Pharyngitis—Principles of Judicious Use of Antimicrobial Agents

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ABSTRACT. Accurate diagnosis of group A streptococcal pharyngitis and appropriate antimicrobial therapy are important, particularly to prevent nonsuppurative sequelae such as rheumatic fever. Most episodes of sore throat, however, are caused by viral agents. Clinical findings cannot reliably differentiate streptococcal from viral pharyngitis and most physicians tend to overestimate the probability of a streptococcal infection based on history and physical examination alone. Therefore, diagnosis should be based on results of a throat culture or an antigen-detection test with throat culture backup. Presumptively starting therapy pending results of a culture is discouraged because treatment often continues despite a negative test result. Other bacterial causes of pharyngitis are uncommon and often can be diagnosed based on nonpharyngeal findings. Penicillin remains the drug of choice for streptococcal pharyngitis because of its effectiveness, relatively narrow spectrum, and low cost. No group A streptococci are resistant to β-lactam antibiotics. High rates of resistance to macrolides has been documented in several areas; in Finland, decreased national rates of pharyngitis, accounts for 15% of all cases. Diagnosis and treatment of streptococcal pharyngitis should be made based on results of appropriate laboratory tests in conjunction with clinical and epidemiologic findings.

PRINCIPLES

1. Diagnosis of group A streptococcal pharyngitis should not be given to a child with pharyngitis in the absence of diagnosed group A streptococcal or other bacterial infection.

2. A penicillin remains the drug of choice for treating group A streptococcal pharyngitis.

BACKGROUND AND JUSTIFICATION

Sore throat is one of the most common complaints in pediatrics, resulting in millions of physician office visits each year. Group A Streptococcus (S. pyogenes), the leading bacterial cause of pharyngitis, accounts for ~15% of all cases. Diagnosis and treatment of streptococcal pharyngitis are important because antimicrobial therapy initiated within 9 days of onset is effective in preventing acute rheumatic fever. In addition, treatment of group A streptococcal infection may prevent supplicative complications, lead to more rapid resolution of illness, and prevent the spread of infection. Nevertheless, because most episodes of sore throat are caused by viral agents, clinical diagnosis is often made based on symptoms alone. However, a more accurate diagnosis is possible through the use of a throat culture or an antigen-detection test with throat culture backup. Presumptively starting therapy pending results of a culture results in patients receiving unnecessary antibiotic treatment, which can lead to the development of antimicrobial resistance.

The Centers for Disease Control and Prevention (CDC) recommends that all children aged 3 to 18 years with pharyngitis be tested for group A streptococcal infection. The CDC also recommends that children aged 3 to 18 years with pharyngitis be tested for group A streptococcal infection if they are at high risk for complications, such as patients with recurrent episodes of pharyngitis, those with a history of rheumatic fever, and those with a history of Kawasaki disease.

The diagnosis of group A streptococcal pharyngitis is based on the presence of characteristic symptoms, such as fever, sore throat, and cervical lymphadenopathy. A positive throat culture or a rapid antigen-detection test with throat culture backup confirms the diagnosis. Antimicrobial therapy is recommended for children with group A streptococcal pharyngitis to prevent complications, such as rheumatic fever, arthritis, and otitis media.

Macrolide-resistant group A streptococci are a concern in some areas, and the use of a β-lactam antibiotic, such as penicillin, remains the drug of choice for treating group A streptococcal pharyngitis. However, the development of resistance to β-lactam antibiotics is a growing concern, and the use of alternative antibiotics, such as clindamycin, may be necessary in areas with high rates of resistance.
by viral agents, treatment of all children with this illness would result in substantial unnecessary antimicrobial use. The recommendations that follow provide an approach to the diagnosis and treatment of children with pharyngitis that are consistent with judicious antimicrobial use.

EVIDENCE IN SUPPORT OF PRINCIPLES

Diagnosis of Group A Streptococcal Pharyngitis Should Be Made Using a Laboratory Test in Conjunction With Clinical and Epidemiologic Findings

Symptoms of classic streptococcal pharyngitis include acute onset of pharyngeal pain, dysphagia, and fever. Malaise, headache, abdominal pain, and vomiting occur commonly. Rhinorrhea, cough, hoarseness, conjunctivitis, and diarrhea are uncommon and strongly suggest a viral etiology. On examination, the pharynx is erythematous, a patchy exudate often is present on the posterior pharynx and tonsils, and palatal petechiae may be observed. The anterior cervical lymph nodes often are enlarged and tender.

Unfortunately, these clinical findings are neither sensitive nor specific for group A streptococcal infection. When a diagnosis is based on clinical impression alone, physicians generally overestimate the probability that patients have streptococcal infection. Several schema have been developed to improve the ability to predict which patients will have group A streptococcal pharyngitis by scoring clinical and epidemiologic findings. None of these systems, however, identifies accurately children who need treatment and those who do not. Although the negative predictive value of a low score is good and may help guide a physician in deciding when a diagnostic test is needed, the positive predictive value of even the highest score is limited. In the evaluation of one system among adults, only 54% of patients in the most predictive group—those with a history of fever, tonsillar exudate, anterior cervical lymphadenopathy, and an absence of cough—had group A streptococci identified by culture.

Because the clinical presentation of pharyngitis does not predict reliably the etiologic agent, when group A streptococcal infection is suspected, diagnosis should be based on results of a throat swab culture or antigen-detection test with culture back-up. Culture of a throat swab specimen is recommended as the standard for diagnosis. Some studies report the sensitivity of antigen-detection tests to be ≥90% in carefully controlled clinical settings, but such tests often have proved less sensitive in routine clinical practice. Consequently, the American Academy of Pediatrics recommends that if an antigen-detection test is negative in a child with suspected group A streptococcal pharyngitis, a culture also be performed. Because the specificity of antigen-detection tests is high, confirmation of a positive test is not required.

Throat cultures may be false-negative if specimens are obtained or cultured improperly. Samples should be obtained by vigorous swabbing of both tonsillar surfaces or fossae and the posterior pharynx; swabbing the soft palate and uvula should be avoided, because it dilutes the inoculum. Culture methods are important as well. In one study, results of throat cultures performed in five physicians’ offices were compared with a duplicate swab cultured at a reference laboratory. The sensitivities of cultures performed in the offices ranged from 73% to 100%; errors occurred both in isolating group A streptococci and in correctly identifying the organism. The sensitivity of culture also has been reported to vary depending on the laboratory methods used. For both culture and antigen detection, the sensitivity of the test is dependent on the quality of the specimen, how well the assay is performed, and the experience of the person reading the results.

Survey results indicate that many physicians initiate antimicrobial therapy for pharyngitis pending results of throat culture and that antimicrobial therapy often is continued despite cultures being reported as negative. This approach results in substantial antimicrobial overuse and obviates the benefits of performing a culture. If antibiotics are provided pending results of culture, physicians should be diligent in contacting parents if cultures are negative and should inform them to stop therapy and discard any remaining antibiotics.

Because early antimicrobial therapy may limit transmission of illness if the infection is caused by group A streptococci and may facilitate a child’s return to school or day care, appropriate therapy should be initiated as soon as the diagnosis is supported by a laboratory test. It is unclear, however, whether immediate therapy offers a clinical benefit compared with symptomatic treatment, and no evidence suggests that early antimicrobial therapy decreases recurrent infection or is necessary to prevent acute rheumatic fever. Negative consequences of empirically starting therapy include selection of resistant bacterial pathogens, the risk of hypersensitivity or other adverse reactions, and cost. Use of a rapid antigen-detection test can help clinicians resist pressure for immediate therapy, because a negative result may facilitate immediate return to school or day care.

Antimicrobial Therapy Should Not Be Given to a Child With Pharyngitis in the Absence of Diagnosed Group A Streptococcal or Other Bacterial Infection

Viral agents cause most pharyngitis episodes. Even in patients with pharyngeal exudate and fever, group A streptococci account for a minority of infections. In one study, diagnostic tests for bacterial and viral pathogens were performed on 110 children who had exudative pharyngitis and fever and had not been treated previously with antibiotics. Group A streptococci were isolated from only 12% of children, whereas viral infection was documented from 31%. In addition, viral agents for which diagnostic testing was not available, including rhinovirus and coronavirus, may have accounted for infection in some of the children in whom no etiologic agent was identified. The predominance of viral infection was especially noted among children who were <3 years of age—a
group in whom classical group A streptococcal pharyngitis occurs less often.

Pharyngeal irritation occurs frequently in persons with rhinovirus, corona virus, parainfluenza, influenza, adenovirus, and Epstein–Barr virus infection.26 The signs and symptoms of pharyngitis associated with these viral infections overlap substantially with those of group A streptococcal pharyngitis; however, differences in clinical presentation also may exist. Children with viral pharyngitis often have prominent extrapharyngeal signs and symptoms such as nasal discharge, cough, and hoarseness. Adenoviral infection, a common cause of prolonged exudative pharyngitis, may be accompanied by conjunctivitis (pharyngoconjunctival fever), whereas an Epstein–Barr virus infection may have other signs of infectious mononucleosis (eg, generalized lymphadenopathy, splenomegaly). Coxsackie viruses and herpes simplex viruses often cause stomatitis as well as pharyngitis; vesicular or ulcerative lesions may be noted on examination.26

Bacteria other than group A Streptococcus are rare causes of pharyngitis, and many such infections can be recognized by extrapharyngeal signs.1 Other β-hemolytic streptococci (groups C and G) may be carried in the pharynx asymptomatically or may cause infection resembling that caused by group A streptococci; the course of these infections is self-limited, and rheumatic fever does not occur. These β-hemolytic streptococci could be identified by culture but not by an antigen-detection test. Neisseria gonorrhea pharyngitis is rare and typically occurs among adolescents; a history of sexual activity would be suggestive of this etiology, and pharyngitis may be accompanied by signs of genital infection or a rash. Arcanobacterium haemolyticum infection is uncommon in the United States, characteristically occurs in adolescents, and often presents with a scarlatiniform rash.27 Diphtheria is a rare cause of pharyngitis in well-immunized populations and may be recognized by an asymmetric gray pharyngeal membrane that may extend beyond the borders of the anterior tonsillar pillars onto the soft palate and/or the uvula. Because each of these etiologic agents is uncommon and sequelae such as acute rheumatic fever do not occur, there is no rationale for empiric antimicrobial therapy of pharyngitis in children.

The significance of Mycoplasma pneumoniae and Chlamydia pneumoniae as causes of pharyngitis is unclear; these infections usually are accompanied by other signs of respiratory illness, especially cough. The benefit of antimicrobial therapy for the pharyngitis caused by these agents has not been documented.

Because the large majority of pharyngitis episodes are not caused by group A streptococci, empiric antimicrobial therapy would result in substantial overtreatment. The widespread availability of accurate, inexpensive, diagnostic tests for group A streptococcal infections makes a diagnostic strategy of culture and/or antigen-detection testing for children with suspected streptococcal pharyngitis both effective and cost-effective,28 and represents an optimal approach to avoiding the overuse of antibiotics. This strategy has been presented in algorithm form.1

Penicillin Remains the Drug of Choice for Treating Group A Streptococcal Pharyngitis

Penicillin has proven highly effective as therapy for group A streptococcal pharyngitis and in preventing acute rheumatic fever. Because of its safety, efficacy, relatively narrow spectrum, and low cost, it remains the drug of choice for this indication. Amoxicillin is an acceptable alternative and often is prescribed because it is more palatable than penicillin and the cost is comparable. Because of its broader antimicrobial spectrum, however, use of amoxicillin results in greater selective pressure for the development of antimicrobial resistance. Penicillin therapy, administered for 10 days, results in bacteriologic and clinical cure in ~90% of children with group A streptococcal pharyngitis.29 Shorter courses of therapy have been less effective.30,31 Although microbiologic cure rates are slightly higher in children treated with cephalosporins,32 this may reflect greater efficacy in eradicating the organism from children who actually are carriers rather than improved outcome in those with acute infection.29 Carriers are at very low risk for developing acute rheumatic fever and transmitting infection; therefore, the excess cost of cephalosporin therapy and the greater selective pressure for resistance associated with use of these broader-spectrum agents are disadvantages that outweigh the small increment in group A streptococcal eradication. To date, no group A streptococci resistant to β-lactam antibiotics have been identified. Resistance to erythromycin, an alternative therapy for patients who are allergic to penicillin, has been reported in several areas.33–35 In both Finland and Japan, increased rates of erythromycin resistance occurred coincident with increasing levels of macrolide use. As macrolide use subsequently declined—in Finland as the result of national guidelines recommending decreased use of erythromycin for respiratory and skin infections—so too has the proportion of erythromycin-resistant group A streptococci.34,35 Because resistance to extended spectrum macrolides (eg, clarithromycin) or azolides (eg, azithromycin) would be similar to that for erythromycin and these agents exert selective pressure for resistance over a broader range of bacterial pathogens, their use in treating pharyngitis should be discouraged.

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REFERENCES

Acute Sinusitis—Principles of Judicious Use of Antimicrobial Agents

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ABSTRACT. Establishing an accurate diagnosis of bacterial sinusitis is challenging but critical, because viral rhinosinusitis is at least 20 to 200 times more common than bacterial infection of the sinuses. Strict criteria for clinical diagnosis that require either prolonged and persistent symptoms or an acute severe presentation are supported with published evidence.

Radiographic imaging of the sinuses should be used only in very selected circumstances. A majority of patients with the common cold will meet radiographic criteria for sinusitis early in the course of their illness. For patients meeting these strict criteria, an appropriate narrow-spectrum antimicrobial agent will be of modest benefit compared with symptomatic treatment alone. Pediatrics 1998;101:174–177; sinusitis, diagnosis, antimicrobial therapy, mucopurulent rhinitis, antimicrobial resistance, pediatrics.

ABBREVIATIONS: URI, upper respiratory tract illness; CT, computed tomography.

PRINCIPLES

1. Clinical diagnosis of bacterial sinusitis requires the following: prolonged nonspecific upper respiratory signs and symptoms (ie, rhinosinusitis and...
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