Predicting Clearance of Colonization with Vancomycin-Resistant Enterococci and Methicillin-Resistant Staphylococcus aureus by Use of Weekly Surveillance Cultures

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We analyzed surveillance cultures for vancomycin-resistant enterococci (VRE) and methicillin-resistant Staphylococcus aureus (MRSA) collected during a multicenter trial to determine if three negative cultures collected at weekly intervals would predict clearance of VRE or MRSA from colonized patients. Seventy-two percent of VRE-colonized patients and 94% of MRSA-colonized patients were culture negative after three consecutive negative cultures.

Infections with oxacillin (methicillin)-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE) have increased dramatically in recent years, and together, they cause 12% of all health care-associated infections (2, 8, 16). Patients infected with MRSA or VRE, as well as asymptptomatically colonized patients, serve as a reservoir for transmission of these bacteria to other hospitalized patients. To prevent spread, national guidelines recommend that health care providers use contact precautions during care of colonized and infected patients until it can be demonstrated that they are no longer colonized (5, 10, 14). Colonization with VRE can be prolonged (1, 3, 7), so the current recommendation by the Hospital Infection Control Practices Advisory Committee (HICPAC) is that isolation precautions should be maintained until VRE-negative results are documented with at least three consecutive negative cultures collected a minimum of 1 week apart (6, 14, 15). Persistent carriage with MRSA is also well documented (11, 13). Criteria for documenting clearance of MRSA from colonized patients are not established, although the standard of three negative weekly cultures is commonly applied to this population.

The National Institute of Allergy and Infectious Diseases (NIAID) supported a large, cluster-randomized trial assessing strategies to reduce transmission of VRE and MRSA in 19 intensive care units (ICUs) (W. C. Huskins, C. M. Huckabee, N. P. O’Grady, P. R. Murray, H. Kopetskie, L. Zimmer, M. E. Walker, R. L. Sinkowitz-Cochran, J. A. Jernigan, M. Samore, D. Wallace, and D. A. Goldmann, submitted for publication). Stool or perianal swabs for VRE and anterior nasal swabs for MRSA were collected at all ICU sites from patients upon admission, weekly thereafter, and on discharge and were processed at a central laboratory. More than 22,000 swabs from ICU populations at multiple geographic sites presented an opportunity to evaluate the HICPAC recommendations for VRE and their applicability for MRSA colonization.

Stool or perianal swabs for VRE were inoculated into bile-esculin azide broth supplemented with 8 μg/ml vancomycin and incubated at 35°C for 18 to 24 h. Broths were subcultured onto bile-esculin azide agar plates with 6 μg/ml vancomycin, incubated at 35°C, and inspected at 24 and 48 h of incubation. Enterococcus isolates were tested for vanA/vanB genes, using the LightCycler VRE detection test (Roche Applied Science, Indianapolis, IN). Nasal swabs for MRSA were inoculated into Mueller-Hinton broth supplemented with 7% NaCl and 2 μg/ml oxacillin and incubated at 35°C for 18 to 24 h. The broths were then subcultured onto mannitol salt agar plates with 4 μg/ml oxacillin, incubated at 35°C, and inspected after 24 and 48 h of incubation. Isolates of S. aureus were tested for the mecA gene by using the LightCycler MRSA detection test (Roche Applied Science, Indianapolis, IN).

We identified all patients with at least one positive surveillance culture for VRE or MRSA, followed by those with a minimum of two additional cultures, the first of which was negative. Of the specimens processed for VRE, slightly more than half (52%) of the cultures were negative after the initial negative culture. After two negative cultures, the next culture was negative in 68% of the culture sets, and 72% were negative after three negative cultures (Table 1). Of the specimens processed for MRSA, the percentages of negative cultures after one, two, and three negative cultures were 70%, 82%, and 94%, respectively.

These data demonstrate that a significant proportion of patients colonized with VRE would not be detected even after three negative weekly cultures. In contrast, the vast majority of previously MRSA-colonized patients were culture negative after three negative cultures.

The results of this study must be viewed with the following caveats. Highly sensitive culture techniques were used, includ-
ing selective broth enrichment, selective differential agar me-
dia, and prolonged incubation (9, 12). If less-sensitive culture
methods were used, then the negative weekly cultures would
have underestimated the number of patients who remained
colonized with VRE or MRSA. This could be responsible for
the findings in this study compared with earlier reports that
three negative weekly cultures could be used to exclude col-

The study was conducted through the Bacteriology and Mycology
Study Group clinical research network with assistance from the data
coordinating center, the Bacteriology and Mycology Statistical and
Operations Unit.

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TABLE 1. Predictive values of negative VRE and MRSA cultures

<table>
<thead>
<tr>
<th>No. of consecutive negative cultures following a positive</th>
<th>VRE</th>
<th>MRSA</th>
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<tbody>
<tr>
<td>No. of culture sets</td>
<td>% (95% CI) sets with next culture negative</td>
<td>No. of culture sets</td>
</tr>
<tr>
<td>1</td>
<td>511</td>
<td>52 (47–56)</td>
</tr>
<tr>
<td>2</td>
<td>148</td>
<td>68 (60–75)</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>72 (59–81)</td>
</tr>
</tbody>
</table>

*Culture sets with one additional culture following the consecutive negative cultures.
*CI, confidence interval.