

Diagnosis of Streptococcal Pharyngitis by Rapid Antigen Detection From the Throat Swab

Emanuel Wolinsky, MD, and William Adams
Cleveland, Ohio

The diagnosis of streptococcal pharyngitis may be substantiated by documentation of the presence of *Streptococcus pyogenes* in significant numbers. Throat culture has been the standard method, but it takes at least 24 hours and sometimes longer for results to be reported. Described here is a test for the rapid detection of group A streptococcal antigen directly from the throat swab that is suitable for performance in a physician's office or small clinic.

METHODS

Cultures were taken with a rayon-tipped plastic swab, and the group A-specific antigen was extracted by an enzyme extraction reagent. The antigen was recognized by the agglutination of latex particles sensitized with specific rabbit antibody. The results were available in approximately 70 minutes, and reagents and

materials were supplied in a self-contained kit.*

Throat swabs were obtained from 575 children suspected of having streptococcal pharyngitis in schools, clinics, and private physicians' offices. The specimens were delivered within two hours to a special throat culture laboratory maintained at Cleveland Metropolitan Hospital under a program originally set up to prevent rheumatic fever in the community. Swabs were rayon-tipped plastic rods, either those supplied in the kits (275 specimens) or those of another manufacturer** (300 specimens). All swabs were transported in sterile tubes in a dry state. For all specimens, a routine culture on sheep blood agar was streaked before proceeding with the rapid antigen detection test. Culture plates were incubated at 35° to 37° C in an aerobic atmosphere for 18 to 24 hours. β -Hemolytic colonies were extracted by the autoclave technique and grouped by the capillary precipitin test.^{1,2}

Immediately after application to the culture plate, the swab was immersed in the extraction reagent in a test tube. The tube was agitated on a vortex mixer for a few seconds and then incubated at 37° C for 60 minutes. After discarding the swab, one drop of the sample extract was mixed with a drop of suspension of sensitized latex particles in ringed circles on a disposable card. Suitable positive and negative controls were included. Positive

From the Division of Microbiology, Department of Pathology, Cleveland Metropolitan General Hospital, Cleveland, Ohio. Requests for reprints should be addressed to Dr. Emanuel Wolinsky, 3395 Scranton Road, Cleveland, OH 44109.

*Kits for this trial were supplied by Clay Adams division of Becton Dickinson and Company as Q Test Strep Kit.

**Marion Scientific.

TABLE 1. LABORATORY RESULTS OF SPECIMENS COLLECTED BY MARION CULTURETTE AND Q TEST

Results	Collection Technique	
	Marion Culturette No. (%)	Q Test Swab No. (%)
Culture		
Group A streptococci	39 (13)	43 (16)
β -streptococci, not group A	11 (04)	13 (04)
Negative for β -streptococci	250 (83)	219 (80)
Q Test		
Positive (% sensitivity)	38/39* (97)	43/43 (100)
Negative (% specificity)	261/261 (100)	232/232 (100)

*Number positive or negative over the total number positive or negative for group A streptococci by culture

tests were easily identified by agglutination of the latex particles after gentle hand-rocking for a few seconds followed by a four-minute rotation of the cards on a mechanical rotator.

Agglutination was recorded as either negative or positive, with the positive tests graded from 1 to 4+ according to the intensity of the reaction. Culture results were evaluated on the following day by the same technologist, but without reference to the antigen detection test reports.

RESULTS

The results are shown in Table 1. Eighty-one specimens were positive for group A streptococci both by culture and by the Q Test Strep Kit, with only one false-negative result generated by the antigen detection test (97 percent sensitivity for the Q Test); 493 specimens were negative by both culture and Q Test (100 percent specificity for the Q Test); and all 24 specimens that yielded non-group A β -hemolytic streptococci by culture were negative by the Q Test.

Continued on page 280

ISOPTIN[®]

(verapamil HCl/Knoll)

80 mg and 120 mg scored, film-coated tablets

Contraindications: Severe left ventricular dysfunction (see *Warnings*), hypotension (systolic pressure < 90 mm Hg) or cardiogenic shock, sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker), 2nd- or 3rd-degree AV block. **Warnings:** ISOPTIN should be avoided in patients with severe left ventricular dysfunction (e.g., ejection fraction < 30% or moderate to severe symptoms of cardiac failure) and in patients with any degree of ventricular dysfunction if they are receiving a beta blocker. (See *Precautions*.) Patients with milder ventricular dysfunction should, if possible, be controlled with optimum doses of digitalis and/or diuretics before ISOPTIN is used. (Note interactions with digoxin under *Precautions*.) ISOPTIN may occasionally produce hypotension (usually asymptomatic, orthostatic, mild and controlled by decrease in ISOPTIN dose). Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Such elevations may disappear even with continued treatment; however, four cases of hepatocellular injury by verapamil have been proven by rechallenge. Periodic monitoring of liver function is prudent during verapamil therapy. Patients with atrial flutter or fibrillation and an accessory AV pathway (e.g. W-P-W or L-G-L syndromes) may develop increased antegrade conduction across the aberrant pathway bypassing the AV node, producing a very rapid ventricular response after receiving ISOPTIN (or digitalis). Treatment is usually D.C.-cardioversion, which has been used safely and effectively after ISOPTIN. Because of verapamil's effect on AV conduction and the SA node, 1° AV block and transient bradycardia may occur. High grade block, however, has been infrequently observed. Marked 1° or progressive 2° or 3° AV block requires a dosage reduction or, rarely, discontinuation and institution of appropriate therapy depending upon the clinical situation. Patients with hypertrophic cardiomyopathy (IHSS) received verapamil in doses up to 720 mg/day. It must be appreciated that this group of patients had a serious disease with a high mortality rate and that most were refractory or intolerant to propranolol. A variety of serious adverse effects were seen in this group of patients including sinus bradycardia, 2° AV block, sinus arrest, pulmonary edema and/or severe hypotension. Most adverse effects responded well to dose reduction and only rarely was verapamil discontinued. **Precautions:** ISOPTIN should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacologic effects. Studies in a small number of patients suggest that concomitant use of ISOPTIN and beta blockers may be beneficial in patients with chronic stable angina. Combined therapy can also have adverse effects on cardiac function. Therefore, until further studies are completed, ISOPTIN should be used alone, if possible. If combined therapy is used, close surveillance of vital signs and clinical status should be carried out. Combined therapy with ISOPTIN and propranolol should usually be avoided in patients with AV conduction abnormalities and/or depressed left ventricular function. Chronic ISOPTIN treatment increases serum digoxin levels by 50% to 70% during the first week of therapy, which can result in digitalis toxicity. The digoxin dose should be reduced when ISOPTIN is given, and the patients should be carefully monitored to avoid over- or under-digitalization. ISOPTIN may have an additive effect on lowering blood pressure in patients receiving oral antihypertensive agents. Disopyramide should not be given within 48 hours before or 24 hours after ISOPTIN administration. Until further data are obtained, combined ISOPTIN and quinidine therapy in patients with hypertrophic cardiomyopathy should probably be avoided, since significant hypotension may result. Clinical experience with the concomitant use of ISOPTIN and short- and long-acting nitrates suggest beneficial interaction without undesirable drug interactions. Adequate animal carcinogenicity studies have not been performed. One study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. **Pregnancy Category C:** There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor and delivery only if clearly needed. It is not known whether verapamil is excreted in breast milk; therefore, nursing should be discontinued during ISOPTIN use. **Adverse Reactions:** Hypotension (2.9%), peripheral edema (1.7%), AV block 3rd degree (0.8%), bradycardia: HR < 50/min (1.1%), CHF or pulmonary edema (0.9%), dizziness (3.6%), headache (1.8%), fatigue (1.1%), constipation (6.3%), nausea (1.6%), elevations of liver enzymes have been reported. (See *Warnings*.) The following reactions, reported in less than 0.5%, occurred under circumstances where a causal relationship is not certain: ecchymosis, bruising, gynecostasia, psychotic symptoms, confusion, paresthesia, insomnia, somnolence, equilibrium disorder, blurred vision, syncope, muscle cramp, shakiness, claudication, hair loss, macules, spotty menstruation. **How Supplied:** ISOPTIN (verapamil HCl) is supplied in round, scored, film-coated tablets containing either 80 mg or 120 mg of verapamil hydrochloride and embossed with "ISOPTIN 80" or "ISOPTIN 120" on one side and with "KNOLL" on the reverse side. Revised August, 1984.



KNOLL PHARMACEUTICAL COMPANY
30 NORTH JEFFERSON ROAD, WHIPPANY, NEW JERSEY 07981

DISCUSSION

It is now possible to recognize specific antigen in various body fluids by the techniques of counterimmunoelectrophoresis, coagglutination, latex particle agglutination, and other immunologic tests. El Kholy and co-workers³ described a technique for the recognition of group A streptococcal antigen extracted from tonsillar scrapings by a modified nitrous acid extraction followed by precipitation with specific antiserum in capillary tubes. Other reports described similar procedures from throat swabs or pharyngeal secretions obtained by gargling.^{4,6} More recent papers were reviewed in an editorial by Gerber.⁷ The test described herein is a modification of the Directigen Group A Strep Test (Hynson, Westcott & Dunning), which was used successfully to recognize streptococcal pharyngitis in a trial involving four different medical centers.⁸

The rapidity with which results are obtained and the fact that rapid antigen detection tests recognize only group A streptococci are features preferred over the conventional culture technique. Although other non-group A β -hemolytic streptococci have occasionally been associated with clinical pharyngitis, rheumatic fever follows group A streptococcal infections only, and there have been very few reports of nephritis as a complication of other than group A disease.⁷

The effect of transportation time on the results of the test procedure was not evaluated in this small study, but Matteson and Anhalt⁹ reported a trend to greater sensitivity of the antigen detection test with longer delays in processing the swabs. In most of the other reports of rapid antigen detection tests for group A streptococci, the sensitivity varied from approximately 80 to 92 percent, in contrast to 97 percent sensitivity in the present study. Of the various factors that could be responsible for these differences, the two most important appear to be the experience and expertise of the technician performing the test, and the number of colonies isolated from the cultured swabs, roughly representing the streptococcal burden in the diseased pharynx. Most of the reported false-negative tests were associated with cultures that yielded only a light growth of group A streptococci.^{7,8} The greater sensitivity of the trial reported here may be

attributed to familiarity with the test procedure and to the happenstance that all of the positive cultures were graded as 2+ (greater than 10 colonies) or more.

Cost will be an important consideration in the choice of a laboratory technique for the recognition of group A streptococci. Items not included in the kit are a vortex mixer and a mechanical rotator. Special training will be necessary before proficiency can be acquired, but gaining proficiency in this procedure should be no more difficult than learning how to process swabs for culture. At the present time, the rapid antigen detection tests are slightly more expensive than routine culture, but it remains to be seen which technique will be more cost effective in the long run.

References

1. Rantz LA, Randall E: Use of autoclaved extracts of hemolytic streptococci for serological grouping. *Stanford Med Bull* 1955; 13:290-291
2. Lancefield RC: The serological differentiation of human and other groups of hemolytic streptococci. *J Exp Med* 1933; 57:572-595
3. El Kholy A, Facklam R, Sabri G, Rotta J: Serological identification of group A streptococci from throat scrapings before culture. *J Clin Microbiol* 1978; 8:725-728
4. Edwards EA, Phillips IA, Suiter WC: Diagnosis of group A streptococcal infections directly from throat secretions. *J Clin Microbiol* 1982; 15:481-483
5. Gerber MA: Micronitrous acid extraction-coagglutination test for rapid diagnosis of streptococcal pharyngitis. *J Clin Microbiol* 1983; 17:170-171
6. Otero JR, Reyes S, Noriega AR: Rapid diagnosis of group A streptococcal antigen extracted directly from swabs by an enzymatic procedure and used to detect pharyngitis. *J Clin Microbiol* 1983; 18:318-320
7. Gerber MA: Culturing of throat swabs: End of an era? *J Pediatr* 1985; 107:85-88
8. Berkowitz CD, Anthony BF, Kaplan EL, et al: Cooperative study of latex agglutination to identify group A streptococcal antigen on throat swabs in patients with acute pharyngitis. *J Pediatr* 1985; 107:89-92
9. Matteson ML, Anhalt JP: Effect of delay in processing on the performance of Directigen for the detection of group A streptococci in throat swabs. *J Clin Microbiol* 1985; 21:993-994