Specificity Study of Kits for Detection of Group A Streptococci Directly from Throat Swabs

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A total of 78 Streptococcus strains, 15 Staphylococcus strains, and 2 Stomatococcus strains were used to test the specificity of 18 different antigen detection systems for group A streptococci and five products that detect a specific enzyme associated with group A streptococci. All streptococcal strains possessing the group A antigen were correctly identified with 31 different lots of reagents in the 18 antigen detection systems. The specificities of the 31 different lots of reagents ranged between 88.5 and 100%. A limited number of nonspecific reactions were observed with Enterococcus gallinarium, group C Streptococcus strain C23, and Staphylococcus aureus F49 and Cowan 1. The antigen detection kits that used enzymes as the extraction reagent gave slightly more specific results than did the kits that used chemical extraction reagents. The reagents in the five kits designed to detect the enzyme pyroglutamic acid arylamidase in Streptococcus pyogenes reacted positively with S. pyogenes (group A streptococcus); however, the reagents also reacted positively with all group D enterococcal streptococci and with about half of the staphylococcal strains treated. The nonspecificity of tests based on pyroglutamic acid arylamidase detection would seem to limit the usefulness of these kits with mixed cultures.

There are approximately 27 million throat swabs processed annually in the United States. Two recent studies have reported that, despite broad use of throat cultures for the detection of group A streptococci (GAS), throat swabs processed by conventional means have very little impact on the management of patients (5, 12). Holmberg and Faich (12), in their survey of physicians practicing in Rhode Island, reported that 87% of primary-care physicians prescribed antimicrobial therapy before culture results were known and that 40% continued antimicrobial therapy for 10 days regardless of culture results. These authors concluded that current throat-culturing practices probably have very little influence on the treatment of streptococcal pharyngitis in the state. Cochi et al. (5), in a nationwide survey of practicing physicians, reported that 25% of physicians always take specimens for culture, 52% selectively do so, and 23% never do so for patients with acute sore throats. Pediatricians were more likely to always take culture specimens (54%) and less likely (5%) to never take culture specimens. When primary-care physicians were asked whether they begin treatment before culture results are known, 42% said yes, always; 55% said yes, selectively; and 3% said no. When physicians who took throat cultures were asked whether they discontinued antimicrobial therapy if the culture was negative, 58% said yes and 42% said no. From these responses, we can conclude that throat cultures as they are now used in the United States have very little impact on the management of patients.

For any microbiologic test to be useful, it should have some influence on the management of patients. The most often stated reason for not using the results of conventional throat cultures to influence the decision to prescribe or not to prescribe antimicrobial therapy was the delay in getting the culture results (5).

The development of new antigen detection systems which claim to identify GAS directly from throat swabs seems to have the potential for improving the management of patients with acute sore throats, because the identification of GAS is made within 10 to 70 min of taking the swab from the patient. Some of these kits have been evaluated for specificity and sensitivity in various clinical settings (2-4, 8-11, 13, 27, 28).

This study was undertaken to attempt to measure the probable specificity of as many kits as could be obtained from commercial suppliers. Most of the kits studied have not had extensive specificity evaluations, and reports of extensive clinical evaluations have been limited to only two of these products.

MATERIALS AND METHODS

Strains. All strains were stock strains from our culture collection and were identified by conventional means (7). The following strains were used in this study: 18 strains with group A antigen; 11 typical beta-hemolytic Streptococcus pyogenes, each with a different M type; 2 nonhemolytic S. pyogenes; 2 beta-hemolytic S. anginosus; 3 alpha-hemolytic S. intermedius; 9 typical group B strains representing 6 different serotypes; 8 group C Streptococcus (7 S. equisimilis and 1 S. zooepidemicus); 10 group D Streptococcus representing 7 different species; 5 group F Streptococcus; 7 group G Streptococcus; and 4 strains representing Otens types I through IV. In addition, I used 14 viridans group Streptococcus strains, all representing different antigenic characteristics (6, 29); 15 Staphylococcus strains representing 7 species; 3 S. pneumoniae strains; and 2 Stomatococcus mucilaginosus strains (1). I believe that these strains are representative of bacteria that are commonly found in the posterior pharynx of humans in high enough concentrations to cause potential reactions with the GAS antigen detection kits.

Antigen detection systems. Culturette Brand 10-Minute Group A Strep ID kits were obtained from Marion Laboratories, Kansas City, Mo. DAI Strep A Latex and Direct Antigen ID Strep A Tests were obtained from Difco Laboratories, Detroit, Mich. Detect-A-Strep kits were obtained from Antibodies, Inc., Davis, Calif. Directigen Group A Strep and Directigen Rapid Group A Strep Tests were obtained from Hynson, Wescott and Dunning, Baltimore,
TABLE 1. Specificity of direct antigen test kits for group A Streptococcus identification

<table>
<thead>
<tr>
<th>Method and kit</th>
<th>Lot tested</th>
<th>Specificity (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Chemical extraction, slide agglutination detection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phadirect Strep A 50</td>
<td>A8326</td>
<td>97.8</td>
</tr>
<tr>
<td></td>
<td>1089</td>
<td>98.7</td>
</tr>
<tr>
<td></td>
<td>8798</td>
<td>98.5</td>
</tr>
<tr>
<td></td>
<td>27200</td>
<td>100</td>
</tr>
<tr>
<td>Culturette Brand 10-minute Test Pack</td>
<td>401603</td>
<td>100</td>
</tr>
<tr>
<td>Group A Strep ID</td>
<td>40667</td>
<td>97.7</td>
</tr>
<tr>
<td>Detect-A-Strep</td>
<td>7AH31W</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>5A0003</td>
<td>100</td>
</tr>
<tr>
<td>PathoDx Strep A</td>
<td>009</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>017</td>
<td>98.3</td>
</tr>
<tr>
<td>Directigen Rapid Group A Strept Test</td>
<td>300</td>
<td>98.3</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>98.3</td>
</tr>
<tr>
<td></td>
<td>502</td>
<td>97.4</td>
</tr>
<tr>
<td>Q Test Stat Strep</td>
<td>303</td>
<td>98.6</td>
</tr>
<tr>
<td>DAI Strep A Latex</td>
<td>R00256</td>
<td>100</td>
</tr>
<tr>
<td>Respiralex</td>
<td>LK14</td>
<td>88.5</td>
</tr>
<tr>
<td></td>
<td>LK16</td>
<td>96.0</td>
</tr>
<tr>
<td>SKD Rapid Test-Strep</td>
<td>2015</td>
<td>97.4</td>
</tr>
<tr>
<td>Streptogen 100</td>
<td>080968</td>
<td>97.4</td>
</tr>
<tr>
<td>B. Chemical extraction, ELISA detection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murex SUDS Group A Strep Test</td>
<td>No lot no.</td>
<td>100</td>
</tr>
<tr>
<td>Quidal Strep Group A</td>
<td>0309D23901</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>0305E0402</td>
<td>120</td>
</tr>
<tr>
<td>Testpack A</td>
<td>89488EG</td>
<td>97.4</td>
</tr>
<tr>
<td>Ventrexscreen Strep A</td>
<td>O944</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>02754</td>
<td>100</td>
</tr>
<tr>
<td>C. Enzyme extraction, slide agglutination detection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct Antigen ID Strep A Test</td>
<td>1964</td>
<td>98.4</td>
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<tr>
<td>Test</td>
<td>733315</td>
<td>100</td>
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<tr>
<td>Directigen Group A Strept Test</td>
<td>202</td>
<td>100</td>
</tr>
<tr>
<td>Q Test Strep</td>
<td>614</td>
<td>100</td>
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<tr>
<td>Streptex Direct A</td>
<td>K878860</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>K967110</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1. Specificity of direct antigen test kits for group A Streptococcus identification

Md. Murex SUDS Group A Strep Tests were obtained from Murex Corp., Norcross, Ga. PathoDx Strep A kits were obtained from Diagnostic Products Corp., Los Angeles, Calif. Phadirect Strep A 50 kits were obtained from Pharmacia, Inc., Pisacatawy, N.J. Quidal Strep A kits were obtained from Quidal, La Jolla, Calif. Q Test Stat Strep and Q Test Strep kits were obtained from Clay Adams, Parsippany, N.J. Respiralex kits were obtained from Medical Technology Corp., Somersett, N.J. SKD Rapid Test-Strep kits were obtained from SmithKline Diagnostics, Sunnyvale, Calif. Streptex Direct A kits were obtained from Wellcome Diagnostics, Research Triangle Park, N.C. The Streptogen 100 test kit was obtained from New Horizon Diagnostics, Columbia, Md. Testpack Strep A kits were obtained from Abbott Laboratories, North Chicago, Ill. Ventrexscreen Strep A kits were obtained from Ventrex Laboratories, Inc., Portland, Maine.

Non-antigen detection systems. Several commercial systems that measure the presence or absence of pyrolyldonylarylamide (PYRase) were also evaluated. Identicult-AE, Minitek PYR Disc, PYR-broth, Strep-A-Fluor, and Strept-A-Chek test kits were obtained from Scott Laboratories, Fiskeville, R.I.; BBL Microbiology Systems, Cockeysville, Md.; BioSpec. Inc., Dublin, Calif.; CarrScarborough Microbiologicals, Inc., Stone Mountain Ga.; and EY Laboratories, Inc., San Mateo, Calif., respectively.

Evaluation procedure. Strains were streaked to coded tryptic soy blood-agar plates containing 5% sheep blood (BBL). Plates were incubated overnight in a candle extraction jar at 35°C. Dacon-tipped swabs with plastic shafts were used, unless swabs of other material were recommended or provided by the supplier. Swabs were streaked over approximately a 30-mm portion of pure growth of the test strains. All extractions, slide agglutination tests, modified enzyme-linked immunosorbent assays (ELISAs), and PYRase tests were performed according to the instructions provided by the manufacturers in the package inserts. All GAS testing for identification test results and all non-group A strains giving positive identification test results were retested with the product being evaluated. Repeated misidentifications were reidentified by conventional tests.

The specificities of the products were calculated by dividing the number of true-negative reactions by the true-negative plus false-negative reactions.

RESULTS

The specificities and lot numbers of 31 different lots of 18 products are listed in Table 1. The products listed in part A of Table 1 are based on chemical extraction of the group A antigen and slide agglutination testing for the antigen in the extract. The time required to process the swabs from patient to final identification (turnaround time) was about 5 to 12 min. The products listed in part B of Table 1 are based on chemical extraction of the group A antigen and modified ELISA detection of the antigen in the extract. The turnaround times for these procedures were 10 to 20 min. The products listed in part C of Table 1 were based on enzyme extraction of the group A antigen and slide agglutination testing for the antigen, in the extract. The turnaround times for these products were 60 to 70 min.

All of the products listed in Table 1 gave positive reactions with all strains possessing the group A antigen.

Only one lot of one product had a specificity of less than 96%. The first lot of Respiralex (LK14) cross-reacted with nearly all the Staphylococcus strains used in this study. These cross-reactions were not present in the second lot (LK16) of reagents.

Staphylococcus aureus strains were more likely to cross-react than other strains used in this study. S. aureus F49 and Cowan 1 reacted with five and four products, respectively, whereas strains 42BP and 64BP reacted with two products each. Of the streptococci, group C strain C23 and Enterococcus gallinarum each reacted with five products. No other strain reacted with more than two lots of reagents.

In general, the specificities for the chemical extraction-ELISA detection systems and enzyme extraction-slide agglutination systems were higher than those for chemical extraction-slide agglutination systems (Table 1).

The test results of five products designed to detect the presence of PYRase are shown in Table 2. Only one of these products (Strep-A-Fluor) is marketed as a direct test for GAS. Of the streptococci possessing group A antigen, only S. pyogenes strains possess PYRase. Strains of S. anginosus and S. intermedius did not react with any of the products for detection of PYRase. PYRase was present in all Enterococcus sp. strains and several of the Staphylococcus sp. strains. Strains of S. haemolyticus, S. saprophyticus, and Stomatococcus mucilaginosus were consistently positive for PYRase in all products. S. aureus strains were negative in all
Streptococcus mucilaginosus were consistently positive for PYRase in all products. *S. aureus* strains were negative in all tests except for PYR-broth, in which two of four strains were positive. Strains of *S. epidermidis* and *S. warneri* were consistently negative for PYRase, whereas strains of *S. simulans* and *S. cohnii* gave variable results with the PYRase tests.

**DISCUSSION**

These results indicate that the rapid antigen detection devices are very specific. The specificities of these products are dependent upon the strains chosen for the study. Do they represent a sample of oral bacteria that may be found in high enough concentrations in the human oral cavity to cause cross-reactions? The true test of specificity must be obtained.

### TABLE 2. Percent positive reactions of test strains in tests designed to detect PYRase

<table>
<thead>
<tr>
<th>Test</th>
<th>Time</th>
<th>Lot no.</th>
<th><em>S. pyogenes</em></th>
<th>Other streptococci</th>
<th>Enterococci</th>
<th>Viridans group streptococci</th>
<th>Staphylococci and stomatococci</th>
</tr>
</thead>
<tbody>
<tr>
<td>PYR-broth</td>
<td>4 h</td>
<td>063272</td>
<td>100</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>48</td>
</tr>
<tr>
<td>Strep-A-Fluor</td>
<td>5 min</td>
<td>A454</td>
<td>100</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>NT</td>
</tr>
<tr>
<td>Strep-A-Chek</td>
<td>10 min</td>
<td>021186</td>
<td>100</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>50</td>
</tr>
<tr>
<td>Identicult-AE</td>
<td>10 min</td>
<td>032203</td>
<td>100</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>33</td>
</tr>
<tr>
<td>Minitek-PYR Disc</td>
<td>10 min</td>
<td>225758</td>
<td>100</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>48</td>
</tr>
</tbody>
</table>

* a — No reaction (all strains).
* b — NT, Not tested.

### TABLE 3. Specificity and sensitivity of direct identification of GAS from throat swabs

<table>
<thead>
<tr>
<th>Reference or source</th>
<th>No. of swabs processed/no. with GAS</th>
<th>Selective media</th>
<th>Incu ATM</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Culturette 10-min GAS ID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Campos and Charilau (3)</td>
<td>445/150</td>
<td>Yes</td>
<td>AN</td>
<td>62.0</td>
<td>99.6</td>
</tr>
<tr>
<td>Chang and Mohlu (4)</td>
<td>339/108</td>
<td>No</td>
<td>CO₂</td>
<td>83.0</td>
<td>99.0</td>
</tr>
<tr>
<td>Gerber (8)</td>
<td>313/257</td>
<td>No</td>
<td>A</td>
<td>88.0</td>
<td>96.0</td>
</tr>
<tr>
<td>Roddey et al. (21)</td>
<td>905/170</td>
<td>No</td>
<td>AN</td>
<td>63.0</td>
<td></td>
</tr>
<tr>
<td>Miceika et al. (17)</td>
<td>813/92</td>
<td>No</td>
<td>AN</td>
<td>92.4</td>
<td>92.8</td>
</tr>
<tr>
<td>Schwartz et al. (22)</td>
<td>425/211</td>
<td>No</td>
<td>AN</td>
<td>93.4</td>
<td>90.2</td>
</tr>
<tr>
<td>Shrinler et al. (24)</td>
<td>400/238</td>
<td>No</td>
<td>?</td>
<td>97.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Slifkin and Gil (25)</td>
<td>557/82</td>
<td>No</td>
<td>AN</td>
<td>95.1</td>
<td>100.0</td>
</tr>
<tr>
<td>Venezia et al. (26)</td>
<td>64/26</td>
<td>No</td>
<td>CO₂</td>
<td>100.0</td>
<td>97.0</td>
</tr>
<tr>
<td>Wagener and Remington (27)</td>
<td>722/105</td>
<td>No</td>
<td>AN</td>
<td>89.5</td>
<td>95.5</td>
</tr>
<tr>
<td>White et al. (28)</td>
<td>589/84</td>
<td>No</td>
<td>CO₂</td>
<td>78.0</td>
<td>88.0</td>
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<td>B. Directigen</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Berkowitz et al. (2)</td>
<td>1.044/214</td>
<td>No</td>
<td>A</td>
<td>88.3</td>
<td>98.0</td>
</tr>
<tr>
<td>Gerber et al. (11)</td>
<td>263/85</td>
<td>No</td>
<td>CO₂</td>
<td>84.0</td>
<td>99.0</td>
</tr>
<tr>
<td>Kamm and Bille (13)</td>
<td>229/46</td>
<td>No</td>
<td>CO₂</td>
<td>93.0</td>
<td>98.0</td>
</tr>
<tr>
<td>Latessa and Anhalt (15)</td>
<td>964/93</td>
<td>No</td>
<td>?</td>
<td>61.0</td>
<td>99.0</td>
</tr>
<tr>
<td>McCusker et al. (16)</td>
<td>500/144</td>
<td>No</td>
<td>AN</td>
<td>90.9</td>
<td>99.2</td>
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<tr>
<td>Miller et al. (18)</td>
<td>149/23</td>
<td>Yes</td>
<td>CO₂</td>
<td>91.0</td>
<td>98.0</td>
</tr>
<tr>
<td>S. Redd, R. Facklam, and M. Cohen, unpublished data</td>
<td>251/85</td>
<td>No</td>
<td>AN</td>
<td>90.6</td>
<td>94.0</td>
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<td>C. Detect-A-Strep</td>
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<td>Campos and Charilau (3)</td>
<td>539/135</td>
<td>Yes</td>
<td>AN</td>
<td>64.4</td>
<td>96.5</td>
</tr>
<tr>
<td>Wagener and Remington (27)</td>
<td>744/109</td>
<td>Yes</td>
<td>AN</td>
<td>83.5</td>
<td>98.6</td>
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<tr>
<td>D. Others</td>
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</tr>
<tr>
<td>DAI, Diño</td>
<td>196/54</td>
<td>No</td>
<td>CO₂</td>
<td>83.0</td>
<td>99.0</td>
</tr>
<tr>
<td>Venezia et al. (26)</td>
<td>307/66</td>
<td>No</td>
<td>CO₂</td>
<td>86.4</td>
<td>90.0</td>
</tr>
<tr>
<td>Phadirect</td>
<td>265/43</td>
<td>No</td>
<td>CO₂</td>
<td>87.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Ogay and Bille (19)</td>
<td>118/45</td>
<td>No</td>
<td>AN</td>
<td>44.0</td>
<td>78.0</td>
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<tr>
<td>Streptex</td>
<td>249/86</td>
<td>No</td>
<td>AN</td>
<td>62.8</td>
<td>96.9</td>
</tr>
</tbody>
</table>

* Incu ATM, Incubation atmosphere: A. aerobic; AN, anaerobic; CO₂, increased CO₂ in atmosphere or CO₂ incubator.
* Office setting: all others, laboratory setting.
* Positive culture only when blood agar plate contains 100 colonies.
from comparing the antigen detection test results with GAS recovery by conventional techniques. However, there is an 
unfortunate problem with this comparison. There is no conventional standard procedure that is universally ac-
cepted. There are a wide variety of techniques available to 
both microbiologists and practicing physicians who perform 
throat cultures. The use of selective media or atmospheres of 
culture incubation (or both) is recommended by some but 
not by others. The recent statement of Gerber (8) that if you 
asked 10 people how they do throat cultures, you would 
probably get 10 different answers is a disconcerting but 
accurate assessment of the current situation.

To help validate the conclusions of this study that the 
antigen detection systems are specific, I compared the 
results of this study to the results of other studies for which 
the sources of the throat swabs were patients with upper-
respiratory-tract illness. The results of several studies are 
summarized in Table 3. Note that the authors of some of 
these reports used selective media, whereas others did not.
Also note that the authors of these reports used three 
different incubation atmospheres for their “conventional” 
isoilation procedures.

All the reports in part A of Table 3 used the Culturette 
10-Minute GAS identification procedure. The specificities 
ranged from 88 to 100%, but most (10 of 12 reports) were 
between 95.5 and 99.0% specific. My results with two lots of 
this product were 97.8 and 98.7% specific.

There are seven reports about the Directigen 
Strep-A-Fluor test. The specificity of the 
Strep-A-Fluor test was also 
100%.

Two studies have evaluated the Detect-A-Strep GAS kit. 
The specificity of the Detect-A-Strep product evaluated in 
this study was 100% (two lots). The specificities reported by 
the other authors were 96.5 and 98.6% (Table 3, part C).

Three of the five studies, each using a different product, 
summarized in Table 3, part D, reported specificities nearly 
identical to those observed in this study. The specificity of 
the Phadirect Strep A test reported by Ogay and Bille (19) 
was lower than I observed, but these authors delayed 
processing some of the swabs. This could have altered both 
the conventional and direct antigen test results. The 
specificity of the Strep-A-Fluor test was also low (78%). I did not 
calculate the specificity of the Strep-A-Fluor test in the present study, because the data could be easily manipulated 
by the choice of test strains. The Strep-A-Fluor test is based 
on detection of the enzyme PRase, which is known to 
occur not only in group A Streptococcus but in Enterococcus 
and Staphylococcus species as well. The results of 
Gerber et al. (10) indicate that either enterococci or staphy-
lococci are among the bacteria found in the oral cavity that 
may give positive PRase reactions. It is dubious whether 
this test should be used as a direct test for the identification of 
GAS.

I have also listed the sensitivities reported by the authors of 
these studies in Table 3. There is a wide range of results, 
62 to 100% sensitive. Even studies using the same product 
with the same conventional procedure have a difference of 
20% in sensitivity (Roddey et al. [21] versus Schwartz et al. 
[22]). There is a general trend that the products using 
enzymes for extraction (Directigen, DAI, and Strepext) have 
sensitivities near or at 90%. Also note how one group of 
authors improved the sensitivity of one product to 97.8% by 
disregarding the cultures with fewer than 100 beta-hemolytic 
colonies (24). There is a controversial theory held by some 
strptococcollogists that if the conventional throat culture 
has between 1 and 10 colonies, then the patient is a probable 
carrier and does not have streptococcal pharyngitis. This 
controversy has not been settled.

In summary, I believe that the results of these studies have 
been substantially validated. This representative collection 
of bacteria appears to be useful in predicting potential 
cross-reactions and, thus, specificities of products.

Users of these products may encounter some difficulty in 
reading slide agglutination tests unless they have some 
experience. I generally found from my personal experience 
and from what I have observed firsthand that after reading 
about 30 reactions the difficulties disappeared. The most 
difficult reactions to interpret were those in which nonspe-
cific agglutination occurred, that is, when both the group A 
and control reagents were positive. These reactions should 
be interpreted as negative, but the tendency is to read them 
as positive. These difficulties were not encountered in inter-
preting the modified ELISAs.

The antigen detection devices offer identification of the 
majority of patients with GAS in much less time than that 
required for conventional culturing. Therefore, they can and 
should be put into use. The high specificity allows for the 
 immediate treatment of patients with positive test results. 
The somewhat-lower-than-desired sensitivity does not allow 
us to discontinue the use of conventional culturing tech-
niques when a negative antigen test is observed. The best 
scenario at this time is for physicians to obtain a pair of swab 
samples from their patients; use a direct antigen test for one 
swab and, if the direct antigen test is negative, prepare a 
culture from the second swab. Physicians should prescribe 
antimicrobial therapy for all patients with positive direct 
antigen tests, prescribe antimicrobial therapy for those 
patients who give the clinical impression of having strep throat 
even in view of a negative test result, and withhold antimi-
crobial therapy from all patients with negative direct antigen 
test results and for whom there is any reasonable doubt 
about clinical impressions. More than likely, this scenario 
would still probably result in the overtreatment of patients, 
as is currently being done, but it should decrease the 
indiscriminate distribution of antimicrobial agents.

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