Although pharyngitis caused by the group A beta-hemolytic streptococcus (GAS) is one of the most common human infections and has been studied intensively for decades, considerable debate remains about the most appropriate method of diagnosis and treatment. Most cases of acute pharyngitis seen in primary care practice are viral in cause; GAS is the only commonly occurring cause of sore throat for which antimicrobial therapy is indicated. Moreover, the signs and symptoms of GAS pharyngitis and viral pharyngitis overlap so broadly that precise diagnosis on clinical grounds is difficult. For this reason, practice guidelines issued by the American Heart Association (1), American Academy of Pediatrics (2), and Infectious Diseases Society of America (3) advocate microbiological confirmation of the diagnosis by throat culture or a rapid antigen diagnostic test. Because the latter is generally less sensitive than throat culture, these guidelines suggest that a negative result be backed up by throat culture. The necessity for this has been questioned, however (4), especially because supposedly more sensitive rapid tests, such as optical immunoassay (OIA), have appeared on the market (5).

Several clinical algorithms help clinicians assess the probability that a given adult patient with acute pharyngitis has GAS infection (6, 7). Recently, a practice guideline of the American College of Physicians (ACP) recommended that one such algorithm may be used to diagnose GAS pharyngitis in adults on clinical grounds alone, eschewing microbiological testing. The Centers for Disease Control and Prevention and the American Academy of Family Physicians have also approved this recommendation.

This algorithm, developed by Centor and associates (8), relates the probability of GAS pharyngitis to four clinical findings: tonsillar exudates, tender anterior cervical adenopathy, absence of cough, and history of fever. The ACP guideline was published in two papers (9, 10) that have slightly differing recommendations. The ACP guidelines allow for using a rapid antigen diagnostic test or, alternatively, empirically treating patients who meet three or four Centor criteria and nontreatment of all others. I think it is unlikely that clinicians will perform cultures or rapid tests when a practice guideline endorsed by so many prestigious organizations states that clinical criteria suffice.

According to the National Ambulatory Care Survey, between 1989 and 1999 adults made an estimated 6.7 million visits to primary care office-based physicians with the chief symptom of sore throat (11). Thus, issues of appropriate diagnosis and treatment have major public health import. Minimizing unnecessary antimicrobial therapy in adults is highly desirable because the prevalence of GAS pharyngitis in this group is low (estimated to be in the 10% range) and the risk for the most feared sequela of this condition, acute rheumatic fever, is remote.

In this issue, Neuner and colleagues (12) report a detailed cost-effectiveness analysis of the diagnosis and management of U.S. adults with pharyngitis. The authors extensively reviewed the pertinent literature and constructed a careful analysis using the best available evidence on the magnitude of the relevant variables. They compared five management strategies: no testing or treatment, empirical treatment with penicillin, throat culture using a two-plate selective technique, OIA backed up by culture if OIA results are negative, or OIA alone. They further examined the effect of the Centor clinical prediction rule on these strategies. Assuming a GAS prevalence of 10% in adults with pharyngitis, they found empirical treatment to be the least effective in terms of quality-adjusted life-days. Although all other strategies were similarly effective, culture was the most cost-effective. When these findings were subjected to sensitivity analysis, empirical treatment based on the Centor criteria was neither most effective nor least expensive at any GAS pharyngitis prevalence likely to be found in U.S. adult populations.

The stated goal of the ACP guideline is “dramatically decreasing excess antibiotic use” (10). As a result, examining in further detail the consequences of the empirical therapy recommendation would be helpful. In Centor and colleagues’ study, only 10% of “adult” patients (>15 years of age) presenting to an urban emergency department met all four criteria, and throat culture was positive in 56% of these patients. In the 20% of patients meeting three criteria, the probability of a positive culture was only 30% to 34%. Therefore, the combined positive predictive value associated with meeting three or four of the clinical criteria would be approximately 40%. This means that 60% of the patients treated empirically would have had a negative result on GAS culture or a rapid antigen diagnostic test (13, 14). Use of the Centor algorithm does indeed identify patients whose risk for GAS infection is so low that microbiological testing or antibiotic treatment is unnecessary.

As pointed out by Neuner and colleagues (12), the risk for preventable severe supplicative or nonsuppurative infections in adults with GAS pharyngitis is small. Antimicrobial therapy may truncate the illness, but only if started early in the illness and only by a day or two. Such treatment may decrease spread of the infection to close contacts. Given this limited benefit, the main purpose of any diagnostic strategy for adults should be to minimize unnecessary antimicrobial therapy. This latter point is of particular importance in view of national data indicating that antibiotics—frequently the more expensive, broader-spectrum ones—are prescribed for approximately three quarters
of adults who consult community primary care physicians because of a sore throat (11). After considering these facts, the Infectious Diseases Society of America, in a revised practice guideline (3) not cited by Neuner and colleagues, now advocates use of the rapid antigen diagnostic test alone to confirm the diagnosis of GAS pharyngitis in adults. This strategy is simpler than throat culture and yields results that allow rapid treatment decisions. The generally high specificity of a rapid test should minimize over-prescription of antibiotics for adults with acute pharyngitis. It is comforting to see that in Neuner and associates’ analysis, the performance of a rapid diagnostic test without culture backup was similar to that of a strategy requiring culture confirmation of negative rapid test results.

There are several caveats. First, a positive result on throat culture or rapid test only confirms GAS presence in the pharynx and does not in itself differentiate acute infection from chronic carriage. In everyday primary care practice, however, this should have a negligible effect because carriage rates in adults are low. Second, the prevalence of positive throat cultures may be higher than the usually quoted 5% to 10% in adults who have intensive exposure to children (such as mothers of school-aged children and schoolteachers); as a result, a higher index of suspicion, and perhaps backup of rapid antigen diagnostic testing with throat culture, might be warranted in such persons.

Once a test result is positive, the American Heart Association, American Academy of Pediatrics, and Infectious Diseases Society of America recommend penicillin as the drug of choice for nonallergic patients. Particularly undesirable is the practice of prescribing the newer macrolide agents as first-line empirical therapy for febrile patients with upper respiratory tract infections (15). While penicillin-resistant group A β-hemolytic streptococci have never been recovered from any clinical source (16), macrolide resistance develops rapidly in communities that use these drugs extensively (17). Fortunately, such resistance has to date been reported from only a few places in the United States (18, 19), but constant surveillance is necessary. The ultimate test of the most cost-effective and beneficial strategy for managing acute GAS pharyngitis would of course be a controlled clinical trial. Indeed, the authors of the ACP guidelines suggest that prospective studies should be conducted to determine relevant patient outcomes and costs (9). Unless and until such studies are performed, and for the reasons outlined above, I do not believe it is prudent to rely exclusively on clinical criteria for diagnosis and management of GAS pharyngitis.

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References


