Development, Implementation, and Impact of Acceptability Criteria for Serologic Tests for Infectious Diseases

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Received 29 August 2002/Returned for modification 7 November 2002/Accepted 13 November 2003

Serologic testing is essential for the diagnosis of some infectious diseases and yet is fraught with potential pitfalls. All parts of the diagnostic process must be optimized to ensure that serologic tests perform adequately. Recognizing that a lack of clinical data and correctly timed, paired sera frequently led to uninterpretable serology results at our laboratory, we developed and implemented simple acceptability criteria for serologic tests. We assessed the impact of these criteria by comparing submissions and results for the year before and the year after implementation of the criteria. The number of serologic tests performed declined by 25% after implementation of the acceptability criteria, despite an increase in requests for serologic tests. Inappropriate testing of acute-phase sera alone fell from 49 to 0% ($P < 0.001$) for the tests monitored. Appropriate submission of paired sera rose from 9 to 19% ($P = 0.006$). The proportion of results classified as interpretable rose from 52 to 100% ($P < 0.001$). We recommend that acceptability criteria be developed and applied to samples submitted to clinical microbiology laboratories for serologic testing.

Serologic testing is central to the diagnosis of some acute, recent, or chronic infectious diseases. Sometimes serologic testing must be relied upon as the only diagnostic test that is practical, because the suspected etiologic agent is impossible, difficult, or dangerous to grow in cultures in a routine diagnostic laboratory or because colonization and disease cannot readily be distinguished by classical microbiological methods. However, failure to optimize all parts of the diagnostic process can render the results of serologic testing difficult or impossible to interpret.

Criteria that guide the decision to test various specimens submitted to clinical microbiology laboratories have been developed and applied in several areas of bacteriology and parasitology, including those for processing cerebrospinal fluid (1, 7), stool (2, 5), and sputum (4, 6). These have been associated with time and cost savings (3). Such measures also improve the utility of data provided to physicians by the clinical laboratory.

We observed that samples submitted to our laboratory for serologic testing for infectious diseases frequently lacked adequate clinical data for the interpretation of results and that correctly timed, paired samples were often not supplied. To address this, we developed, implemented, and assessed the impact of acceptability criteria for serologic tests for infectious diseases. We studied all serum samples submitted for serologic tests conducted on behalf of Duke University Medical Center patients by the North Carolina State Laboratory of Public Health and the Centers for Disease Control and Prevention (Table 1) between 1 December 1998 and 30 November 2000.

The findings described in this work were presented in part at the 41st Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, Ill., abstract D-1400, 18 December 2001.

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Simple acceptability criteria for these tests were developed on the basis of the recommendations of the manufacturer and the performing laboratory. According to those recommendations, serologic assays are performed only when the following conditions are satisfied: (i) the date of onset is provided and (ii) a correctly timed acute-phase sample (in cases in which a reliable immunoglobulin M assay is available), or acute- and convalescent-phase serum samples (in cases in which they are needed or recommended), or a convalescent-phase sample alone (in cases in which acute-phase sera are not available and results can be interpreted in the clinical context on the basis of the date of onset) is submitted.

The acceptability criteria were introduced on 1 December 1999 in conjunction with notification and education of medical center staff in the monthly clinical microbiology newsletter. Each sample submitted during this second year of the study was reviewed for compliance with the acceptability criteria. For each serum sample, the clinical microbiology laboratory issued an interim report to the clinician indicating that an onset date and/or a convalescent-phase serum sample was needed before the serologic test would be done. Exceptions to the acceptability criteria were considered only after consultation with, and approval by, the Medical Microbiology Fellow, Clinical Microbiology Faculty, Serology Section Head, or Laboratory Director. Such exceptions were tracked in a logbook. Samples not meeting acceptability criteria were not forwarded for testing but were held for 3 months before being discarded.

To assess the impact of the acceptability criteria, we compared the number of test submissions and the proportions of rejected, inappropriately tested, positive, and interpretable tests during the year prior to the intervention compared to the year after the intervention. Statistical analyses were done using Epi Info 6.04 software (Centers for Disease Control and Prevention, Atlanta, Ga.).

We rejected 41% of tests submitted during the postintervention year, because they did not meet acceptability criteria (Ta-
ble 2). Requests for rickettsial, Legionella, Bartonella, and arbovirus serology were most frequently rejected (Table 3). No exceptions to the acceptability criteria were required during the year after implementation. The number of serologic tests performed declined by 25% after implementation of the acceptability criteria, despite an increase in requests for serologic tests. Inappropriate testing of acute-phase sera alone fell from 49 to 0% (P < 0.001). Appropriate submission of paired sera rose from 9 to 19% (P = 0.006). The proportion of results classified as interpretable rose from 52 to 100% (P < 0.001).

It is our impression that samples submitted for serologic testing might not receive the scrutiny given other types of specimens received by the clinical microbiology laboratory. Consequently, opportunities to improve the value of the test to the clinician and patient are lost. Furthermore, inappropriate testing of samples may result in diagnostic errors and waste of healthcare resources, including taxpayers’ money, for state and federal laboratories. After documenting that a lack of clinical exposure history and causes of potentially misleading results are necessary to determine pretest probability of disease (e.g., travel and medical history), adequate clinical data need to be supplied. The onset date is vital for interpretation of a result, appropriate handling of the sample in the laboratory, and selection of the best assay and testing strategy. Other clinical data are necessary to determine pretest probability of disease (e.g., travel and exposure history) and causes of potentially misleading results (e.g., vaccination and past medical history). A frequent deficiency is the failure to submit both acute- and convalescent-phase sera when they are needed.

We recommend that acceptability criteria should be developed and applied to samples submitted to clinical microbiology laboratories for serologic testing. Our acceptability criteria can be easily implemented when done in conjunction with education of health providers and clear lines of communication for consultation about individual patients. Criteria should be reviewed regularly to adapt them to inevitable changes in sero-

<table>
<thead>
<tr>
<th>Test category</th>
<th>Specific infections</th>
<th>Testing of acute-phase sample alone acceptable?</th>
<th>Testing of convalescent-phase sample alone acceptable?</th>
<th>Are paired sera the “gold standard”?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial agglutinins panel</td>
<td>Brucella abortus, Francisella tularensis</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Rickettsial panel</td>
<td>Ehrlichia chaffeensis, Anaplasma phagocytophilum, Rickettsia rickettsii, Rickettsia typhi</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Arboviral panel</td>
<td>Eastern equine encephalitis, La Crosse virus, St. Louis encephalitis</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Bacterial respiratory panel</td>
<td>Chlamydia psittaci, Coxiella burnetii, Legionella, Mycoplasma pneumoniae</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Viral respiratory panel</td>
<td>Adenovirus group, influenza virus A/B, parainfluenza virus 1–3, respiratory syncytial virus</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Parasitic</td>
<td>Babesia, Echinococcus, Entamoeba histolytica, Leishmania, Paragonimus westermanii, Plasmodium, Taenia solium, Toxocara, Trichinella spiralis, Trypanosoma cruzi, Schistosoma, Strongyloides</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Others</td>
<td>Bartonella, Chlamydia trachomatis, dengue, hantavirus, Japanese encephalitis, Leptospira, lymphocytic choriomeningitis, measles, mumps</td>
<td>No&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<sup>a</sup> Paired sera recommended for individuals from areas of endemicity.
<sup>b</sup> Testing acute sample alone acceptable for measles.

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<tr>
<th>Time period</th>
<th>No. of sera submitted</th>
<th>No. (%) of sera rejected&lt;sup&gt;a&lt;/sup&gt;</th>
<th>No. (%) of acute-phase sera inappropriately tested&lt;sup&gt;a&lt;/sup&gt;</th>
<th>No. (%) of paired sera submitted&lt;sup&gt;a&lt;/sup&gt;</th>
<th>No. (%) of positive results&lt;sup&gt;a&lt;/sup&gt;</th>
<th>No. (%) of interpretable results&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preintervention</td>
<td>204</td>
<td>0 (0)</td>
<td>100 (49)</td>
<td>18 (9)</td>
<td>16 (8)</td>
<td>106 (52)</td>
</tr>
<tr>
<td>Postintervention</td>
<td>262</td>
<td>108 (41)</td>
<td>0 (0)</td>
<td>29 (19)</td>
<td>17 (11)</td>
<td>154 (100)</td>
</tr>
</tbody>
</table>

<sup>a</sup> P < 0.001.
<sup>b</sup> P = 0.006.
<sup>c</sup> P, not significant.
logic assays, particularly those conducted at reference centers. Reference centers should inform the referring laboratories of changes in the tests that they provide and indicate the optimal sample requirements for each assay. Future refinements might include closer tailoring of criteria to individual assays and requirements for more detailed clinical information that would allow thorough evaluation of pretest probability before each assay is conducted.

**REFERENCES**


