BACTERIOLOGICAL EXAMINATION OF PHARYNGEAL SECRETIONS

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There are more than 225 pathogens including more than 200 viruses which are currently known to cause upper respiratory infection(1). Group A streptococci are the principal bacterial agents in patients between the ages of 2 and 14 years, with peak incidence in 5 to 8 years old patients. Studies have demonstrated recovery of this agent in 35 to 50% of children less than 3 years of age(2). *Corynebacterium diphtheriae, Neisseria meningitidis* and *N. gonorrhoeae* also primarily infect the upper respiratory tract. *Hemophilus influenzae, Streptococcus pneumoniae* and *Staphylococcus aureus* may infect the upper respiratory tract secondarily. The initial manifestations of pertussis are those of nasopharyngitis.

Indications

Throat cultures are usually performed to distinguish between viral pharyngitis and Streptococcal sore throat. Group A beta hemolytic Streptococcus (GABHS) is the organism associated with the most morbidity and is the object of most diagnostic and therapeutic regimens. The primary goal of diagnosis is to avoid the recognized suppurative and non-suppurative (rheumatic fever and glomerulonephritis) complications of such an infection, to reduce spread to close contacts and to relieve symptoms. The necessity for a correct diagnosis of GABHS pharyngitis has been recently emphasized by the resurgence of acute rheumatic fever in the United States(3). Primary prevention of rheumatic fever depends upon the identification of all patients with GABHS pharyngitis and their adequate treatment. Occasionally, cultures are taken to diagnose whooping cough, diphtheria or gonococcal infection of the pharynx. Nasopharyngeal cultures can also be used for eipdemiological purposes to detect carrier states of potential pathogens such as *N. meningitidis* and *C. diphtheriae.* The *Table* shows several recommended criteria for obtaining throat cultures in patients with pharyngitis.

Streptococcal *vs* Viral Pharyngitis

Clinical manifestations differ somewhat in streptococcal and viral upper respiratory infection. Several clinical grading systems for assessing the likelihood of Group A streptococcal pharyngitis have been published(4-6). However, there is much overlapping of signs and symptoms and it is often impossible to clinically distinguish between viral and streptococcal pharyngitis. Conjunctivitis, rhinitis, cough and hoarseness rarely occur with proven Streptococcal pharyngitis and the presence of two or more of these signs or symptoms is

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Received for publication: October 23, 1991; Accepted: November 22, 1991

TABLE—*Indications for Obtaining a Throat Culture*

Any child above 3 years with significant temperature elevation and diffuse redness of tonsils.
Petechial mottling of soft palate.
Associated lymphadenitis involving anterior cervical nodes.
Follicular exudations.
Scarlatiniform rash.
Exposure to a person with Streptococcal pharyngitis.
History of rheumatic fever.
Membrane over pharynx.
Known epidemic caused by:
Group A beta hemolytic Streptococcus
N. meningitidis
C. diphtheriae

suggestive of viral infection. The physical findings most likely to be associated with streptococcal disease are diffuse redness of the tonsils and tonsillar pillars with a petechial mottling of the soft palate with or without lymphadenitis or follicular exudations(7).

A positive throat culture may indicate streptococcal pharyngitis, but (*i*) hemolytic streptococci are common inhabitants of the nasopharynx in healthy children, and (*ii*) some children with a viral upper respiratory infection have positive throat cultures for Beta hemolytic streptococci. Thus, isolation of a GABHS from the pharynx of a child with pharyngeal infection does not necessarily indicate that the disease is caused by this organism. However, when the child is having moderate or severe exudative pharyngitis with petechiae on the palate and cervical adenitis, the diagnosis is more secure.

Collection and Transportation

The specimen from throat can be collected using a cotton tipped swab. Tonsillar areas, pharynx and areas of purulance, ulceration, inflammation or capsule formation must be swabbed, with minimal oral contamination(8). If there is likely to be delay of more than three hours in transporting the specimen to the laboratory, serum coated swabs or transport medium should be used(9). Swabs of the nose should be moistened first with saline or sterile water. Ordinarily, cultures for GABHS suffice. However, the laboratory must be notified when diphtheria, pertussis or gonococcal infection is suspected clinically, appropriate selective media can be inoculated. The swabs are routinely plated on blood agar and incubated.

Diphtheria

For recovery of *C. diphtheriae* material from beneath the membrane or a portion of the membrane itself should be obtained for culture. *C. diphtheriae* is relatively resistant to drying. Use of non-nutritive moisture reducing transport medium helps to prevent the overgrowth of other microorganisms. Loeffler, Tellurite, and blood agar media are inoculated. Smears can be stained with Albert stain and Gram stain. The fluorescent antibody technique is reliable only with experienced personnel.

Pertussis

Recovery of *B. pertussis* is best accomplished during the early phases of illness by culture of nasopharyngeal swabs obtained at the bed side. Some also recommend use of a concurrent throat swab. Cough plates are not recommended. Bordet-Gengou medium is used for isolation. Fluorescent antibody staining of pharyngeal specimens

may provide a rapid specific diagnosis. IgA antibody to B pertussis can be detected by an enzyme linked immunosorbent assay (ELISA) in nasopharyngeal secretions. These antibodies appear during second or third week of illness and persist for at least 3 months. They are not induced by immunization.

Interpretation

Interpretation of results of cultures is difficult because microbial flora are normally recovered from these areas. Some organisms are considered pathogenic wherever found, such as *Corynebacterium diphtheriae, Bordetella pertussis* and *Neisseria gonorrhoeae*. Others such as *Streptococcus pyogenes, Neisseria meningitidis, Hemophilus influenzae* or Staphylococci may be pathogenic or non-pathogenic depending on whether the patient is symptomatic or not. Still others such as *Streptococcus viridans* are rarely considered pathogenic. Candida can be found on normal mucosa. Only their abundant presence is of significance. Demonstration of mycelial forms indicates colonization and tissue invasion and is, therefore, of greater significance.

Accuracy of Throat Culture

Throat culture has remained the 'gold standard' for determining the presence of GABHS in the upper respiratory tract. However, several investigators have de-monstrated that the throat culture is unreliable because of a discordance between duplicate throat cultures taken at the time of the initial visit(5,10). Reviewing the existing data, Gerber concluded that the discordance rate for all throat cultures was less than 5%. The positive culture in most of the discordant cultures was only weakly positive suggesting that many of these patients may be streptococcal carriers (positive throat culture without a serologic response to the GABHS) and not truly infected (positive throat culture with a serologic response to the GABHS)(11).

Strongly positive cultures are more likely in (*i*) acute pharyngitis as compared to asymptomatic children, and (*ii*) patients with true streptococcal infection as compared to streptococcal carriers. However, there is significant overlapping and true streptococcal infection cannot be accurately differentiated from carrier stage on the basis of the degree of positivity alone(11).

Rapid Strep Tests

One of the most exciting developments in recent years in the area of GABHS pharyngitis has been the appearance of commercial rapid strep tests for the rapid identification of GABHS directly from throat swabs. Rapid strep tests are based on the extraction (by nitrous acid) and subsequent detection of the group specific polysaccharide from the streptococcal cell wall using methods like agglutination, coagglutination and ELISA. The entire process takes 5-15 minutes depending upon the particular kit used. ELISA methods are about as accurate as Latex Agglutination tests and are easier to read, but are more expensive. There are several reviews of around 20 rapid antigen detection systems currently commercially available(12,13). The specificity of rapid tests is quite satisfactory. Facklam recorded specificities of more than 95% in 74% of the Group A streptococci kits tested. However, 44% of the kits that had been evaluated prior to 1987 had sensitivities of less than 85%. Some were as low as 60%. Less than 40% of those examined had a sensitivity of more than 90%(12). One plus culture (usually 10 or fewer colonies on the culture

plate) are most frequently associated with false negative rapid test results.

It has been suggested that since streptococcal carriers very frequently have few organisms, most 'false negative' rapid test results are from carriers, are of little clinical consequence and can be ignored. However, recent studies have indicated that such an assumption cannot be made. One third to half of the cases with false negative rapid tests had a significant streptococcal antibody response representing true streptococcal infection and not the carrier state(14,15). Hence, when a rapid test result is negative in a patient suspected of having streptococcal pharyngitis, a back-up throat culture should be performed(16,17). There are no Indian studies evaluating the rapid test. Six different versions of this test are in the market (Testpack, Abbot Laboratories; Quest Group A Strep Test, Quiedel; Icon Strep A Test, Hybritech; SUDS Group A Strep Test, Murex Corp; Hygeia Flow-through Immunosorbent Assay, Hygeia; Venter screen Strep A Test, Ventrex Laboratories, Inc.)(18).

Generally, the costs for rapid antigen detection systems are greater than for performance of a routine throat culture. However, the total medical cost for the illness could be considerably reduced if the rapid test is positive and treatment is started immediately, reducing time off from work to care for the child or to make a second visit. Early diagnosis and treatment also prevents spread of this organism to others.

In conclusion, sensitive, specific and if possible rapid diagnostic tests for distinguishing the minority of individuals who have streptococcal pharyngitis from the majority with self limited non-streptococcal infection remains desirable. Clinical and epidemiological features provide important clues, while supplemental throat culture yields sufficient precision for maximal prevention of acute rheumatic fever.

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