is probably the bacitracin disk test. This test provides a presumptive identification based on the observation that $>95\%$ of group A streptococci show a zone of inhibition around a disk containing 0.04 units of bacitracin, while 83%–97% of non-group A streptococci do not [21, 22].

An alternative and highly specific method of identifying streptococcal serogroups is the detection of the group-specific cell-wall carbohydrate antigen directly on isolated bacterial colonies. Commercial kits containing group-specific antisera are available for this purpose. Such tests are appropriate for use by microbiology laboratory personnel, but most physicians who perform throat cultures would find it difficult to justify the additional expense for the minimal improvement in accuracy that serogrouping with an antigen detection test would provide [19].

Rapid Antigen Detection Tests

A disadvantage of culturing a throat swab on blood agar plates is the delay (overnight or longer) in obtaining the culture results. RADTs have been developed for the identification of group A β -hemolytic streptococci directly from throat swabs. Although these rapid tests are more expensive than blood agar cultures, the advantage they offer over the traditional procedure is the speed with which they can provide results. Rapid identification and treatment of patients with streptococcal pharyngitis can reduce the risk of the spread of group A β -hemolytic streptococci, allowing these patients to return to school or work sooner, and can reduce the acute morbidity associated with this illness [13, 23–25] (category A, grade II). The use of RADTs vs. throat cultures for certain populations (e.g., patients seen in emergency departments) has been shown to significantly increase the number of patients appropriately treated for streptococcal pharyngitis [26].

Most of the RADTs that are currently available have an excellent specificity ($\geq 95\%$) when compared with blood agar plate cultures [13] (category A, grade II). This specificity means that false-positive test results are unusual and, therefore, that therapeutic decisions can be made on the basis of a positive test with a great degree of confidence. Unfortunately, the sensi-

tivity of most of these tests is between 80% and 90%, or even lower, when compared with the blood agar plate culture (category A, grade II). It has been suggested that most of the false-negative RADT results occur for patients who are merely streptococcal carriers and are not truly infected. Studies have demonstrated, however, that a large proportion of patients in whom RADTs are falsely negative are truly infected with group A β -hemolytic streptococci and are not merely streptococcal carriers [27]. Therefore, a negative RADT result should be confirmed with conventional blood agar plate culture results (category A, grade II).

The first RADTs were based on latex agglutination methodology, were relatively insensitive, and had unclear endpoints. Newer tests based on EIA techniques offer more sharply defined endpoints as well as increased sensitivity. More recently, RADTs for which optical immunoassay and chemiluminescent DNA probes are used have become available. Data on these newer tests suggest that they may be more sensitive than other RADTs and perhaps even as sensitive as standard throat cultures on sheep blood agar plates. However, in view of somewhat conflicting data [28], additional corroborative information is needed before these tests can be recommended for routine use without confirmatory throat cultures for negative test results.

Titers of antibodies to streptococci reflect past and not present immunologic events and are of no value in the diagnosis of acute pharyngitis. These titers are valuable for confirming prior streptococcal infections in patients suspected of having acute rheumatic fever or acute glomerulonephritis. They also are helpful in prospective epidemiological studies that are conducted to separate patients with acute infection from those who are carriers.

Guideline: The diagnosis of acute group A streptococcal pharyngitis should be suspected on clinical and epidemiological grounds and then supported by the results of a laboratory test. Either a positive throat culture or RADT provides adequate confirmation of the presence of group A β -hemolytic streptococci in the pharynx, but a negative RADT result should be confirmed with a throat culture (category A, grade II).

Repeated Diagnostic Testing

Most asymptomatic patients with group A β -hemolytic streptococci present in the upper respiratory tract after a complete course of appropriate therapy are streptococcal carriers [29, 30]. Therefore, follow-up throat cultures are not routinely indicated for asymptomatic patients who have received a complete course of therapy for group A streptococcal pharyngitis (category A, grade II). However, there are special situations when follow-up throat cultures should be performed for asymptomatic patients. Throat cultures should be performed routinely for patients with histories of rheumatic fever. Such cultures should also be considered for patients who develop acute pharyngitis during outbreaks of either acute rheumatic fever or poststreptococcal acute glomerulonephritis as well as during outbreaks of group A streptococcal pharyngitis in closed or semiclosed communities [30, 31]. Follow-up throat

cultures may also be indicated when "Ping-Pong" spread of group A streptococci has been occurring within a family (category B, grade III).

Guideline: With rare exceptions, follow-up throat cultures are not indicated for asymptomatic patients who have received a complete course of therapy for group A streptococcal pharyngitis.

B. Management of Group A Streptococcal Pharyngitis

Antimicrobial therapy is indicated for individuals with symptomatic pharyngitis after the organism's presence in the throat is confirmed by microbiological or immunologic means (figure 1). When there is clinical or epidemiological evidence that results in a high index of suspicion, antimicrobial therapy can be initiated while laboratory confirmation is pending provided such therapy is discontinued if the diagnosis of streptococcal pharyngitis is not confirmed. Early initiation of antimicrobial therapy results in faster resolution of the signs and symptoms [23–25] (category A, grade I) of the infection, but two facts should be recalled. First, group A streptococcal pharyngitis is usually a self-limited disease; fever and constitutional symptoms disappear spontaneously within 3 or 4 days of onset, even when antimicrobial therapy is not administered [32]. Second, it has been shown that therapy can be safely postponed ≤ 9 days after the onset of symptoms and still prevent the occurrence of the major nonsuppurative sequel, acute rheumatic fever [33] (category A, grade I).

These facts allow the clinician flexibility in initiating therapy during the evaluation of an individual patient with presumed group A streptococcal pharyngitis. The results of the initial therapeutic studies were reported nearly 50 years ago; since then numerous antimicrobial agents have been examined in

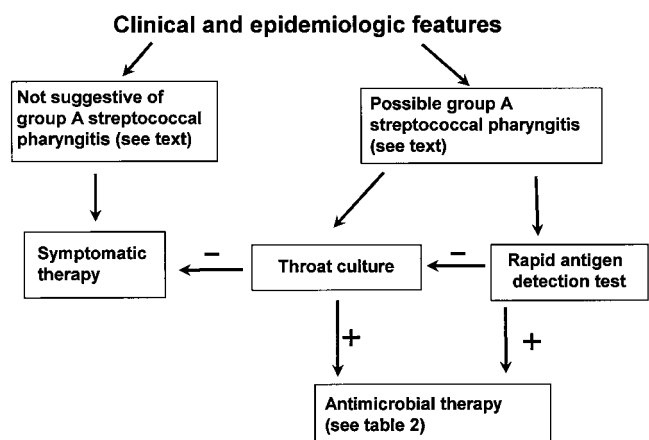


Figure 1. Diagnosis and management of acute pharyngitis. This algorithm applies to uncomplicated cases of acute pharyngitis; additional diagnostic and therapeutic measures may be necessary for patients with suppurative complications (e.g., peritonsillar abscess or cervical lymphadenitis) or when infection with uncommon pharyngeal bacterial pathogens (e.g., *Corynebacterium diphtheriae* or *Neisseria gonorrhoeae*) is suspected. (– = if negative; + = if positive).

clinical trials and have been shown to be capable of eradicating group A streptococci from the upper respiratory tract. However, it must be recognized that the only antimicrobial actually examined in controlled studies and shown to be capable of preventing initial attacks of rheumatic fever has been intramuscular repository penicillin [34, 35] (category A, grade I). These studies were performed with procaine penicillin G in oil containing aluminum monostearate [34, 35], a preparation that has since been supplanted by benzathine penicillin G. (For this reason, no regimens listed in table 2 have been assigned a grade of A1.) There are data, although not definitive, indicating that benzathine penicillin G is effective in primary prevention of rheumatic fever (prevention of an initial attack of rheumatic fever following an episode of group A streptococcal pharyngitis) [36, 37]. Benzathine penicillin G has also been shown to decrease the occurrence of rheumatic fever cases during epidemics of streptococcal pharyngitis in military recruit camps [38]. Moreover, benzathine penicillin G has been proven effective for preventing rheumatic fever in patients who have had a previous attack of the disease (secondary prophylaxis) [39] (category A, grade I). Other antimicrobials can effectively eradicate group A streptococci from the upper respiratory tract, and it is assumed that such eradication is an adequate measure of effectiveness in the primary prevention of rheumatic fever.

Antimicrobial resistance has not been a significant issue in the treatment of group A streptococcal pharyngitis in the United States. There has never been a clinical isolate of group A streptococcus documented to be resistant to penicillin anywhere in the world. Although there have been geographic areas where isolates have been highly resistant to macrolide antibiotics (specifically erythromycin), this has not been and currently is not a clinically significant problem in North America. Less than 5% of group A streptococci isolated in the United States have

been shown to be resistant to erythromycin [40]. Sulfonamides and tetracyclines are not recommended for treatment of group A streptococcal pharyngitis because of the higher rates of resistance to these agents among group A streptococci and the frequent failure of these agents to eradicate even susceptible organisms from the pharynx.

Antimicrobial therapy. When selecting an antimicrobial for treatment of group A streptococcal pharyngitis, important issues include efficacy, safety, antimicrobial spectrum (narrow vs. broad), dosing schedules, compliance (or adherence), and cost. These factors influence the cost-effectiveness of antimicrobial therapy.

A number of antibiotics have been shown to be effective for treating group A streptococcal pharyngitis. These agents include penicillin and its congeners (such as ampicillin and amoxicillin), as well as numerous cephalosporins, macrolides, and clindamycin. However, penicillin remains the treatment of choice because of its proven efficacy, safety, narrow spectrum, and low cost [31, 41, 42]. Erythromycin is a suitable alternative for patients who are allergic to penicillin. First- or second-generation cephalosporins are also acceptable for penicillin-allergic patients who do not manifest immediate hypersensitivity to β -lactam antibiotics.

Most oral antibiotics must be administered for 10 days to achieve maximal pharyngeal eradication of group A streptococci, but certain new agents have been administered in shorter courses. It has been reported that azithromycin [43–45], cefuroxime [46], cefixime [47], and cefpodoxime [48] can be used to achieve comparable bacteriologic and clinical cure rates among patients with streptococcal pharyngitis when these drugs are given for ≤ 5 days. However, definitive results from comprehensive studies are not available, and thus it is not possible to endorse these proposed shorter courses of oral antibiotic ther-

Table 2. Antimicrobial therapy for group A streptococcal pharyngitis.

Antimicrobial agent	Dose	Duration	Category	Grade
Oral				
Penicillin V*	Children: 250 mg	b.i.d. or t.i.d. \times 10 d	A	II
	Adolescents and adults: 250 mg	t.i.d. or q.i.d.	A	II
	or 500 mg	b.i.d. \times 10 d	C	III
Parenteral				
Benzathine penicillin G	1.2×10^6 units	1 dose	A	II [†]
	6.0×10^5 units	1 dose [‡]	A	II
	1.2×10^6 units	1 dose	B	II
C-R bicillin (900/300) [§]	1.2×10^6 units	1 dose	B	II
For penicillin-allergic patients				
Erythromycin estolate	20–40 mg/kg/d [#]	b.i.d. or t.i.d. \times 10 d	A	II
Erythromycin ethyl succinate	40 mg/kg/d [#]	b.i.d. or t.i.d. \times 10 d	A	II

* Amoxicillin is often used in place of oral penicillin V in young children; the efficacy of amoxicillin appears to be equal to that of penicillin V, and this choice is primarily related to acceptance of the taste of the suspension.

[†] See text.

[‡] For patients weighing less than 60 lbs (27 kg).

[§] Two milliliters of C-R bicillin(900/300) contains 900,000 units of benzathine penicillin G and 300,000 units of procaine penicillin G; this preparation thus contains less benzathine penicillin G than is conventionally used in the treatment of adolescents or adults.

^{||} Available data indicate that orally administered first- and second-generation cephalosporins also are effective in eradicating group A streptococci from the upper respiratory tract; these agents should not be used in patients with immediate hypersensitivity to β -lactam antibiotics.

[#] First-generation cephalosporin A II Second-generation cephalosporin A II.

[#] These are total daily doses (maximum daily dose, 1 g per day).

apy at this time. Moreover, the spectra of these antibiotics are much broader than that of penicillin, and, even when they are administered for short courses, they are more expensive.

Antimicrobials for group A streptococcal upper respiratory tract infections may be given either orally or parenterally. Table 2 shows suggested regimens for several antimicrobials that have proven to be effective for the treatment of uncomplicated group A streptococcal pharyngitis. Intramuscular benzathine penicillin G is preferred for patients who are unlikely to complete a full 10-day course of oral therapy.

Guideline: patients with acute streptococcal pharyngitis should receive therapy with an antimicrobial agent in a dosage and for a duration that is likely to eradicate the infecting organism from the pharynx. On the basis of penicillin's narrow spectrum of antimicrobial activity, the infrequency with which it produces adverse reactions, and its modest cost, it is the drug of choice for nonallergic patients.

Management of close contacts and pharyngeal carriers. Approximately 25% of individuals within the household of an index patient may also harbor group A streptococci in their upper respiratory tracts. However, it is usually not necessary to perform throat cultures for these contacts or treat them if they are asymptomatic. In those situations in which repeated testing is indicated (see the section on Repeated Diagnostic Testing), performing cultures for asymptomatic family contacts and treating those who are positive are advisable. When a larger group (e.g., schools, day care centers, or domiciliary institutions) is involved in a documented outbreak of group A streptococcal upper respiratory infections or scarlet fever, throat cultures should be performed for all patients; however, only those with positive throat cultures should be treated with antimicrobials. The administration of intramuscular injections of benzathine penicillin G has been shown to be very effective in terminating such outbreaks.

Strains of group A streptococci that cause invasive infections may spread to close contacts of the index case. Secondary cases of severe invasive infection have rarely occurred in family and institutional contacts and in health care workers [49–51]. Data are as yet too limited to assess with precision the risk of secondary illness or to make a firm recommendation regarding the advisability of routinely performing cultures and treating close contacts of patients with group A streptococcal infections such as necrotizing fasciitis or the toxic shock-like syndrome.

Guideline: It is not necessary to perform throat cultures or provide treatment for household contacts of patients with group A streptococcal pharyngitis, except in specific situations in which there is increased risk of frequent infections or of non-suppurative sequelae (category B, grade III).

C. Management of Patients with Repeated Episodes of Acute Pharyngitis and Cultures or RADTs Positive for Group A β -Hemolytic Streptococci

Performing routine throat cultures (or rapid antigen testing) for asymptomatic patients after completion of antibiotic therapy for group A streptococcal pharyngitis is not necessary unless

special circumstances are present (see the section on Repeated Diagnostic Testing). Because routine retesting is no longer advised, only those patients whose signs and symptoms of acute pharyngitis return within the succeeding few weeks will return for reassessment. If such patients' cultures or RADTs are again positive for group A streptococci, there are several possible explanations: persistence of the carrier state during intercurrent viral infection [29], noncompliance with the prescribed antimicrobial regimen [52], or a new infection with a group A streptococcus acquired from family, classroom, or community contacts. A second episode of pharyngitis with the original infecting group A streptococcal strain (i.e., treatment failure) cannot be ruled out, but this occurs only rarely.

Streptococcal carriers do not ordinarily require further antimicrobial therapy. These individuals have group A β -hemolytic streptococci present in their throats but have no evidence of an immunologic reaction to this organism [53]. During the winter and spring in temperate climates, $\leq 20\%$ of asymptomatic school-aged children may be streptococcus carriers. They may be colonized by group A β -hemolytic streptococci for several months, and during that period they may have episodes of intercurrent viral pharyngitis. When tested, these patients are found to have group A β -hemolytic streptococci in their pharynges and appear to have acute streptococcal pharyngitis. Streptococcal carriers are unlikely to spread the organism to their close contacts and are at low risk, if any, for developing suppurative complications or nonsuppurative complications (e.g., acute rheumatic fever) [53].

Moreover, it is more difficult to eradicate group A streptococci from the upper respiratory tracts of streptococcal carriers [29]. This has been shown to be true with penicillin therapy and also may be true with some other antimicrobials. In fact, many of the published studies showing relatively high rates of failure to eradicate group A streptococci from the upper respiratory tract with penicillin therapy were likely "contaminated" with carriers.

In practice it is difficult to differentiate a carrier with an intercurrent non-group A streptococcal infection from a patient with acute streptococcal pharyngitis. Helpful clues include the patient's age, season of the year, local epidemiology (e.g., the presence of influenza or enteroviral illnesses), and the precise nature of the presenting signs and symptoms (see the section on clinical diagnosis above).

In many instances, however, the clinician may not be able confidently to distinguish persistent carriage from acute infection and will elect to administer another course of antimicrobials. For single episodes of symptomatic, culture-confirmed or RADT-confirmed group A streptococcal pharyngitis that occur shortly after completion of a course of appropriate antimicrobial therapy, any of the agents listed in table 2 is appropriate. Because patient compliance with oral antimicrobials often is an issue, a regimen of intramuscular benzathine penicillin G should be considered. For these single repeated episodes, it is not necessary to reculture the throat after the second course of therapy unless the patient remains or becomes symptomatic or

unless special circumstances are present (see the section on Repeated Diagnostic Testing above).

An even more challenging clinical circumstance is a patient—usually a school-aged child or adolescent—who has multiple episodes of acute pharyngitis and cultures or RADTs positive for group A streptococci within a period of months to years. It is likely that most patients in this category are streptococcal carriers with nonstreptococcal infections. For patients who have frequent distinct episodes of infection, information regarding the clinical response to antibiotic therapy and the presence or absence of group A streptococci in throat cultures performed during asymptomatic intervals is helpful in distinguishing persistent carriage from repeated episodes of streptococcal pharyngitis. Serotyping of repeated streptococcal isolates from an individual patient may also assist in arriving at this determination, but such studies can be done only in specialized research laboratories.

When physicians suspect Ping-Pong spread to be associated with multiple repeated episodes of group A streptococcal infections in one family, performing simultaneous cultures for all family contacts and treating those whose cultures are positive may be helpful (category **B**, grade III). There is no credible evidence that family pets are reservoirs for group A streptococci or that they contribute to familial spread.

Continuous antimicrobial prophylaxis for group A streptococcal infection is not recommended because there is insufficient evidence to show that it is effective, except for preventing recurrences of acute rheumatic fever. Surgical removal of the tonsils may be considered for the rare patient whose symptomatic episodes do not diminish in frequency over time and for whom no alternative explanation for the recurrent pharyngitis is evident. Tonsillectomy may decrease recurrences of symptomatic pharyngitis in selected patients, but only for a limited period of time [54] (category **A**, grade I).

There have been no definitive controlled studies of therapy for multiple, repeated symptomatic episodes of culture-positive acute pharyngitis in the same patient; however, the regimens listed in table 3 have been reported to result in low bacteriologic failure rates [55–58].

Guideline: A small percentage of patients will have recurrences of acute pharyngitis and throat cultures (or RADTs) positive for group A streptococci within a short period of time following completion of a course of antimicrobial therapy. A single such episode may be retreated with the regimens listed in table 2. When multiple episodes occur over the course of months or years, it may be difficult to differentiate viral infections from true group A streptococcal infections in a streptococcal carrier. Use of certain antimicrobial agents has been shown to yield high rates of streptococcal eradication in the pharynx under these particular circumstances (category **A**, grade II). Suggested regimens with these agents are listed in table 3.

D. Indicators of Quality

Indicators of quality of care for patients with acute pharyngitis include: (1) performance of throat cultures or RADTs for patients suspected of having group A streptococcal pharyngitis; (2) performance of throat cultures for patients with negative RADTs; (3) prescription of one of the antimicrobial regimens recommended in table 2 for patients with acute pharyngitis and positive tests for group A streptococci; (4) withholding or discontinuing antimicrobial therapy for patients with throat cultures negative for group A streptococci; (5) omission of routine follow-up cultures for patients who have received an adequate course of antimicrobial therapy; (6) avoidance of routine throat cultures for asymptomatic family contacts of patients with group A streptococcal pharyngitis; (7) avoidance of con-

Table 3. Retreatment of symptomatic patients with multiple repeated culture-positive episodes of pharyngitis.

Antimicrobial agent	Dose	Category	Grade
Oral*†			
Clindamycin	Children: 20–30 mg/(kg · d) for 10 d Adults: 600 mg/d in 2–4 equally divided doses for 10 d	B	II
Amoxicillin/clavulanate	40 mg/(kg · d) in 3 equally divided doses for 10 d‡	B	II
Parenteral agents			
Benzathine penicillin G	(for dose, see table 2)§	B	II

* Macrolides (e.g., erythromycin) and cephalosporins are not included in this table, as there are insufficient data to support their efficacy in this specific circumstance.

† Although shorter courses of some newer macrolides and cephalosporins have been reported to be effective for treating group A streptococcal upper respiratory tract infections, the evidence is not yet sufficient to recommend these agents for therapy at this time (this is also true for patients with repeated infections or for those in whom the organism is difficult to eradicate).

‡ Maximum dose, 750 mg of amoxicillin per day.

§ Benzathine penicillin G is useful for patients whose compliance with previous courses of oral antimicrobials is questionable. Limited data suggest that the addition of rifampin (10 mg/kg b.i.d. × 4 days; maximum dose, 300 mg b.i.d.) to a benzathine penicillin G regimen may be beneficial for eradicating streptococci from the pharynx [58].

tinuous long-term antimicrobial prophylaxis for preventing recurrent episodes of acute pharyngitis.

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