Diagnosis of Group A Streptococcal Pharyngitis

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Acute pharyngitis is one of the most common reasons children are seen by a physician. Group A beta-hemolytic streptococci (GABHS) are the most common cause of bacterial pharyngitis and this infection is the only common form of acute pharyngitis that requires antimicrobial therapy. However, most cases of acute pharyngitis are caused by viral agents. Therefore, when confronted with a patient with acute pharyngitis, the clinical decision that usually needs to be made is whether the pharyngitis is attributable to GABHS. GABHS pharyngitis is important because of the acute morbidity associated with it, and because it may be followed by the nonsuppurative sequelae (acute rheumatic fever or acute glomerulonephritis). GABHS is spread by person-to-person contact with infectious nasal or oral secretions, and transmission is more common in situations of crowding such as schools.

**Using Epidemiologic and Clinical Findings to Decide When to Test for GABHS**

When attempting to decide whether to perform a throat culture or rapid antigen detection test on a patient presenting with acute pharyngitis, a careful consideration of the epidemiologic and clinical findings should take place (Table). GABHS pharyngitis is primarily a disease of children between 5 and 15 years of age, so this is the age range when throat swabs have most value. In temperate climates, GABHS is most common in the winter and early spring. An awareness of a high prevalence of GABHS infections in the community is helpful, and should reduce the threshold for a diagnostic test. The same is true for a history of close contact with a well-documented case of GABHS pharyngitis.

Patients with GABHS pharyngitis commonly present with the sudden onset of a sore throat, pain on swallowing, and fever. Headache, nausea, vomiting, and abdominal pain (especially in children) may also

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**Educational Objectives**

1. Describe the clinical and epidemiologic features of group A streptococcal pharyngitis.
2. Review the role of rapid antigen tests and blood agar plate cultures in the management of children with acute pharyngitis.

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be present. On examination, these patients have been more likely to demonstrate tonsillopharyngeal erythema with or without exudate, a red, swollen uvula, petechiae on the palate, and tender, enlarged anterior cervical lymph nodes, as compared to those with usual pharyngitis. Tonsils, if visible, are usually described as enlarged and erythematous with patchy exudates on their surfaces. The papillae of the tongue may be red and swollen, leading to the designation “strawberry tongue.”

Younger children may have a more prolonged course following infection with GABHS. They tend to present with chronic, low-grade fever, generalized lymphadenopathy, and coryza with crusting below the nares and little or no evidence of pharyngeal inflammation. This infantile form of GABHS upper respiratory infection has been called streptococcosis.

When a fine, diffuse erythematous rash accompanies the acute GABHS pharyngitis, the illness is called scarlet fever. Most pediatricians will initiate treatment for GABHS based solely on a chemical diagnosis of scarlet fever, although a diagnostic test may be obtained if there is any uncertainty. Scarlet fever is rarely seen in children younger than 3 years of age and is less common in adults than in children. The rash of scarlet fever has a texture similar to fine sandpaper and blanches with pressure. The face is usually flushed but without actual involvement with the rash. The area around the mouth remains pale in comparison to the extremely red cheeks, giving the appearance of “circumoral pallor.” The rash usually appears about 24 hours after the onset of symptoms and is noticed initially on the upper chest. The flexor skin creases, especially in the antecubital fossae, may be unusually prominent (Pastia’s lines). Within Pastia’s lines, small petechiae can sometimes be seen and can be induced by placing a tourniquet on the upper arm. The erythema begins to fade within a few days with treatment, and, within a week of onset, desquamation may occur. The desquamation begins on the face and progresses downward, often resembling that seen after a mild sunburn. Occasionally sheet-like desquamation may occur around the free margins of the finger nails, the palms, and the soles.

THE ACCURACY OF THE CLINICAL DIAGNOSIS OF GABHS PHARYNGITIS

With the exception of the rash of scarlet fever, none of the above clinical findings is specific for GABHS pharyngitis and may occur with other forms of acute pharyngitis as well. The presence of other clinical features such as conjunctivitis, cough, hoarseness, coryza, anterior stomatitis, discrete ulcerative lesions, viral exanthem, and diarrhea strongly suggests a viral agent rather than GABHS as the etiology.

Being selective about when to use diagnostic studies for GABHS pharyngitis will increase the proportion of positive results, and the proportion of patients with positive test results who have a clinical infection, rather than those who are merely streptococcal carriers. Diagnostic testing usually not be performed on patients with acute pharyngitis when the clinical and epidemiologic findings do not suggest GABHS. The negative predictive value in their absence is usually high.

In contrast, the positive predictive value of these clinical and epidemiologic findings is relatively low. Efforts have been made to incorporate clinical and epidemiologic findings of acute pharyngitis into scoring systems that attempt to predict the probability that a particular illness is caused by GABHS. However, at best these clinical scoring systems predict positive results of throat cultures or rapid antigen tests no more than 80% of the time. Therefore, the correct diagnosis of GABHS pharyngitis cannot be made with consistency based on clinical findings. Even the most experienced physicians must rely on bacteriologic confirmation.

The clinical assessment of the pharyngeal findings in most of these earlier investigations was reported in relatively general terms (eg, “abnormal pharynx”), and little attention was paid to specific abnormalities of the uvula, tonsils, or pharyngeal mucosa. To determine if a careful examination of specific pharyngeal findings could allow one to accurately distinguish between viral and GABHS pharyngitis, we recently examined, using otoscopic lens magnification, 192 children presenting with acute pharyngitis. We looked for the presence of nine specific pharyngeal findings. Of the 192, 133 (89%) had GABHS isolated from their throat culture. There was no significant difference in the proportion of children with GABHS and non-GABHS pharyngitis who had palatal petechiae. Children with
GABHS pharyngitis were significantly more likely than those with non-GABHS pharyngitis to have pharyngeal erythema, palatal enanthern, uvular erythema, uvular petechiae, uvular enanthern, uvular edema, tonsillar erythema, and tonsilar exudate ($P < 0.01$). The sensitivities and positive predictive values for these eight pharyngeal findings for identifying GABHS ranged from 0.37 to 0.95 and from 0.73 to 0.91, respectively. "Doughnut" lesions, reported by some to be diagnostic of GABHS pharyngitis, were present in only five (3%) of the children with GABHS pharyngitis and in none with non-GABHS pharyngitis. The positive predictive values of various combinations of two or three of these pharyngeal findings were greater than 90%. However, these combinations were never present in more than 30% to 40% of the patients with GABHS pharyngitis, and the negative predictive values of these combinations were never greater than 50% to 60%.

THROAT CULTURE

Culture of a throat swab on a sheep blood agar plate remains the standard for documenting GABHS in the upper respiratory tract and for confirming the clinical diagnosis of acute GABHS pharyngitis. If performed correctly, a single throat swab cultured on a blood agar plate has a sensitivity of 90% to 95% in detecting the presence of GABHS in the pharynx. Several variables may impact the accuracy of the throat culture. For example, the manner in which the swab is obtained has an important impact on the yield of GABHS. Throat swab specimens should be obtained from the surface of both tonsils (or tonsillar fossae) and from the posterior pharyngeal wall. Other areas of the oral pharynx and mouth are unacceptable, and these sites should not be touched either before or after culturing the appropriate areas. Health care providers who compromise in trying to obtain a throat swab from an uncooperative child may obtain a specimen that is neither adequate nor representative. False-negative throat culture results may be obtained if the patient has received antibiotics either shortly before or at the time the throat swab is taken. The use of anaerobic incubation and selective culture media has been reported to increase the proportion of positive cultures. However, the data regarding the impact of the atmosphere of incubation and the culture media are conflicting, and, in the absence of a definite benefit, the increased cost and effort associated with anaerobic incubation and selective culture media is difficult to justify, particularly for physicians processing throat cultures in their own offices.

Another variable that can impact the yield of the throat culture is the duration of incubation. Once plated, cultures should be incubated at 35° to 37° C for 18 to 24 hours prior to reading. An additional overnight incubation at room temperature will identify a considerable number of positive throat cultures that would not otherwise have been identified. Therefore, although initial therapeutic decisions may be made on the basis of an overnight culture, it is advisable to reexamine plates, that are negative at 24 hours, and again at 48 hours.

The clinical significance of the number of colonies of GABHS present on the throat culture plate is problematic. Although patients with bona fide acute GABHS pharyngitis are likely to have more strongly positive cultures than patients who are streptococcal carriers, there is so much overlap that this differentiation cannot be made accurately on the basis of degree of positivity of the throat culture alone.

It is important to determine whether a betahemolytic streptococcus that grows from a throat culture is group A or some other type. This is true because the former cause nonsuppurative complications and are much more likely to be the ideology of pharyngitis.

The most widely used test for differentiation of GABHS from other beta-hemolytic streptococci in physicians' offices is the bacitracin disk test. This test provides a presumptive identification based on the observation that more than 95% of GABHS demonstrate a zone of inhibition around a disk containing 0.04 units of bacitracin, whereas 83% to 97% of non-GABHS streptococci do not. An alternative and very specific method for differentiation of GABHS from other beta-hemolytic streptococci is the detection of the group-specific cell wall carbohydrate antigen on isolated bacterial colonies (serogrouping). Commercial kits employing group-specific antiserum are available for this purpose. Such tests are appropriate for use by microbiology laboratories, but most physicians performing throat cultures would find it difficult to justify the additional expense for the minimal improvement in accuracy that serogrouping of beta-hemolytic streptococci would provide over the bacitracin disk test.

RAPID ANTIGEN DETECTION TESTS

The major disadvantage of culturing throat swabs on a blood agar plate is the delay (overnight or longer) in obtaining the culture results. Rapid antigen detection tests have been developed for the identification of GABHS directly from throat swabs. Although these rapid tests are more expensive than blood agar culture plate, the advantage they offer over the traditional procedure is the speed with which they can provide results. Rapid identification and treatment of patients with GABHS pharyngitis can reduce the risk of the spread of GABHS, allow the patient to return to school or work sooner, and reduce the acute morbidity of this illness. The use of rapid antigen detection tests in certain populations (eg, emergency rooms) has been shown to significantly increase the number of patients appropriately treated for GABHS pharyngitis when compared with the use of traditional throat cultures.

The great majority of the rapid antigen detection
tests that are currently available have an excellent specificity (ie, 95% or greater) when compared with blood agar plate cultures.3 This means that false-positive test results are unusual, and, therefore, therapeutic decisions can be made on the basis of a positive test with a great degree of confidence. Unfortunately, the sensitivity of most of these tests is only between 80% and 90% when compared with the blood agar plate culture. It has been suggested that most of the false-negative rapid test results occur in patients who are merely streptococcal carriers and not truly infected. However, studies have demonstrated that a large proportion of patients with false-negative rapid antigen detection test results are truly infected with GABHS and are not merely streptococcal carriers.14 Therefore, it is currently recommended that a negative rapid antigen detection test result be confirmed with a conventional blood agar plate culture.15

CURRENT PRACTICES
Several surveys have examined the actual strategies currently used by physicians in practice to diagnose GABHS pharyngitis. In 1993, Schwartz and colleagues surveyed pediatricians about their diagnostic approaches to children with pharyngitis.16 An optimal approach, defined as use of culture alone or as a backup to a negative rapid antigen test for at least 80% of patients, was used by only 44% of pediatricians who responded to the survey. Seventeen percent reported using clinical findings or rapid tests without culture for most children with pharyngitis. Recently, Hofer and colleagues obtained similar results from a national survey of US pediatricians: 38% used cultures alone, 42% used throat cultures when the rapid test was negative, and 20% used strategies that are not recommended.17 Thus, it appears that many physicians do not follow recommended guidelines for diagnosing GABHS pharyngitis.

NEW ANTIGEN DETECTION TESTS
The first rapid antigen detection tests used latex agglutination techniques. These were relatively insensitive and had unclear end points. Newer tests based on enzyme immunoassay techniques offered a more sharply defined end point and an increased sensitivity. More recently, rapid antigen detection tests using optical immunoassay (OIA) and chemiluminescent DNA probes have become available. Data suggest these newer tests may be more sensitive than other rapid antigen detection tests and perhaps even as sensitive as standard throat cultures on blood agar plates. However, in view of somewhat conflicting data,18,19 there has been a reluctance to recommend these newer tests for routine use without a confirmatory throat culture for negative test results.

We recently compared the accuracy of an OIA with that of a blood agar plate culture for the rapid diagnosis of GABHS pharyngitis in 983 consecutive patients with acute pharyngitis in three private pediatric offices in Connecticut, and for 1130 consecutive patients with acute pharyngitis in Chicago.20 The sensitivities and specificities of the OIA and the blood agar plate culture (both performed and interpreted in the pediatric offices) were determined using a research laboratory's interpretation of a combination of blood agar plate culture and Todd Hewitt broth culture of transport tube pledget as the gold standard. Among patients in Connecticut, the sensitivities of the OIA and blood agar plate culture were 94% and 89%, respectively (P<0.01), whereas the specificities were 96% and 99%, respectively (P<0.01). Among patients in Chicago, the sensitivities of the OIA and blood agar plate culture were 78% and 72%, respectively (P<0.01), whereas the specificities were 88% and 98%, respectively (P<0.01). In each of the six pediatric offices, the OIA was more sensitive than the blood agar plate culture. Combining the data from Connecticut and Chicago, the overall sensitivities of the OIA and blood agar plate culture were 84% and 78%, respectively (P<0.01), whereas the specificities were 93% and 99%, respectively (P<0.01). We concluded that with adequately trained personnel, negative OIA test results may not always need to be routinely confirmed with blood agar plate cultures.

REPEAT DIAGNOSTIC TESTING
Follow-up throat cultures are not routinely indicated for asymptomatic patients who have received a complete course of antimicrobial therapy for GABHS pharyngitis. The majority of such patients with persistent GABHS present in their upper respiratory tract are streptococcal carriers.21 It is known that approximately 25% of individuals within a household of an index patient may also harbor GABHS in their upper respiratory tracts. However, it is usually not necessary to perform a throat culture (or rapid antigen test) on or to treat household contacts of a patient with GABHS pharyngitis who are asymptomatic. Laboratory testing and treatment of positive asymptomatic patients who have received a complete course of antimicrobial therapy for GABHS pharyngitis or of asymptomatic family contacts is advisable only in special situations. These would include the following: when there is someone in the family with a history of rheumatic fever, during outbreaks of either acute rheumatic fever or post-streptococcal acute glomerulonephritis, during outbreaks of GABHS pharyngitis in closed or semi-closed communities, and when "ping pong" spread of GABHS has been occurring within a family.21 When a larger group (eg, school, day care center, or domiciliary institution) is involved in documented outbreaks of GABHS upper respiratory tract infections,
all individuals should have throat cultures or rapid antigen tests performed, but only those with positive results should be treated with antimicrobials.

SEROLOGIC TESTS

Demonstrating serological evidence of an antibody response to extracellular products or cellular components of GABHS is not useful for the diagnosis of acute GABHS pharyngitis. However, this can help determine if a recent GABHS infection has occurred when considering a diagnosis of rheumatic fever or glomerulonephritis. These observations are true because serum antibody levels require at least 10 to 14 days to rise, so streptococcal antibody tests are useful only for determining past infection. Antibodies that are often measured when evaluating for a possible post-streptococcal illness include anti-streptolysin O (ASO), antideoxyribonuclease B, and anti-hyaluronidase (AHT). Performance of more than one of these tests improves sensitivity to detect a response to a recent (but not current) GABHS infection. The Streptozyme® test (Wampole Laboratories, Cranbury, NJ) is a slide agglutination test for the detection of antibodies to several streptococcal antigens. Although this test is rapid, relatively simple to perform, and widely available, it is less standardized and less reproducible than most of the other antibody tests. Therefore, the Streptozyme® test should not be used as a definitive test for evidence of antecedent GABHS infection.

REFERENCES