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

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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.

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 submitted (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-
able 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 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 for infectious diseases. By comparing submissions and results for the year before and the year after implementation of the criteria, we showed improved correct submission of specimens and improved interpretability of results. These changes promote improved patient care and judicious use of healthcare resources. This study was not designed to determine whether diagnoses were missed because samples were rejected. However, considerable efforts were made to educate healthcare providers and to encourage consultation with laboratory staff about specific diagnostic questions in individual patients.

Although serology for establishing immune status respecting an infectious agent is relatively straightforward, its use for the diagnosis of acute, recent, or chronic infections is fraught with pitfalls. Consequently, all parts of the diagnostic process must be optimized to ensure that the serological test performs adequately. In each case an assessment needs to be made of the value of a serologic test compared with other available diagnostic methods. If a serologic test is found to be both indicated and useful, 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-

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**TABLE 1. Serologic tests studied**

<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><em>Brucella abortus</em>, <em>Francisella tularensis</em></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Rickettsial panel</td>
<td><em>Ehrlichia chaffeensis</em>, <em>Anaplasma phagocytophilum</em>, <em>Rickettsia rickettsii</em>, <em>Rickettsia typhi</em></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Arboviral panel</td>
<td>Eastern equine encephalitis, <em>La Crosse virus</em>, <em>St. Louis encephalitis</em>, Western equine encephalitis</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Bacterial respiratory panel</td>
<td><em>Chlamydia psittaci</em>, <em>Coxiella burnetti</em>, <em>Legionella</em>, <em>Mycoplasma pneumoniae</em></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Viral respiratory panel</td>
<td><em>Adenovirus</em> 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><em>Babesia</em>, <em>Echinococcus</em>, <em>Entamoeba histolytica</em>, <em>Leishmania</em>, <em>Paragonimus westermanii</em>, <em>Plasmodium</em>, <em>Taenia solium</em>, <em>Toxocara</em>, <em>Trichinella spiralis</em>, <em>Trypanosoma cruzi</em>, <em>Schistosoma</em>, <em>Strongyloides</em></td>
<td>No</td>
<td>Yes</td>
<td>No†</td>
</tr>
<tr>
<td>Others</td>
<td><em>Bartonella</em>, <em>Chlamydia trachomatis</em>, dengue, hantavirus, Japanese encephalitis, <em>Leptospira</em>, lymphocytic choriomeningitis, measles, mumps</td>
<td>No‡</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

† Paired sera recommended for individuals from areas of endemicity.
‡ Testing acute sample alone acceptable for measles.

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**TABLE 2. Impact of acceptability criteria**

<table>
<thead>
<tr>
<th>Time period</th>
<th>No. of sera submitted</th>
<th>No. (%) of sera rejected*</th>
<th>No. (%) of acute-phase sera inappropriately tested*</th>
<th>No. (%) of paired sera submitted*</th>
<th>No. (%) of positive results*</th>
<th>No. (%) of interpretable results*</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>

* $P < 0.001$.
† $P < 0.006$.
‡ $P$, 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