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Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America[a]

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The guideline is intended for use by healthcare providers who care for adult and pediatric patients with group A streptococcal pharyngitis. The guideline updates the 2002 Infectious Diseases Society of America guideline and discusses diagnosis and management, and recommendations are provided regarding antibiotic choices and dosing. Penicillin or amoxicillin remain the treatments of choice, and recommendations are made for the penicillin-allergic patient, which now include clindamycin.

EXECUTIVE SUMMARY

Group A streptococcal (GAS) pharyngitis is a significant cause of community-associated infections. This document constitutes a revision of the 2002 guideline of the Infectious Diseases Society of America (IDSA) on the treatment of GAS pharyngitis [1]. The primary objective of this guideline is to provide recommendations on the management of this very common clinical condition among adult and pediatric patients. The guideline addresses issues related to the diagnosis of streptococcal pharyngitis and its treatment in patients who are or are not allergic to penicillin. The guideline does not discuss active surveillance testing or other prevention strategies. Each section of the guideline begins with a specific clinical question and is followed by numbered recommendations and a summary of the most-relevant evidence in support of the recommendations. Areas of controversy in which data are limited or conflicting and in which additional research is needed are indicated throughout the document and are highlighted in the Future Research section.

Summarized below are the recommendations made in the updated guidelines for the diagnosis and management GAS pharyngitis. The Panel followed a process used in the development of other IDSA guidelines, which included a systematic weighting of the strength of recommendation (ie, "strong" or "weak") and quality of evidence (ie, "high," "moderate," "low," or "very

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[a]It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. IDSA considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

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low"), using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system [2–8] (Table 1). A detailed description of the methods, background, and evidence summaries that support each of the recommendations can be found in the full text of the guidelines. Specific treatment recommendations regarding streptococcal pharyngitis are included in Table 2.

RECOMMENDATIONS FOR THE DIAGNOSIS OF GAS PHARYNGITIS

I. How Should the Diagnosis of GAS Pharyngitis Be Established?

Recommendations

1. Swabbing the throat and testing for GAS pharyngitis by rapid antigen detection test (RADT) and/or culture should be performed because the clinical features alone do not reliably discriminate between GAS and viral pharyngitis except when overt viral features like rhinorrhea, cough, oral ulcers, and/or hoarseness are present. In children and adolescents, negative RADT tests should be backed up by a throat culture (strong, high). Positive RADTs do not necessitate a back-up culture because they are highly specific (strong, high).

2. Routine use of back-up throat cultures for those with a negative RADT is not necessary for adults in usual circumstances, because of the low incidence of GAS pharyngitis in adults and because the risk of subsequent acute rheumatic fever is generally exceptionally low in adults with acute pharyngitis (strong, moderate). Physicians who wish to ensure they are achieving maximal sensitivity in diagnosis may continue to use conventional throat culture or to back up negative RADTs with a culture.

3. Anti-streptococcal antibody titers are not recommended in the routine diagnosis of acute pharyngitis as they reflect past but not current events; strong, high).

II. Who Should Undergo Testing for GAS Pharyngitis?

Recommendations

4. Testing for GAS pharyngitis usually is not recommended for children or adults with acute pharyngitis with clinical and epidemiological features that strongly suggest a viral etiology (eg, cough, rhinorrhea, hoarseness, and oral ulcers; strong, high).

5. Diagnostic studies for GAS pharyngitis are not indicated for children <3 years old because acute rheumatic fever is rare in children <3 years old and the incidence of streptococcal pharyngitis and the classic presentation of streptococcal pharyngitis are uncommon in this age group. Selected children <3 years old who have other risk factors, such as an older sibling with GAS infection, may be considered for testing (strong, moderate).

6. Follow-up posttreatment throat cultures or RADT are not recommended routinely but may be considered in special circumstances (strong, high).

7. Diagnostic testing or empiric treatment of asymptomatic household contacts of patients with acute streptococcal pharyngitis is not routinely recommended (strong, moderate).

RECOMMENDATIONS FOR THE TREATMENT OF PATIENTS WITH GAS PHARYNGITIS

III. What Are the Treatment Recommendations for Patients With a Diagnosis of GAS Pharyngitis?

Recommendations

8. Patients with acute GAS pharyngitis should be treated with an appropriate antibiotic at an appropriate dose for a duration likely to eradicate the organism from the pharynx (usually 10 days). Based on their narrow spectrum of activity, infrequency of adverse reactions, and modest cost, penicillin or amoxicillin is the recommended drug of choice for those non-allergic to these agents (strong, high).

9. Treatment of GAS pharyngitis in penicillin-allergic individuals should include a first generation cephalosporin (for those not anaphylactically sensitive) for 10 days, clindamycin or clarithromycin for 10 days, or azithromycin for 5 days (strong, moderate).

IV. Should Adjunctive Therapy With Nonsteroidal Anti-inflammatory Drugs (NSAIDs), Acetaminophen, Aspirin, or Corticosteroids Be Given to Patients Diagnosed With GAS Pharyngitis?

Recommendation

10. Adjunctive therapy may be useful in the management of GAS pharyngitis.

(i) If warranted, use of an analgesic/antipyretic agent such as acetaminophen or an NSAID for treatment of moderate to severe symptoms or control of high fever associated with GAS pharyngitis should be considered as an adjunct to an appropriate antibiotic (strong, high).
(ii) Aspirin should be avoided in children (strong, moderate).
(iii) Adjunctive therapy with a corticosteroid is not recommended (weak, moderate).

V. Is the Patient With Frequent Recurrent Episodes of Apparent GAS Pharyngitis Likely to Be a Chronic Pharyngeal Carrier of GAS?

Recommendations

11. We recommend that clinicians caring for patients with recurrent episodes of pharyngitis associated with laboratory evidence of GAS pharyngitis consider that they may be experiencing >1 episode of bona fide streptococcal pharyngitis at close intervals, but they should also be alert to the possibility that the patient may actually be a chronic pharyngeal GAS carrier who is experiencing repeated viral infections (strong, moderate).

Table 1. Strength of Recommendations and Quality of the Evidence

Strength of Recommendation and Quality of Evidence	Clarity of Balance Between Desirable and Undesirable Effects	Methodological Quality of Supporting Evidence (Examples)	Implications
Strong recommendation, high-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research is unlikely to change our confidence in the estimate of effect.
Strong recommendation, moderate quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Strong recommendation, low-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence	Recommendation may change when higher-quality evidence becomes available. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Strong recommendation, very-low-quality evidence (very rarely applicable)	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher-quality evidence becomes available. Any estimate of effect for at least 1 critical outcome is very uncertain.
Weak recommendation, high-quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patients or societal values. Further research is unlikely to change our confidence in the estimate of effect.
Weak recommendation, moderate-quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Alternative approaches likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Weak recommendation, low-quality evidence	Uncertainty in the estimates of desirable effects, harms, and burden; desirable effects, harms, and burden may be closely balanced	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Weak recommendation, very-low-quality evidence	Major uncertainty in the estimates of desirable effects, harms, and burden; desirable effects may or may not be balanced with undesirable effects	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of effect, for at least 1 critical outcome, is very uncertain.

Information is based on GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria [2–8]

Abbreviation: RCT, randomized controlled trial.

12. We recommend that GAS carriers do not ordinarily justify efforts to identify them nor do they generally require antimicrobial therapy because GAS carriers are unlikely to spread GAS pharyngitis to their close contacts and are at little or no risk for developing suppurative or nonsuppurative complications (eg, acute rheumatic fever; strong, moderate).

13. We do not recommend tonsillectomy solely to reduce the frequency of GAS pharyngitis (strong, high).

INTRODUCTION

GAS is the most common bacterial cause of acute pharyngitis, responsible for 5%–15% of sore throat visits in adults and

Table 2. Antibiotic Regimens Recommended for Group A Streptococcal Pharyngitis

Drug, Route	Dose or Dosage	Duration or Quantity	Recommendation Strength, Quality[a]	Reference(s)
For individuals without penicillin allergy				
Penicillin V, oral	Children: 250 mg twice daily or 3 times daily; adolescents and adults: 250 mg 4 times daily or 500 mg twice daily	10 d	Strong, high	[125, 126]
Amoxicillin, oral	50 mg/kg once daily (max = 1000 mg); alternate: 25 mg/kg (max = 500 mg) twice daily	10 d	Strong, high	[88–92]
Benzathine penicillin G, intramuscular	<27 kg: 600 000 U; ≥27 kg: 1 200 000 U	1 dose	Strong, high	[53, 125, 127]
For individuals with penicillin allergy				
Cephalexin,[b] oral	20 mg/kg/dose twice daily (max = 500 mg/dose)	10 d	Strong, high	[128–131]
Cefadroxil,[b] oral	30 mg/kg once daily (max = 1 g)	10 d	Strong, high	[132]
Clindamycin, oral	7 mg/kg/dose 3 times daily (max = 300 mg/dose)	10 d	Strong, moderate	[133]
Azithromycin,[c] oral	12 mg/kg once daily (max = 500 mg)	5 d	Strong, moderate	[97]
Clarithromycin,[c] oral	7.5 mg/kg/dose twice daily (max = 250 mg/dose)	10 d	Strong, moderate	[134]

Abbreviation: Max, maximum.

[a] See Table 1 for a description.

[b] Avoid in individuals with immediate type hypersensitivity to penicillin.

[c] Resistance of GAS to these agents is well-known and varies geographically and temporally.

20%–30% in children [9, 10]. Accurate diagnosis of streptococcal pharyngitis followed by appropriate antimicrobial therapy is important for the prevention of acute rheumatic fever; for the prevention of suppurative complications (eg, peritonsillar abscess, cervical lymphadenitis, mastoiditis, and, possibly, other invasive infections); to improve clinical symptoms and signs; for the rapid decrease in contagiousness; for the reduction in transmission of GAS to family members, classmates, and other close contacts of the patient [11]; to allow for the rapid resumption of usual activities; and for the minimization of potential adverse effects of inappropriate antimicrobial therapy.

Although acute pharyngitis is one of the most frequent illnesses for which pediatricians and other primary care physicians are consulted, with an estimated 15 million visits per year in the United States [10], only a relatively small percentage of patients with acute pharyngitis (20%–30% of children and a smaller percentage of adults) have GAS pharyngitis. Moreover, the signs and symptoms of GAS and nonstreptococcal pharyngitis overlap so broadly that accurate diagnosis on the basis of clinical grounds alone is usually impossible [12].

With the exception of very rare infections by certain other bacterial pharyngeal pathogens (eg, *Corynebacterium diphtheriae* and *Neisseria gonorrhoeae*) (Table 3), antimicrobial therapy is of no proven benefit as treatment for acute pharyngitis due to organisms other than GAS. Therefore, it is extremely important that physicians exclude the diagnosis of GAS pharyngitis to prevent inappropriate administration of antimicrobials to large numbers of patients with nonstreptococcal pharyngitis. Such therapy unnecessarily exposes patients to the expense and hazards of antimicrobial therapy. Despite improvements in antimicrobial prescribing for children and adults with acute pharyngitis, a substantial number of patients continue to receive inappropriate antimicrobial therapy [13–15]. Inappropriate antimicrobial use for upper respiratory tract infections, including acute pharyngitis, has been a major contributor to the development of antimicrobial resistance among common pathogens [15]. Estimated economic costs of pediatric streptococcal pharyngitis in the United States range from $224 million to $539 million per year, including indirect costs related to parental work losses [16].

In addition to acute disease, streptococcal pharyngitis is important because it can lead to the nonsuppurative postinfectious disorders of acute rheumatic fever with and without carditis, as well as to poststreptococcal glomerulonephritis. Although acute rheumatic fever is now uncommon in most developed countries, it continues to be the leading cause of acquired heart disease in children in areas such as India, sub-Saharan Africa, and parts of Australia and New Zealand [17]. This guideline updates the 2002 practice guidelines of the IDSA [1]. The following 5 clinical questions are addressed in the guidelines:

(I) How should the diagnosis of GAS pharyngitis be established?

Table 3. Microbial Etiology of Acute Pharyngitis

Organisms	Clinical Syndrome(s)
Bacterial	
Group A streptococcus	Pharyngotonsillitis, scarlet fever
Group C and group G streptococcus	Pharyngotonsillitis
Arcanobacterium haemolyticum	Scarlatiniform rash, pharyngitis
Neisseria gonorrhoeae	Tonsillopharyngitis
Corynebacterium diphtheriae	Diphtheria
Mixed anaerobes	Vincent's angina
Fusobacterium necrophorum	Lemierre's syndrome, peritonsillar abscess
Francisella tularensis	Tularemia (oropharyngeal)
Yersinia pestis	Plague
Yersinia enterocolitica	Enterocolitis, pharyngitis
Viral	
Adenovirus	Pharyngoconjunctival fever
Herpes simplex virus 1 and 2	Gingivostomatitis
Coxsackievirus	Herpangina
Rhinovirus	Common cold
Coronavirus	Common cold
Influenza A and B	Influenza
Parainfluenza	Cold, croup
EBV	Infectious mononucleosis
Cytomegalovirus	CMV mononucleosis
HIV	Primary acute HIV Infection
Mycoplasma	
Mycoplasma pneumoniae	Pneumonitis, bronchitis
Chlamydia	
Chlamydophila pneumoniae	Bronchitis, pneumonia
Chlamydophila psittaci	Psittacosis

Abbreviations: CMV, cytomegalovirus; EBV, Epstein-Barr virus; HIV, human immunodeficiency virus.

(II) Who should undergo testing for GAS pharyngitis?

(III) What are the treatment recommendations for patients with a diagnosis of GAS pharyngitis?

(IV) Should adjunctive therapy with NSAIDs, acetaminophen, aspirin, or corticosteroids be given to patients with a diagnosis of GAS pharyngitis?

(V) Is the patient with frequent recurrent episodes of apparent GAS pharyngitis likely to be a chronic pharyngeal carrier of GAS?

METHODOLOGY

Practice Guidelines

"Practice guidelines are systematically developed statements to assist practitioners and patients in making decisions about appropriate healthcare for specific clinical circumstances" [18]. Attributes of good guidelines include validity, reliability, reproducibility, clinical applicability, clinical flexibility, clarity, multidisciplinary process, review of evidence, and documentation [18].

Panel Composition

A panel of 8 multidisciplinary experts in the management of streptococcal pharyngitis in children and adults was convened in 2009. The panel consisted of internists and pediatricians, including adult and pediatric infectious disease specialists and a general pediatrician.

Process Overview

The group convened a face-to-face meeting in 2009 in which an outline of the guideline was discussed and the process of guideline development using the GRADE approach was explained. The GRADE approach offers a structured, systematic, and transparent process to formulate recommendations on the basis of explicit criteria that go beyond just the quality of available evidence (Table 1) [2–8]. This was followed by a series of teleconferences in which a list of clinical questions to be addressed in the guideline was generated, discussed, and prioritized.

Literature Review and Analysis

We identified up-to-date valid systematic reviews from the MEDLINE database, PubMed, and the Cochrane Library, and in selected cases we also reference lists of the most recent narrative reviews or studies on the topic. Unless specified otherwise, the search period was 1980–2012 and was restricted to the English-language literature. Articles were also retrieved by searches for clinical diagnosis, laboratory diagnosis, symptoms and signs, and microbiology. The panel members contributed reference lists in these areas. The quality of evidence was evaluated after the literature review. We based our judgments on these systematic reviews and, if applicable, on additional studies published after the reviews were done. When systematic reviews were unavailable, we evaluated the original studies to inform judgments about the quality of the underlying evidence that were based on examination of these studies. Primary key search terms were as follows:

- Pharyngitis
- Streptococci
- Throat culture
- Rapid streptococcal tests
- Pharyngeal carriers
- Tonsillectomy
- Streptococcal antibody tests

Consensus Development Based on Evidence

The Panel met on >4 occasions via teleconference (including subgroup calls) and once in person to complete the work on

the guideline. The purpose of the teleconferences was to discuss the questions, distribute writing assignments, and finalize recommendations. All members of the Panel participated in the preparation and review of the draft guideline. Feedback was obtained from external peer reviews. The guideline was reviewed and approved by the IDSA Standards and Practice Guidelines Committee (SPGC) and the IDSA Board of Directors prior to dissemination.

Guidelines and Conflict of Interest

All members of the expert panel complied with the IDSA policy regarding conflicts of interest, which requires disclosure of any financial or other interest that might be construed as constituting an actual, potential, or apparent conflict. Members of the expert Panel were provided a conflict of interest disclosure statement from the IDSA and were asked to identify ties to companies developing products that might be affected by promulgation of the guideline. Information was requested regarding employment, consultancies, stock ownership, honoraria, research funding, expert testimony, and membership on company advisory committees. The Panel made decisions on a case-by-case basis about whether an individual's role should be limited as a result of a conflict. No limiting conflicts were identified.

Revision Dates

At annual intervals, the Panel chair, the liaison advisor, and the SPGC chair will determine the need for revisions to the updated guideline on the basis of an examination of current literature. If necessary, the entire Panel will reconvene to discuss potential changes. When appropriate, the Panel will recommend full revision of the guideline to the IDSA SPGC and the IDSA Board of Directors for review and approval.

RECOMMENDATIONS FOR THE DIAGNOSIS OF GROUP A STREPTOCOCCAL PHARYNGITIS

I. How Should the Diagnosis of Group A Streptococcal Pharyngitis Be Established?

Recommendations

1. Swabbing the throat and testing for GAS pharyngitis by rapid antigen detection test (RADT) and/or culture should be performed because the clinical features alone do not reliably discriminate between GAS and viral pharyngitis except when overt viral features like rhinorrhea, cough, oral ulcers, and/or hoarseness are present. In children and adolescents, negative RADT tests should be backed up by a throat culture (strong, high). Positive RADTs do not necessitate a back-up culture because they are highly specific (strong, high).

Table 4. Epidemiologic and Clinical Features Suggestive of Group A Streptococcal and Viral Pharyngitis

Feature, by Suspected Etiologic Agent
GROUP A STREPTOCOCCAL
• Sudden onset of sore throat • Age 5–15 years • Fever • Headache • Nausea, vomiting, abdominal pain • Tonsillopharyngeal inflammation • Patchy tonsillopharyngeal exudates • Palatal petechiae • Anterior cervical adenitis (tender nodes) • Winter and early spring presentation • History of exposure to strep pharyngitis • Scarlatiniform rash
VIRAL
• Conjunctivitis • Coryza • Cough • Diarrhea • Hoarseness • Discrete ulcerative stomatitis • Viral exanthema

2. Routine use of back-up throat cultures for those with a negative RADT is not necessary for adults in usual circumstances, because of the low incidence of GAS pharyngitis in adults and the risk of subsequent acute rheumatic fever is generally exceptionally low in adults with acute pharyngitis (strong, moderate). Physicians who wish to ensure they are achieving maximal sensitivity in diagnosis may continue to use conventional throat culture or to back up negative RADTs with a culture.
3. Anti-streptococcal antibody titers are not recommended in the routine diagnosis of acute pharyngitis as they reflect past but not current events (strong, high).

Evidence Summary

Acute GAS pharyngitis has certain characteristic epidemiological and clinical features [9, 12] (Table 4). The disorder is primarily a disease of children 5–15 years of age, and, in temperate climates, it usually occurs in the winter and early spring. Patients with GAS pharyngitis commonly present with sore throat (generally of sudden onset), pain on swallowing, and fever. Headache, nausea, vomiting, and abdominal pain may also be present, especially in children. On examination, patients have tonsillopharyngeal erythema, with or without

exudates, often with 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 are specific for GAS pharyngitis. Conversely, the absence of fever or the presence of clinical features such as conjunctivitis, cough, hoarseness, coryza, anterior stomatitis, discrete intra-oral ulcerative lesions, viral exanthema, and diarrhea strongly suggest a viral rather than a streptococcal etiology.

Clinical Diagnosis

There is broad overlap between the signs and symptoms of streptococcal and nonstreptococcal (usually viral) pharyngitis, and the ability to identify streptococcal pharyngitis accurately on the basis of clinical grounds alone is generally poor [12, 19–21]. Therefore, except when obvious viral clinical and epidemiological features are present, a laboratory test should be performed to determine whether GAS is present in the pharynx [9, 21]. Efforts have been made to incorporate the clinical and epidemiological features of acute pharyngitis into scoring systems that attempt to predict the probability that a particular illness is caused by GAS pharyngitis [19, 20, 22]. These clinical scoring systems are helpful in identifying patients who are at such low risk of streptococcal infection that performance of a throat culture or an RADT is usually unnecessary. However, the signs and symptoms of streptococcal and nonstreptococcal pharyngitis overlap too broadly for diagnosis to be made with the requisite diagnostic precision on the basis of clinical grounds alone. Even subjects with all clinical features in a particular scoring system can be confirmed to have streptococcal pharyngitis only about 35%–50% of the time, and this is particularly the case in children [20, 23]. The clinical diagnosis of GAS pharyngitis cannot be made with certainty even by the most experienced physicians, and bacteriologic confirmation is required.

Differential Diagnosis

Nonbacterial Infectious Agents. Viruses are the most common cause of acute pharyngitis (Table 3) [9]. Respiratory viruses, such as adenovirus, influenza virus, parainfluenza virus, rhinovirus, and respiratory syncytial virus, frequently cause acute pharyngitis. Other viral agents of acute pharyngitis include coxsackievirus, echoviruses, and 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 (eg, generalized lymphadenopathy and splenomegaly). Systemic infections with cytomegalovirus, rubella virus, measles virus, and a number of other viral agents may be associated with acute pharyngitis. Human metapneumovirus and human bocavirus may cause lower respiratory tract infection in children, but their respective roles, if any, in causing pharyngitis are unknown [24].

Bacteria. GAS is the most common cause of bacterial pharyngitis, but other bacteria can also cause acute pharyngitis (Table 3). *Arcanobacterium haemolyticum* is a rare cause of acute pharyngitis that may be associated with a rash similar to that seen in scarlet fever, particularly in teenagers and young adults [25, 26]. *N. gonorrhoeae* can occasionally cause acute pharyngitis in sexually active persons, and infections with other bacteria, such as *Francisella tularensis* and *Yersinia enterocolitica*, and mixed infections with anaerobic bacteria (eg, Vincent's angina) are rare causes of acute pharyngitis**.** Other pathogens, such as *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*, are uncommon causes of acute pharyngitis. Other bacterial causes of acute pharyngitis include groups C and G β-hemolytic streptococci and *C. diphtheriae* [27–30].

Group C streptococcus (GCS) is a relatively common cause of acute pharyngitis among college students and adults [28, 29]. In addition to endemic pharyngitis, GCS can cause epidemic food-borne pharyngitis after ingestion of contaminated products, such as unpasteurized cow's milk. Family and school outbreaks of GCS pharyngitis have also been described. Even though there are several well-documented food-borne outbreaks of group G streptococcal (GGS) pharyngitis, as well as a community-wide respiratory outbreak of GGS pharyngitis in children [30], the etiologic role of GGS in acute, endemic pharyngitis remains unclear. Acute rheumatic fever has not been described as a complication of either GCS or GGS pharyngitis. Reports have attempted to link acute glomerulonephritis with GGS pharyngitis, but a causal relationship has not been established. Acute glomerulonephritis as a complication of GCS pharyngitis is extremely unusual. Therefore, the primary reason to identify either GCS or GGS as the etiologic agent of acute pharyngitis is to initiate antibiotic therapy that may reduce the clinical impact of the illness. Currently, there is no convincing evidence from controlled studies of a clinical response to antibiotic therapy in patients with acute pharyngitis and either GCS or GGS isolated from the throat.

Several recent reports have documented the isolation of *Fusobacterium necrophorum* from throat swabs of adolescents and young adults with nonstreptococcal pharyngitis [31–35]. Some studies also suggest a role for *F. necrophorum* in cases of recurrent or persistent pharyngitis (with or without bacteremia or Lemierre's syndrome) [33]. *F. necrophorum* is the causative agent of most cases of Lemierre's syndrome, which requires urgent antibiotic therapy, [33, 35], but at present, the evidence for *F. necrophorum* as a primary pathogen in acute pharyngitis in adolescents and young adults is only suggestive. Further study is required to determine the role of *F. necrophorum* in acute pharyngitis, as well as the necessity for and effectiveness of antibiotic therapy.

As is evident from this list of potential etiologic agents, GAS pharyngitis is the only commonly occurring form of acute pharyngitis for which antibiotic therapy is definitely indicated. Therefore, for a patient with acute pharyngitis, the clinical decision that usually needs to be made is whether or not the pharyngitis is attributable to GAS.

Laboratory Diagnosis

Throat Culture. Culture of a throat swab on a sheep-blood agar plate has been the standard for the documentation of the presence of GAS pharyngitis in the upper respiratory tract and for the confirmation of the clinical diagnosis of acute streptococcal pharyngitis [9, 36, 37]. If performed correctly, culture of a single throat swab on a blood agar plate is 90%–95% sensitive for detection of GAS pharyngitis [37].

Several variables affect the accuracy of throat culture results. For example, the manner in which the swab is obtained has an important impact on the yield of streptococci [37–40]. Throat swab specimens should be obtained from the surface of either tonsils (or tonsillar fossae) and the posterior pharyngeal wall. Other areas of the oral pharynx and mouth are not acceptable sites. Healthcare professionals who try to obtain a throat swab from an uncooperative child without immobilizing the neck may obtain a specimen that is neither adequate nor representative. In addition, false-negative results may be obtained if the patient has received an antibiotic shortly before the throat swab is obtained.

The use of anaerobic incubation and selective culture media may increase the proportion of positive culture results [39], but there are conflicting data in this regard. 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.

Another variable that can affect the throat culture result is the duration of incubation. Once plated, a culture should be incubated at 35°C–37°C for 18–24 hours before reading. Additional incubation overnight at room temperature may identify a number of additional positive throat culture results. Thus, although initial therapeutic decisions may be made on the basis of overnight culture, it is advisable to reexamine plates at 48 hours that yield negative results at 24 hours [41].

The clinical significance of the number of GAS colonies on the throat culture plate is problematic. Although patients with true acute GAS pharyngitis are likely to have more strongly positive cultures than patients who are streptococcal carriers (ie, individuals with chronic GAS colonization of the pharynx), there is too much overlap in this regard to permit accurate differentiation on this basis alone [37].

RADTs. A major disadvantage of throat cultures is the delay (overnight or longer) in obtaining results. RADTs have been developed for the identification of GAS pharyngitis directly from throat swabs, with shorter turnaround time. Rapid identification and treatment of patients with GAS pharyngitis can reduce the risk of spread, allowing the patient to return to school or work sooner, and can reduce the acute associated morbidity [42, 43]. The use of RADTs for certain populations (eg, patients in emergency departments) was reported to significantly increase the number of patients appropriately treated for streptococcal pharyngitis, compared with traditional throat cultures [34].

RADTs currently available are highly specific (approximately 95%) when compared with blood agar plate cultures [38, 43, 44]. False-positive test results are highly unusual, and therefore therapeutic decisions can be made with confidence on the basis of a positive test result [43–45]. Unfortunately, the sensitivity of most of these tests is 70%–90%, compared with blood agar plate culture [43, 44].

The first RADTs used latex agglutination methods, were relatively insensitive, and had unclear end points. Newer tests based on enzyme immunoassay techniques offer increased sensitivity and a more sharply defined end point [43, 44]. More recently, RADTs that use chemiluminescent DNA probes or optical immunoassay have been developed; however, optical immunoassays are no longer commercially available. A variety of RADTs are available, and they are not all equal in their performance characteristics [43, 44].

The practitioner should be aware that, for some of these tests, the Clinical Laboratory Improvement Act of 1988 does not waive the need for certification; use of nonwaived tests requires proper certification of the physician's laboratory. Neither conventional throat culture nor RADTs accurately differentiate acutely infected persons from asymptomatic streptococcal carriers with intercurrent viral pharyngitis. Nevertheless, they allow physicians to withhold antibiotics from the great majority of patients with sore throats for whom results of culture or RADT are negative. This is of extreme importance, because nationally up to 70% of patients with sore throats seen in primary care settings receive prescriptions for antimicrobials [46], while only 20%–30% are likely to have GAS pharyngitis [9, 10, 12].

Both RADTs and throat cultures may be affected by spectrum bias. This refers to the phenomenon that, with a greater pretest probability of GAS pharyngitis, the sensitivities of RADTs and throat culture are greater [44]. Because the sensitivities of the various RADTs are <90% in most studied populations of children and adolescents [38, 43, 44] and because the proportion of acute pharyngitis due to GAS in children and adolescents is sufficiently high (20%–30%), a negative RADT should be accompanied by a follow-up or back-up throat culture in children and adolescents, while this is not necessary in adults under usual circumstances, as noted above.

Measurement of anti-streptococcal antibody titers is often useful for diagnosis of the nonsuppurative sequelae of GAS

pharyngitis, such as acute rheumatic fever and acute glomerulonephritis [47]. However, such testing is not useful in the diagnosis of acute pharyngitis because antibody titers of the 2 most commonly used tests, antistreptolysin O (ASO) and anti-DNase B, may not reach maximum levels until 3–8 weeks after acute GAS pharyngeal infection and may remain elevated for months even without active GAS infection [23, 48].

II. Who Should Undergo Testing for Group A Streptococcal Pharyngitis?

Recommendations

4. Testing for GAS usually is not recommended for children or adults with acute pharyngitis with clinical and epidemiological features that strongly suggest a viral etiology (eg, cough, rhinorrhea, hoarseness, and oral ulcers; strong, high).
5. Diagnostic studies for GAS are not indicated for children <3 years old because acute rheumatic fever is rare in children <3 years old and the incidence of streptococcal pharyngitis and the classic presentation of streptococcal pharyngitis are uncommon in this age group. Selected children <3 years old who have other risk factors, such as an older sibling with GAS infection, may be considered for testing (strong, moderate).

Evidence Summary

GAS as a cause of pharyngitis is most commonly observed in children 5–15 years of age in winter and early spring in temperate climates (ie, November–May), with characteristics as noted above (see special considerations in the diagnosis of acute pharyngitis in adults section below). Many studies have shown that clinical scoring systems can be useful in predicting the likelihood of streptococcal infection [19, 20, 22, 49] but that laboratory confirmation is essential in making a precise diagnosis because physicians often greatly overestimate the probability that GAS is the cause of pharyngitis [21]. A test negative for GAS provides reassurance that the patient likely has a viral cause of pharyngitis. A negative test result also allows the clinician to safely avoid the use of antibiotics. Selective use of diagnostic studies for GAS on the basis of clinical features increases not only the proportion of positive test results but also the proportion of patients who have positive test results and who are truly infected rather than mere carriers of streptococcus [50].

Because of the general increase in rates of resistance to antibiotics, antimicrobial therapy should be prescribed only for proven episodes of GAS pharyngitis [1, 36, 51, 52]. The vast majority of children and adults with acute pharyngitis have a viral etiology and do not need antibiotic treatment, even during peak months. Additionally, many experts support the idea of being selective about which children should have a diagnostic throat culture performed, to avoid identifying carriers rather than acutely infected youngsters. GAS testing should be performed on selected patients with clinical symptoms and signs on physical examination that are suggestive of GAS.

While treatment early in the course leads to a more rapid clinical cure in patients with acute GAS pharyngitis and decreases transmission of GAS to other children, the predominant rationale for treatment of this self-limited illness is to prevent suppurative and nonsuppurative complications [53]. In particular, treatment within 9 days of the onset of illness is effective in preventing acute rheumatic fever (ARF) [53]. However, treatment of pharyngitis does not affect the development of poststreptococcal glomerulonephritis [54].

Special Considerations in the Diagnosis of Acute Pharyngitis in Adults. GAS causes only 5%–15% of cases of acute pharyngitis in adults [9, 10, 55–57]. However, the risk of acute pharyngitis due to GAS among adults is higher for parents of school-age children and for those whose occupation brings them into close association with children. The risk of a first attack of ARF is extremely low in adults, even with an undiagnosed and untreated episode of streptococcal pharyngitis.

Because of these epidemiological distinctions, the use of a clinical algorithm without microbiological confirmation has been suggested as an acceptable alternative basis for diagnosis of infection in adults [36, 57]. In emergency department practice, a 4-factor algorithm predicted a positive result of GAS throat culture with an accuracy of 32%–56%, depending on the number of required clinical features present [22]. However, use of this diagnostic strategy would result in treatment of an unacceptably large number of adults with nonstreptococcal pharyngitis; that is an undesirable result in this age group, which has a low prevalence of GAS pharyngitis and a very low risk of rheumatic fever or rheumatic carditis. However, because of the above noted features of acute pharyngitis in adults, exclusion of the diagnosis on the basis of negative RADT results without confirmation by negative culture results is an acceptable alternative to diagnosis on the basis of throat culture results [36]. The generally high specificity of RADT should minimize overprescription of antimicrobials for treatment of adults. This latter point is of particular importance in view of national data indicating that antibiotics—frequently, the more expensive, broader-spectrum antibiotics—are prescribed for approximately three-quarters of adults who consult community primary care physicians because of a sore throat [14]. Physicians who wish to ensure they are achieving maximal sensitivity in diagnosis may continue to use conventional throat culture or to back up negative RADT results with a culture [20, 58].

Children <3 Years Old With Pharyngitis. It should be noted that GAS infection in children <3 years old is often associated with fever, mucopurulent rhinitis, excoriated nares, and diffuse adenopathy and that exudative pharyngitis is rare in this age group [59].

A recent meta-analysis estimated higher prevalence rates of GAS pharyngitis among school-age children (37%) compared to children <5 years. (24%) [60–63], providing support for routine diagnostic tests in this age group. However, the prevalence of GAS pharyngitis is significantly lower for children <3 years of age, ranging from 10% to 14%, and if a corresponding rise in ASO is required, the prevalence can be as low as 0%–6% [61, 62]. Thus, diagnostic testing for GAS pharyngitis is not routinely indicated in children <3 years of age.

One of the main indications for prompt testing and treatment of GAS pharyngitis is the prevention of ARF. Reports of ARF in children <3 years of age are very rare [17, 64–68]. Of 541 new cases of ARF reported from Salt Lake City, Utah, only 5% involved individuals <5 years of age. For those patients, the median age was 4 years [64]. In countries where ARF is more common than in the United States, the rate among young children is also low [66, 68, 69]. This is thought to be because it may take repeated exposures to GAS or priming of the immune system before there is an immune response to streptococcal pharyngitis that can lead to rheumatic fever [70]. The low prevalence of GAS pharyngitis and the low risk of developing ARF in children <3 years of age limits the usefulness of diagnostic testing in this age group.

However, if a child is <3 years of age and there is household contact with a school-aged sibling with documented streptococcal pharyngitis, then it is reasonable to consider testing the child if the child is symptomatic. Previous family studies demonstrate a high rate of secondary streptococcal infections among household contacts. The likelihood of the spread of infection in a family is as high as 25% if the index subject has symptomatic pharyngitis [11, 71], and studies demonstrate that up to one-third of persons in a semiclosed community developed symptomatic pharyngitis during an outbreak [72–74]. Therefore, if a child is in day care or another setting with a high rate of cases of GAS infections, then it is reasonable to test symptomatic children and treat them if they are found to be positive for GAS.

Recommendations

6. Follow-up posttreatment throat cultures or RADT are not recommended routinely, but may be considered in special circumstances (strong, high).
7. Diagnostic testing or empiric treatment of asymptomatic household contacts of patients with acute streptococcal pharyngitis is not routinely recommended (strong, moderate).

Evidence Summary

When a patient is prescribed an antibiotic for treatment of streptococcal pharyngitis, a clinical response is usually achieved within 24–48 hours of therapy. It is important to note that streptococcal pharyngitis is usually a self-limited disease. Even without treatment, fever and symptoms commonly resolve within a few days of the onset of illness [75–80]. The persistence of symptoms beyond that period suggests either the development of a suppurative complication or that the child may be a chronic carrier of GAS (rather than acutely infected) with an intercurrent community-acquired viral pharyngitis (see question V about streptococcal carriers). Therefore, follow-up cultures are not routinely recommended. Follow-up testing after a course of treatment with an appropriate antibiotic should be reserved for those patients who are at particularly high risk of ARF or who have recurrence of classic symptoms compatible with GAS pharyngitis, as described previously.

Despite the universal susceptibility of GAS to penicillin, 7%–37% of children treated with an appropriate antibiotic for apparent streptococcal pharyngitis have a throat culture positive for GAS at the end of therapy [81–83]. These children are considered bacteriologic failures. Under most circumstances, these children are actually streptococcal carriers, and further antimicrobial therapy is not indicated (see question V about streptococcal carriers).

Asymptomatic Household Contacts

Asymptomatic carriage of GAS has been frequently noted among household contacts of patients with GAS pharyngitis [71–74]. Up to one-third of households include individual(s) who will develop symptomatic GAS pharyngitis that warrants diagnostic testing and treatment [11]. In studies examining the role of antibiotic prophylaxis of household contacts of patients with GAS pharyngitis, penicillin prophylaxis has not been shown to reduce the incidence of subsequent GAS pharyngitis [72, 84, 85], although a small, statistically significant effect on secondary illness has been shown for cephalosporin prophylaxis [84]. Antibiotic use has been associated with adverse side effects such as rash, diarrhea, and, rarely, anaphylaxis, and unnecessary use of broad-spectrum antibiotics leads to concerns about the potential spread of antibiotic-resistant organisms in the population. Given the self-limited nature of GAS pharyngitis, high frequency of GAS throat carriage, limited efficacy of antibiotic prophylaxis, and potential concerns about the direct and indirect risks associated with antibiotic use, routine testing or treatment of asymptomatic household contacts of patients with GAS pharyngitis is not warranted.

RECOMMENDATIONS FOR THE MANAGEMENT OF PATIENTS WITH GAS PHARYNGITIS

III. What Are the Treatment Recommendations for Patients Diagnosed With GAS Pharyngitis?

Recommendations

8. Patients with acute GAS pharyngitis should be treated with an appropriate antibiotic at an appropriate dose for a

duration likely to eradicate the organism from the pharynx (usually 10 days). Based on their narrow spectrum of activity, infrequency of adverse reactions, and modest cost, penicillin or amoxicillin is the recommended drug of choice for those non-allergic to these agents (strong, high).

9. Treatment of GAS pharyngitis in penicillin-allergic individuals may include a first generation cephalosporin (for those not anaphylactically sensitive) for 10 days, clindamycin or clarithromycin for 10 days, or azithromycin for 5 days (strong, moderate).

Evidence Summary

When selecting an antimicrobial for treatment of GAS pharyngitis, important issues to consider include efficacy, safety, antimicrobial spectrum (narrow vs broad), dosing schedule, compliance with therapy (ie, adherence), and cost. These factors influence the cost-effectiveness of antimicrobial therapy.

A number of antibiotics have been shown to be effective in treating GAS pharyngitis (Table 2). These include penicillin and its congeners (eg, ampicillin and amoxicillin), as well as numerous cephalosporins, macrolides, and clindamycin. Penicillin, however, remains the treatment of choice because of its proven efficacy and safety, its narrow spectrum, and its low cost [51, 52, 86, 87]. Penicillin-resistant GAS has never been documented. Amoxicillin is often used in place of penicillin V as oral therapy for young children; the efficacy appears to be equal. This choice is primarily related to acceptance of the taste of the suspension.

In comparative clinical trials, once-daily amoxicillin (50 mg/kg, to a maximum of 1000 mg) for 10 days has been shown to be effective for GAS pharyngitis [88–92]. This somewhat broader-spectrum agent has the advantage of once-daily dosing, which may enhance adherence, and is relatively inexpensive and palatable.

Most oral antibiotics must be administered for the conventional 10 days to achieve maximal rates of pharyngeal eradication of GAS. Currently, the US Food and Drug Administration has approved cefdinir [93, 94], cefpodoxime [95, 96], and azithromycin [97] for a 5-day course of therapy for GAS pharyngitis. However, many studies of short-course cephalosporin therapy lack strict entry criteria, include no assessment of compliance with therapy, and do not include serotypic or genotypic differentiation between infections for which treatment failed and newly acquired infections. In addition, the spectra of these antibiotics are much broader than the spectrum of penicillin, and, even when the antibiotics are administered for short courses, they are more expensive [89]. Therefore, use of these shorter courses of oral cephalosporins cannot be endorsed at this time [51, 89].

Antimicrobials for GAS pharyngitis may be given either orally or parenterally. Intramuscular benzathine penicillin G therapy is preferred for patients deemed unlikely to complete a full 10-day course of oral therapy.

Certain antimicrobials are not recommended for treatment of GAS pharyngitis. Tetracyclines should not be used because of the high prevalence of resistant strains. Sulfonamides and trimethoprim-sulfamethoxazole should not be used because they do not eradicate GAS from patients with acute pharyngitis [98, 99]. Older fluoroquinolones (eg, ciprofloxacin) have limited activity against GAS pharyngitis and should not be used to treat GAS pharyngitis [99]. Newer fluoroquinolones (eg, levofloxacin and moxifloxacin) are active in vitro against GAS, but they are expensive and have an unnecessarily broad spectrum of activity and are therefore not recommended for routine treatment of GAS pharyngitis [100].

A 10-day course of an oral cephalosporin is recommended for most penicillin-allergic individuals (Table 2). Narrow-spectrum cephalosporins, such as cefadroxil or cephalexin, are much preferred to broad-spectrum cephalosporins, such as cefaclor, cefuroxime, cefixime, cefdinir, and cefpodoxime. Most oral broad-spectrum cephalosporins are considerably more expensive than penicillin or amoxicillin, and the former agents are more likely to select for antibiotic-resistant flora [101, 102]. Some penicillin-allergic persons (up to 10%) are also allergic to cephalosporins, and these agents should not be used in patients with immediate (anaphylactic-type) hypersensitivity to penicillin [103].

Clindamycin resistance among GAS isolates in the United States is approximately 1%, and this is a reasonable agent for treating penicillin-allergic patients [104].

An oral macrolide (erythromycin or clarithromycin) or azalide (azithromycin at a dose of 12 mg/kg/day, up to a maximum of 500 mg) is also reasonable for patients allergic to penicillin. Ten days of therapy is indicated for all but azithromycin, which is given for 5 days. Erythromycin is associated with substantially higher rates of gastrointestinal side effects than the other agents. Strains of GAS resistant to these agents have been highly prevalent in some areas of the world and have resulted in treatment failures [105]. In recent years, macrolide resistance rates among pharyngeal isolates in most areas of the United States have been around 5%–8% [104]. One study suggests that 10 days of clarithromycin may be more effective in eradicating GAS pharyngitis than 5 days of azithromycin [82].

USE OF ADJUNCTIVE THERAPEUTICS FOR STREP THROAT

IV. Should Adjunctive Therapy With NSAIDs, Acetaminophen, Aspirin, or Corticosteroids Be Given to Patients Diagnosed With GAS Pharyngitis?

Recommendation

10. Adjunctive therapy is often useful in the management of GAS pharyngitis.

(i) If warranted, use of an analgesic/antipyretic agent such as acetaminophen or an NSAID for treatment of moderate to severe symptoms or control of high fever associated with GAS pharyngitis should be considered as an adjunct to an appropriate antibiotic (strong, high).

(ii) Aspirin should be avoided in children (strong, moderate).

(iii) Adjunctive therapy with a corticosteroid is not recommended (weak, moderate).

Evidence Summary

Multiple studies, including randomized, double-blind, and placebo-controlled studies, support the benefits of NSAIDs such as ibuprofen in reducing fever and pain relative to placebo among both children and adults with pharyngitis. No significant adverse events were noted. In other randomized, double-blind, and placebo-controlled studies, significantly greater pain relief with use of acetaminophen compared with placebo has been documented among both children and adults, although improvement in symptoms was not always equivalent to that obtained through use of ibuprofen [106–109].

Although aspirin has also been shown to reduce pain in adults with upper respiratory tract infection, we recommend against the use of aspirin for pain relief of pharyngitis in children because of the risk of Reye syndrome.

Results from randomized, double-blind, placebo-controlled studies demonstrate that corticosteroids decrease the duration and severity of signs and symptoms in GAS pharyngitis in adults and children, although the actual decrease in pain duration is minimal (approximately 5 hours) [110, 111]. It is difficult to compare the magnitude of the effect across the various studies because of differences in the agent selected, route, and dosage used; method of assessing pain; time of follow-up; and limitations of follow-up by telephone [112]. The effect of concomitant administration of NSAIDs and acetaminophen in these patients is unclear. Although adverse effects of the therapy were not evident in the published data, long-term follow-up had not been done. Given the efficacy of antimicrobials, the self-limited nature of GAS pharyngitis, the efficacy of systemic and some topical analgesics in decreasing the acute symptoms of GAS pharyngitis, and the potential of adverse effects of systemic steroids, we do not recommend use of corticosteroids in therapy of this illness.

A variety of topical agents have been marketed for therapy of acute pharyngitis. These include rinses, sprays, and lozenges. Several contain topical anesthetics, such as ambroxol, lidocaine, and benzocaine, that may give temporary symptomatic relief. Lozenges may be effective but represent a choking hazard for young children [109]. Topical agents for pharyngitis in both children and adults have recently been reviewed [113]. A remedy commonly used in patients old enough to gargle—warm salt water rinses—has not been studied in detail.

V. Is the Patient With Frequent Recurrent Episodes of Apparent GAS Pharyngitis Likely to Be a Chronic Pharyngeal Carrier of GAS?

Recommendations

11. We recommend that clinicians caring for patients with recurrent episodes of pharyngitis associated with laboratory evidence of GAS consider that they may be experiencing >1 episode of bona fide streptococcal pharyngitis at close intervals, but they should also be alert to the possibility that the patient may actually be a chronic pharyngeal GAS carrier who is experiencing repeated viral infections (strong, moderate).
12. We recommend that GAS carriers do not ordinarily justify efforts to identify them nor do they generally require antimicrobial therapy because GAS carriers are unlikely to spread GAS pharyngitis to their close contacts and are at little or no risk for developing suppurative or nonsuppurative complications (eg, acute rheumatic fever; strong, moderate).
13. We do not recommend tonsillectomy solely to reduce the frequency of GAS pharyngitis (strong, high).

Evidence Summary

Because routine posttherapy retesting is no longer advised for patients with acute GAS pharyngitis, only those with recurrent signs and symptoms of acute pharyngitis within weeks or months of completing therapy for an acute pharyngitis are likely to seek reassessment. If such symptomatic patients again have positive culture and/or RADT results, there are several possible explanations: noncompliance with the prescribed antibiotics; a new GAS pharyngeal infection acquired from family contacts, classroom contacts, or other community contacts; or chronic GAS carriage with intercurrent viral infections [114–116]. A second episode of pharyngitis caused by the original infecting strain of GAS cannot be ruled out but is less common [114].

Chronic pharyngeal carriers have GAS present in the pharynx but have no evidence of an active immunologic response to the organism, such as rising anti-streptococcal antibody titers [48, 116]. During the winter and spring in temperate climates, as many as 20% of asymptomatic school-age children may be GAS carriers. They may be colonized by GAS pharyngitis for ≥6 months and during that time may experience episodes of intercurrent viral pharyngitis [115, 117]. Testing of such patients often demonstrates evidence of GAS in the pharynx, and thus they may mimic patients with acute streptococcal pharyngitis. Individuals who are identified as chronic pharyngeal GAS carriers do not ordinarily require further antimicrobial therapy. Carriers appear to be unlikely to spread the organism to their close contacts and are thought to be at very low risk, if any, for developing suppurative or invasive complications or nonsuppurative complications (eg,

Table 5. Treatment Regimens for Chronic Carriers of Group A Streptococci

Route, Drug	Dose or Dosage	Duration or Quantity	Recommendation Strength, Quality[a]	Reference
Oral				
Clindamycin	20–30 mg/kg/d in 3 doses (max = 300 mg/dose)	10 d	Strong, high	[119]
Penicillin and rifampin	Penicillin V: 50 mg/kg/d in 4 doses × 10 d (max = 2000 mg/d); rifampin: 20 mg/kg/d in 1 dose × last 4 d of treatment (max = 600 mg/d)	10 d	Strong, high	[118]
Amoxicillin–clavulanic acid	40 mg amoxicillin/kg/d in 3 doses (max = 2000 mg amoxicillin/d)	10 d	Strong, moderate	[120]
Intramuscular and oral				
Benzathine penicillin G (intramuscular) plus rifampin (oral)	Benzathine penicillin G: 600 000 U for <27 kg and 1 200 000 U for ≥27 kg; rifampin: 20 mg/kg/d in 2 doses (max = 600 mg/d)	Benzathine penicillin G: 1 dose; rifampin: 4 d	Strong, high	[81]

Abbreviation: Max, maximum.

[a]See Table 1 for a description.

acute rheumatic fever) [48, 114, 116]. Additionally, it is much more difficult to eradicate GAS pharyngitis from the throats of carriers than from patients with bona fide acute streptococcal infections [81, 116, 117]. This is particularly true for penicillin or amoxicillin therapy and may also be true for some other antimicrobials [114, 116, 117]. Clinical and epidemiological evidence suggests that, in published studies showing penicillin or amoxicillin to have relatively high failure rates for eradicating GAS pharyngitis, the patient population was likely "contaminated" with chronic carriers [114, 117].

Antimicrobial therapy is not indicated for the large majority of chronic streptococcal carriers. However, there are special situations in which eradication of carriage may be desirable, including the following: (1) during a community outbreak of acute rheumatic fever, acute poststreptococcal glomerulonephritis, or invasive GAS infection; (2) during an outbreak of GAS pharyngitis in a closed or partially closed community; (3) in the presence of a family or personal history of acute rheumatic fever; (4) in a family with excessive anxiety about GAS infections; or (5) when tonsillectomy is being considered only because of carriage. A number of antimicrobial schedules have been demonstrated to be substantially more effective than penicillin or amoxicillin in eliminating chronic streptococcal carriage (Table 5).

In routine practice, it is often difficult to differentiate a GAS carrier with an intercurrent viral infection from a patient with acute streptococcal pharyngitis. Helpful clues include patient age, season, local epidemiological characteristics (eg, the local prevalence of influenza and/or enteroviral illnesses), and the precise nature of the presenting signs and symptoms (Table 4).

In many instances, however, the clinician may not be able to distinguish persistent carriage from acute infection and will elect to administer another course of antimicrobials. For a single episode of pharyngitis associated with laboratory confirmation of GAS that occurs shortly after completion of a course of appropriate antimicrobial therapy, treatment with any of the agents listed in Table 2 is appropriate. Since patient adherence to oral antimicrobial therapy often is an issue, intramuscular benzathine penicillin G should be considered. For these individual second episodes, it is not necessary to obtain additional throat swab specimens for culture after the second course of therapy unless the patient remains or becomes symptomatic or unless one of the special circumstances noted above is present.

An even more challenging clinical circumstance is the person (usually a school-aged child or adolescent) who, within a period of months to years, experiences multiple episodes of acute pharyngitis for which culture and/or RADT results identify GAS. It is likely that most of these patients are chronic streptococcal carriers who are experiencing repeated viral infections. For patients with frequent discrete episodes, information regarding the precise nature of the presenting signs and symptoms (Table 4), the clinical response to antibiotic therapy, and the presence or absence of GAS pharyngitis in cultures of throat swabs obtained during asymptomatic intervals is helpful in distinguishing persistent carriage from recurrent episodes of acute GAS pharyngitis. Serotyping or genotyping of streptococcal isolates recovered from specimens obtained during distinct episodes from an individual patient may also assist in arriving at this determination because a carrier has persistence of the same strain of GAS over time. Unfortunately, such studies are available only from specialized research laboratories and are unlikely to be available within a practical time frame. There have been no definitive controlled studies of treatment of multiple repeated symptomatic episodes of culture-positive acute pharyngitis in the

same person. However, the regimens listed in Table 5 have been reported to result in low rates of bacteriologic failure [81, 118–120]. Continuous antimicrobial prophylaxis is not recommended except to prevent recurrent ARF in patients who have experienced a previous episode of rheumatic fever.

If a physician suspects that "ping-pong" spread of infections is the explanation for multiple recurrent episodes of infections within a family, it may be helpful to obtain throat swabs from all family contacts simultaneously and to treat those for whom culture or RADT results are positive. There is no credible evidence that family pets are reservoirs for GAS pharyngitis or that they contribute to familial spread.

Tonsillectomy may be considered in the rare patient whose symptomatic episodes do not diminish in frequency over time and for whom no alternative explanation for recurrent GAS pharyngitis is evident. However, tonsillectomy has been demonstrated to be beneficial only for a relatively small group of these patients, and any benefit can be expected to be relatively short-lived [121–124].

FUTURE RESEARCH

Future research should focus on the following: (1) improved rapid methods for diagnosis of acute GAS pharyngitis and for distinguishing acute infection from chronic pharyngeal carriage, (2) development of simpler or shorter therapeutic regimens for acute GAS pharyngitis, and (3) development of an affordable, safe, and effective GAS vaccine against the broad spectrum of GAS organisms.

Notes

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