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Acute pharyngitis is a common illness in both children and adults, caused by a wide variety of microbial agents. In children, approximately 20% of pharyngitis is caused by group A beta-hemolytic streptococci (GABHS); in adults, 5% of pharyngitis is due to GABHS. The signs and symptoms of infection are variable, ranging from mild sore throat with minimal physical findings to high fever and severe pain. The differential diagnosis of GABHS pharyngitis is extensive. Most cases of acute pharyngitis in both children and adults are caused by viruses. The gold standard diagnostic test for GABHS remains the throat culture. It is important to select appropriate candidates for culture to maintain the sensitivity of the test. Penicillin is still recommended as first-line treatment for documented GABHS infections. Prompt treatment is important to prevent serious sequelae of infection. (Prim Care Update Ob/Gyns 2002; 9:222–225. © 2002 Elsevier Science Inc. All rights reserved.)

Epidemiology

Acute pharyngitis may be caused by a wide variety of microbial agents, but some of the most common and potentially dangerous microorganisms are group A beta-hemolytic streptococci (GABHS). Lancefield group A consists of a single species, *S. pyogenes*. GABHS are gram-positive bacteria that grow in culture as pairs or chains of variable length. They cause complete hemolysis of red blood cells on sheep blood agar and grow as transparent to opaque, round, small colonies. The pathogenesis of GABHS is mediated by a variety of factors, including streptolysins O and S; streptokinase; DNases; proteases; pyrogenic exotoxins A, B, and C; and a hyaluronic acid capsule that protects the organism from phagocytosis. Streptolysins O and S are toxins that damage cell membranes and account for the hemolysis demonstrated on sheep blood agar. In addition to pharyngitis, GABHS are also one of the etiologic agents of impetigo, cellulitis, and scarlet fever. However, it is as a cause of pharyngitis that GABHS can be the most dangerous because of the postinfection syndromes of acute rheumatic fever and poststreptococcal glomerulonephritis.

GABHS had been a huge problem in both industrialized and developing countries of the world until the end of the 1960s. At this time, infections caused by GABHS and the sequelae of such infections declined markedly in industrialized nations. No changes in the epidemiologic pattern for developing nations were seen, however. During the past 10 years, this discrepancy has changed. For the first time in many decades, reports of individual cases and even outbreaks of acute rheumatic fever were reported from various parts of the United States. For example, >270 cases of acute rheumatic fever occurred in the Salt Lake City, Utah area between 1985 and the end of 1992. Outbreaks have been documented at military training centers, and surveys among pediatric cardiologists indicate significant increases in rheumatic fever in half of the 50 states. The most disturbing fact is that mortality has been >30% in some reported series. The reason for this sudden increase in GABHS infection has not been completely elucidated. One prominent theory suggests the emergence of dominant serotypes of bacteria that produce virulent clones. These clones cause outbreaks by producing specific virulence factors and thus escape the host defense mechanisms.
mechanism of spread because the nasopharynx and oropharynx are the primary carriage sites for this organism. The skin and anus also are potential sites, as evidenced by foodborne outbreaks of disease. Contact with contaminated objects, such as toothbrushes, is probably not important in the spread of the organism. This observation was confirmed by a recent study examining possible treatment failures caused by reinfection from a patient’s toothbrush or bedclothes. Of 114 patients with documented GABHS, 54 patients and their families were given hygienic precautions, including the use of new toothbrushes and frequent changing of bedclothes. No difference in treatment failure rates was found between the groups.5

The incubation period of streptococcal pharyngitis is 1 to 4 days, leading to a self-limited, localized inflammation of the tonsillopharynx lasting 3 to 5 days. Symptoms include sore throat, fever and chills, malaise, and occasionally abdominal complaints and vomiting, especially in children. Both symptoms and signs are quite variable, ranging from mild sore throat with minimal physical findings to high fever and severe pain. Pain may be associated with intense erythema and swelling of the pharyngeal mucosa and the presence of purulent exudates over the posterior pharyngeal wall and tonsillar pillars. Exudative pharyngitis may be associated with enlarged, tender anterior cervical lymph nodes. Notable is the absence of rhinorrhea and cough. Infection with GABHS most typically occurs in midwinter to early spring. When the above constellation of symptoms is present, the likelihood of infection approaches 60–70% in children and 20–30% in adolescents.4

**Differential Diagnosis**

The differential diagnosis of GABHS pharyngitis is extensive. Most cases of acute pharyngitis in both children and adults are caused by viruses. Viruses such as rhinovirus, coronavirus, influenza A and B, and parainfluenza virus may involve the pharynx and other portions of the respiratory tract in the form of the common cold, influenza, or croup. Viruses that frequently produce a purulent tonsillar exudate include the Epstein-Barr virus, adenovirus, and herpes virus. A more recently recognized cause of viral pharyngitis is the acute retroviral syndrome associated with human immunodeficiency virus infection.6 Sore throat is only part of a constellation of symptoms simulating mononucleosis.

GABHS are the most common bacterial cause of acute pharyngitis. Other important bacterial causes, especially in adolescents, are streptococci from Lancefield groups C and G. These streptococci are often the cause of epidemics of pharyngitis associated with contaminated foods. Other bacterial etiologies include *Arcanobacterium hemolyticum*, a rare cause of pharyngitis and tonsillitis in young adults, which closely mimics GABHS pharyngitis by producing a scarlatiniform rash. Other bacterial infections in the differential diagnosis include those caused by *Neisseria gonorrhoea*, *Corynbacterium diphtheriae*, *Treponema pallidum*, *Yersinia species*, *Francisella tularensis*, *Mycoplasma pneumoniae*, and possibly *Chlamydia trachomatis*.

**Diagnosis**

The pertinent clinical issue in the diagnosis of acute pharyngitis is the differentiation of GABHS from non-GABHS causes. The gold standard diagnostic test remains the throat culture. The specimen must be properly collected by vigorously rubbing a sterile swab over both tonsillar pillars, placing the swab in an appropriate culture medium, and then transporting the specimen to the laboratory in a timely manner. Although this test is the most sensitive and specific means available to make a diagnosis, a major disadvantage is the delay in obtaining results. Delay can range from 18–48 hours. Another disadvantage is the inability of the test to differentiate between an acute infection and a chronic state. Thus, treating all patients with positive cultures invariably leads to a degree of overtreatment.

A means of overcoming the time delay with throat cultures was the development of rapid tests for detection of GABHS antigen. Numerous kits are available that use techniques such as agglutination and enzyme immunoassay to detect GABHS carbohydrate in a matter of minutes. The most recent tests employ nucleic acid hybridization techniques. Although these rapid assays are highly specific, a disadvantage is their lower sensitivity compared with routine throat culture. A recent comparison of three second-generation immune assays for detection of GABHS showed similar sensitivities and specificities.7 Strep A Plus had an 84.2% sensitivity and 88.9% specificity, Concise Strep A an 82.4% sensitivity and 92.3% specificity, and Cards Plus, an 84.2% sensitivity and 90.7% specificity. Thus, it is recommended that a negative rapid test be confirmed with a throat culture. However, findings show that with a positive rapid test, it is reasonable to start antibiotic treatment without performing a bacterial culture. These recommendations are particularly important when treating children. In adults, the low prevalence of GABHS pharyngitis leads to an increase in false-positive results, with subsequent unnecessary antibiotic treatment.

Physicians can maintain the sensitivity of GABHS detection by carefully selecting which patients to culture. Appropriate candidates for
culture include those with fever, pharyngeal exudates, swollen anterior cervical lymph nodes, and absence of cough. Adults are three times more likely to have a positive culture with all of these findings than when only two are present. When none of these signs or symptoms are present, only 2.5% of adults with pharyngitis will have a positive culture for GABHS.

### Treatment

Treatment of GABHS infections should relieve the symptoms of the acute illness, eliminate transmissibility, and prevent both suppurative and nonsuppurative sequelae. Acute rheumatic fever is one of the sequelae that can be prevented by initiating antimicrobial therapy within 9 days of symptom onset. The gold standard of therapy for GABHS is penicillin. To date, no GABHS have been documented as resistant to beta-lactam antibiotics. GABHS are also highly susceptible to ampicillin, amoxicillin, and cephalosporins. Another family of antibiotics that is effective against GABHS is the macrolides, specifically erythromycin, clarithromycin, azithromycin, lincomycin, and clindamycin. GABHS can develop resistance to macrolides, especially within a community, and cross-resistance among macrolides has been observed. An important point to remember in treatment is that antimicrobial therapy should not be given in the absence of a GABHS diagnosis confirmed by throat culture and/or rapid assay tests.

Ten days of penicillin treatment is required to achieve maximum bacteriologic cure rate for GABHS pharyngitis. Three to 7 days of therapy has not been proven to achieve maximum eradication. A regimen of 5 days with several kinds of cephalosporins or azithromycin has been shown to be as effective as 10 days of oral penicillin V. The specific cephalosporins studied include cefadroxil, cefuroxime axetil, cefpodoxime proxetil, and cefdinir.

Failure rates with penicillin therapy have ranged from 5% to 35% for GABHS pharyngitis in various studies. Reasons for treatment failures include poor compliance, repeated exposure to the organisms, and co-pathogens that elaborate beta-lactamase. Despite these failure rates, penicillin is still recommended as first-line therapy. One reason is because evidence shows that increased empiric use of broad-spectrum antibiotics, including macrolides and cephalosporins, may lead to antibiotic resistance among respiratory pathogens. Table 1 lists the appropriate doses for the antibiotics commonly used to treat GABHS pharyngitis.

### Sequelae of Pharyngitis

Rheumatic fever is a nonsuppurative sequela of infections with GABHS. The major manifestations include carditis, arthritis, chorea, erythema marginatum, and subcutaneous nodules. Minor manifestations include arthralgia, fever, laboratory documentation of GABHS infection, elevated erythrocyte sedimentation rate, and prolonged P-R interval on electrocardiogram. It is of interest to note that the most recent focal outbreaks of rheumatic fever have occurred in predominantly middle-income families. Another dangerous sequelae of GABHS pharyngitis is poststreptococcal glomerulonephritis. The principal clinical findings are hematuria and edema. It is the most common form of glomerulonephritis in children and is primarily a disease of preschool and school-age children.

#### Summary

In summary, GABHS are potentially dangerous microorganisms that must be correctly diagnosed and promptly treated to prevent serious sequelae. The new rapid streptococcal assays for diagnosis have equal specificity to throat culture but are not as sensitive. Thus, all negative rapid assays should be followed by a throat culture. If a rapid assay is positive, it is appropriate to begin antibiotic therapy. It is important, especially in adults, to perform these tests only on those patients with the clinical manifestations of GABHS, including fever, tonsillar exudates, swollen anterior lymph nodes, and absence of cough. The American Academy of Pediatrics and the American Heart Association continue to recommend penicillin as first-line treatment for documented GABHS infections. Erythromycin is recommended as the alternative in those allergic to penicillin.

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