

Principles of Appropriate Antibiotic Use for Acute Pharyngitis in Adults

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In this guideline, we present the evidence and make specific recommendations on how clinicians can distinguish and diagnose pharyngitis caused by group A β -hemolytic streptococcus (GABHS). We also discuss when antibiotic use is beneficial and which antibiotics should be used. This guideline will not cover gonococcal pharyngitis and diphtheria, for which the appropriateness of immediate antibiotic treatment is well established. The numbers in square brackets are cross-references to the numbered sections in the accompanying background paper, "Principles of Appropriate Antibiotic Use for Acute Pharyngitis in Adults: Background," which is part 2 of this guideline (see pages 509-517).

ACUTE PHARYNGITIS

Acute pharyngitis accounts for 1% to 2% of all visits to outpatient departments, physician offices and emergency departments. A wide range of infectious agents produces acute pharyngitis, but viruses are the most common cause. Approximately 5% to 15% of adult cases are caused by GABHS. In some patients, it can be important to identify an infectious cause other than GABHS (for example, gonococcal pharyngitis, Epstein-Barr virus, and acute HIV infection), but in the vast majority of cases, acute pharyngitis in an otherwise healthy adult is self-limited and rarely produces significant sequelae [1.1].

Antimicrobial agents are prescribed to a substantial majority of patients with acute pharyngitis because of perceived patient expectations or physician desires to avoid such potential complications as rheumatic fever and acute glomerulonephritis. Consequently, this discussion will focus on the diagnosis and treatment of acute GABHS pharyngitis in adult patients. These guidelines do not apply to patients with a history of

rheumatic fever, valvular heart disease, immunosuppression, or recurrent or chronic pharyngitis (symptoms > 7 days) or to patients whose sore throats are not due to acute pharyngitis. They are also not intended to apply during a known epidemic of acute rheumatic fever or streptococcal pharyngitis, or in nonindustrialized countries in which the endemic rate of acute rheumatic fever is much higher than in the United States [1.2].

Although it has been more than 50 years since treatment of streptococcal pharyngitis with penicillin was shown to prevent acute rheumatic fever, diagnosing GABHS infection remains a subject of controversy. This is in part because the best criterion standard for the diagnosis has not been definitively established, and testing for a significant increase in antistreptolysin titers and use of throat swab cultures cannot provide "real-time" results—that is, results that are available when a decision regarding antibiotic use must be made. Because only patients with GABHS (and a few other rare bacterial agents) benefit from antimicrobial therapy, the goal of the diagnostic evaluation should be to predict which patients have a high likelihood of GABHS pharyngitis.

Diagnosis

Although recovery of GABHS from throat cultures is reported in many clinical trials and may be the best available predictor of treatment response, it has poor test-retest agreement; does not always correlate with antistreptolysin titers; and produces results that vary depending on technique, the site in which the sample is obtained and plated, the culture medium, the conditions in which the culture is incubated, and whether results are checked at 24 or 48 hours. Throat cultures also fail to distinguish acute infection from the carrier state. Furthermore, because culture results are not avail-

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able at the time of the index visit, and a delayed decision about use of antibiotics eliminates the primary benefit of antimicrobial therapy in adults (symptom relief), we do not include use of throat culture for clinical decision making in this set of management principles. In addition, there are several reasonable approaches to the diagnosis of GABHS in an otherwise healthy adult, such as use of clinical criteria alone or use of rapid antigen testing as an adjunct to clinical screening. Either of these strategies is associated with reasonable diagnostic accuracy (approximate sensitivity $\geq 70\%$, specificity $\geq 70\%$) and allows treatment decisions to be made early in the course of illness, when patients can receive symptomatic benefit [4.0–4.2].

Although use of clinical screening (history and physical examination) alone would leave some patients with GABHS untreated and would result in overtreatment of others, it would prompt treatment of most patients with GABHS while dramatically decreasing excess antibiotic use. The most reliable predictors include tonsillar exudates, tender anterior cervical lymphadenopathy, absence of cough, and history of fever. Several studies examining these four criteria in a clinical decision rule indicate that in patients who have three or four of the criteria, the sensitivity and specificity (compared with those of throat culture) are approximately 75% and 75%, respectively [4.2.1].

Rapid antigen tests for GABHS, when compared with the “criterion standard” of throat culture, have widely variable reported sensitivity (58% to 96%) and specificity (63% to 100%), depending on the type of test and practice setting of the trial. These rapid antigen tests can be done at the bedside, and treatment decisions can be made in real time. The potential advantage of the rapid antigen tests compared with clinical models is that they have approximately the same sensitivity and perhaps greater specificity for predicting results of throat culture. The disadvantage is that many patients would need to be tested to achieve the possible gain in specificity beyond that provided by clinical information alone. This would shift economic costs from a few extra prescriptions to many extra rapid antigen tests. Performing rapid antigen testing only in individual patients with an intermediate clinical probability of GABHS (those with three, or perhaps two, of the four clinical variables) and withholding antimicrobial agents from those with negative results would decrease antimicrobial use, com-

pared with a clinical decision alone, at the cost of potentially undertreating an additional small group of patients with GABHS. Unfortunately, although many physicians currently perform rapid antigen tests, there is evidence that they frequently prescribe antimicrobial agents even when test results are negative [4.2.2].

Treatment

Reasons to consider prescribing antimicrobials to treat streptococcal pharyngitis include a desire to prevent rheumatic fever, prevent acute glomerulonephritis, prevent suppurative complications, decrease contagion, and ameliorate symptoms. Although reported rates may underestimate the true incidence of acute rheumatic fever, repeatedly low and unchanging reported rates over more than a decade prompted the Centers for Disease Control and Prevention to drop acute rheumatic fever from active national surveillance in 1994. It is still important to consider local epidemics and to be prepared to revise the approach to treatment if evidence of an outbreak exists, although the number of discrete outbreaks of acute rheumatic fever in the United States is very small and should not overly influence physician behavior. Similarly, poststreptococcal acute glomerulonephritis does occur but is extremely rare, even in the absence of antibiotic treatment. Furthermore, there is no evidence that antimicrobial therapy decreases incidence of this complication [3.0, 3.1].

The incidence of suppurative complications, regardless of treatment with antimicrobials, is also small. The most common complication today is peritonsillar abscess (“quinsy”). Recent clinical trials provide some evidence that targeting antimicrobials to a subset of patients with higher clinical likelihood of GABHS may prevent quinsy. In another recent review of GABHS pharyngitis in practice, however, the authors reported that the risk for peritonsillar abscess was not reduced because many affected patients do not present for care until after the complication has developed [3.2, 3.3].

Streptococcal infection often occurs in epidemics, and contagion is a problem in areas of overcrowding or close contacts. Antimicrobial agents lead to far greater microbiological eradication of streptococcus by 48 to 72 hours. However, the presymptomatic incubation period for GABHS is 2 to 5 days, during which the infection can be unknowingly transmitted to others. The effect of treatment on spread of disease in a noninstitutionalized

adult population is unknown. Nevertheless, it is not unreasonable to consider whether an adult is living in close quarters with small children when making clinical decisions about treatment [3,4].

The relief of patient suffering is an appropriate concern of physicians as well as patients. Antimicrobial agents, when instituted within 2 to 3 days of symptom onset, hasten symptomatic improvement among patients in whom throat culture ultimately grows GABHS or in populations in which a high likelihood of GABHS pharyngitis is identified clinically, but not in those with a negative culture. Symptoms seem to resolve 1 to 2 days sooner when antipyretics and other comfort measures are also instituted. One recent trial among unselected patients with acute pharyngitis found that symptom duration was strongly related to patient satisfaction, and patient satisfaction was closely related to whether the physician addressed the patient's concerns rather than to use of antibiotics. This further supports limiting antimicrobials to the subset of patients most likely to benefit and reemphasizes the importance of the quality of the physician-patient interaction [3,5].

If antimicrobial treatment is to be instituted, physicians should choose an agent with the narrowest possible spectrum of action that still covers GABHS. Thus, penicillin is the first choice for patients without a penicillin allergy, and erythromycin is the first choice for penicillin-allergic patients. To date, there is no evidence of GABHS resistance to or tolerance of penicillin, and erythromycin resistance rates are low in the United States [6,0].

Summary

Antimicrobial treatment of GABHS pharyngitis leads to a decreased risk for already rare complications and a decrease in the duration of some patient symptoms by 1 or 2 days. Symptomatic improvement requires that treatment begin within 48 to 72 hours of symptom onset. For otherwise healthy adult patients with GABHS pharyngitis who are averse to antimicrobial agents or medication, it is reasonable to suggest a policy of no antimicrobial treatment and expect few measurable adverse consequences. An appropriate strategy in most adult patients is to limit antimicrobial therapy to the minority of adults with a high likelihood of GABHS pharyngitis, who are most likely to benefit.

RECOMMENDATIONS

Recommendation 1. All patients with pharyngitis should be offered appropriate doses of analgesics, antipyretics, and other supportive care.

The overwhelming majority of adults with acute pharyngitis have self-limited illness, which would do well with supportive care only. Some suggested supportive care includes analgesics (both systemic and topical), antipyretics, and gargles.

Recommendation 2. Physicians should limit antimicrobial prescriptions to patients who are most likely to have GABHS.

Group A β -hemolytic streptococcus is the causal agent in approximately 10% of adult cases of pharyngitis. The benefits of antibiotic treatment of adult pharyngitis are limited to patients with GABHS infection. Recommended strategies include a) empirical antibiotic treatment of adults with at least three of four clinical criteria (history of fever, tonsillar exudate, tender anterior cervical lymphadenopathy, and absence of cough) shown to be associated with GABHS pharyngitis and nontreatment of all others; or b) empirical treatment of adults with all four clinical criteria, rapid antigen testing of patients with three (or perhaps two) clinical criteria, and treatment of those with positive test results and nontreatment of all others.

Recommendation 3. The preferred antimicrobial agent for treatment of acute GABHS pharyngitis is penicillin, or erythromycin in penicillin-allergic patients.

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