Rapid Diagnosis of Streptococcal Pharyngitis in Adult Emergency Room Patients

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A rapid latex agglutination slide test for group A beta-hemolytic streptococcal throat infections was prospectively evaluated. Resident physicians, working in an adult non-acute emergency room, recorded clinical data and collected throat swabs from 729 adult patients with sore throats. Research assistants obtained throat swabs from 329 control patients. Sensitivity and specificity, compared with routine cultures, were 96% and 97%, respectively. Analyses of clinical predictions and of test results for control patients, however, suggest that this test may perform better than routine culture. The test provides a rapid, accurate, potentially useful alternative for diagnosing group A beta-hemolytic streptococcal pharyngitis in adults. Key words: streptococcal infections; latex agglutination slide test. J Gen Intern Med 1986;1:248-251.

A recent study evaluated clinical signs and symptoms, without waiting for culture results. While some authors recommend antibiotic therapy for patients with positive throat cultures only, others recommend treatment based on clinical signs and symptoms. 1-3 \textsuperscript{1} The latter group argues that the gains from immediate antibiotic therapy for those patients who have streptococcal pharyngitis outweigh the risks of treating some patients who do not have a bacterial infection. Furthermore, in the emergency room setting, the difficulty in insuring follow-up for all patients with strep throat argues against the "culture, then treat" approach. Most authors, however, would agree on treating all patients with bona fide group A beta-hemolytic streptococcal infection, if one could easily identify such patients. Thus, a rapid test for diagnosing group A streptococcal infection would be useful.

Recently, investigators developed and studied latex agglutination slide tests for detecting group A antigen from throat swabs. \textsuperscript{4} The costs of materials for these tests range from 1 to 2 dollars, similar to the material costs for most office culture kits. \textsuperscript{5} The laboratory technician places rayon-tipped throat swabs into extraction media and incubates for 7-60 minutes (depending on the specific kit). After this incubation, the technician mixes the extracted fluid with antibody and reads the slide for agglutination. Our study has examined the performance of one of these tests (Directigen; Hynson, Westcott, and Dunning) in an adult, non-acute care emergency room.

Prior evaluations of this technology have been in vitro comparisons: they do not report clinical data. Also, all studies have used throat culture as the gold standard for the diagnosis of streptococcal pharyngitis. This discounts the possibility that a false-negative culture could have a concomitant positive slide test. By analyzing the clinical features of those patients having discordant test results, we can discover whether these patients resemble patients having the same culture result or the same slide test result. Such analyses can help us understand the reasons for discordant test results.

No previous study has included a control group consisting of patients having no upper respiratory tract symptoms. Since throat cultures have a sensitivity of approximately 90%, some patients who have group A beta-hemolytic streptococcal pharyngitis will have negative cultures. Either a false-negative culture or a false-positive slide test could cause the combination of a negative culture with a positive slide test. By studying control patients, we were able to better evaluate the specificity of the slide test.

METHODS

Between June 1984 and April 1985, medical residents working in an adult (16 years old or older) non-acute emergency room recorded demographic and clinical information and obtained throat swabs from all patients seeking care for a sore throat. They collected the swabs using routine techniques and sent specimens to the laboratory in the Cytotest transport system (Marion Scientific Corp, Rockville, Md.).

Demographic data included the patient's age, race, and gender. Using an ordinal scale (absent, mild, moderate, severe), the physicians evaluated several clinical signs and symptoms: tonsillar exudates, pharyngeal exudates, swollen tender anterior cervical nodes, swollen tender posterior cervical nodes, pharyngeal redness, tonsillar swelling, cough, coryza, difficulty swallowing, and fever history. They also recorded the oral temperature.
Based on clinical findings, the residents recorded their estimates of the probabilities that the individual throat cultures would yield group A beta-hemolytic streptococcus. We gave no specific instructions on how to make these estimates. We also calculated a logistic regression estimate based upon the recorded clinical data. This regression equation, which assumes a prevalence of 17%, uses the presence or absence of tonsillar exudates, swollen tender anterior cervical nodes, cough and fever history. For example, if a patient has exudates, swollen tender nodes, no cough, and a history of fever, the model estimates the probability of a positive culture as 55%. Three of these features corresponds to an estimate of 33%; two gives an estimate of 15%; one, 6%; and a patient who has a cough, no history of fever, no exudates, and normal nodes gets an estimate of 2%.

During the study, research assistants obtained throat swabs from patients coming to the emergency room for complaints not involving the upper respiratory tract. We did not identify to the microbiology laboratory which throat swabs came from sore throat patients and which swabs came from control patients.

A microbiology laboratory technician inoculated two rayon swabs onto the surface of two Trypticase soy agar plates (BBL Microbiology Systems, Cockeysville, Md.) containing 5% sheep blood (BAP). A technician streaked the plates and incubated one plate aerobically and the other plate anaerobically, both at 35°C. The laboratory grouped all beta-hemolytic streptococcal isolates as A, B, C, G, or ungroupable using the Phadebact system (Pharmacia Diagnostic, Uppsala, Sweden).

Using one of the rayon swabs, the technician performed the Directigen group A Streptococcus (DGAS) test as outlined by the manufacturer, paying particular attention to reading the test results at the recommended time. One technician performed more than 80% of both tests.

Using standard formulas we calculated sensitivity and specificity of the DGAS test with the culture result as the gold standard. To test indirectly the validity of both test results, we used analysis of variance (ANOVA) and type III sums of squares to compare the DGAS test and the culture result (as independent variables) with both the residents' estimates and the regression estimates (as the dependent variables). Thus, one ANOVA modelled the residents' probability estimates as a function of the DGAS test result and the culture result. The other ANOVA evaluated the regression derived probability estimate as a function of both the DGAS test result and the culture result.

Type III sums of squares tests whether an independent variable explains a significant part of the variance (of the dependent variable) given that the model contains all other independent variables. Thus, in models with the DGAS test and the culture results as the two independent variables, a finding of statistical significance suggests that the tested independent variable adds information beyond that provided by the other independent variable. We used the Statistical Analysis System (SAS) for all ANOVA analyses.

## RESULTS

We collected throat swabs from 729 sore throat patients and 329 control patients. The patients were primarily young adults residing in the city of Richmond. The patients had an average age of 27 (range 16–73), while the controls averaged 33 (range 16–85). Both sore throat patients and control patients were predominately black (89% and 77%) and female (68% and 52%).

For patients with sore throats, the sensitivity of the DGAS test was 208/217 (96%), while the specificity equaled 498/512 (97%) (Table 1). For control patients, we found no false-positive DGAS test result, yielding an observed specificity of 100% (325/325).

The ANOVA results showed both the DGAS test results and the culture results accounting for a significant proportion of the variance in both the resident physicians' and regression model estimates. However, using Type III sums of squares and physicians' estimates as the dependent variable, the DGAS test accounted for an additional proportion of the variance (p < 0.0001), while the culture did not account for an additional proportion of the variance (p = 0.4317). Similarly, using the regression estimate as the dependent variable, the DGAS test added to the culture while the culture did not add to the DGAS test (p < 0.0001 vs. p = 0.6317).

## DISCUSSION

Clinical assessment of new diagnostic tests should consider both the accuracy of the test compared with a gold standard of disease and comparison with currently used methods of diagnosis. Ideally, one should compare diagnostic tests with a gold standard for the disease in question.

### Table 1

<table>
<thead>
<tr>
<th>Patients</th>
<th>Group A Beta Strep</th>
<th>Non-group-A Beta Strep</th>
<th>Normal Flora</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGAS +</td>
<td>208</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>DGAS -</td>
<td>9</td>
<td>82</td>
<td>416</td>
</tr>
<tr>
<td>Controls</td>
<td>DGAS +</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>DGAS -</td>
<td>2</td>
<td>22</td>
<td>303</td>
</tr>
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</table>