Look before You Leap: Active Surveillance for Multidrug-Resistant Organisms

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Hospitals in the United States are under increasing pressure to perform active surveillance cultures for detection of methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE) among newly admitted patients. Results of such cultures can then be used to direct contact precautions to prevent transmission of MRSA and VRE in the health care setting. However, using active surveillance cultures to expand contact precautions is a complicated and resource-intensive intervention that has the potential for several unintended adverse consequences. Therefore, careful forethought and preparation should precede the institution of any active surveillance culture program. We review the following important steps that should be performed when planning any such intervention: preparing the laboratory and reducing the turnaround time for screening tests, monitoring and optimizing the intervention of instituting contact precautions, monitoring and ameliorating the known adverse effects of contact precautions, and measuring important outcomes to evaluate the effectiveness of a program of active surveillance cultures and contact precautions.

The US Centers for Disease Control and Prevention (CDC) recently released updated guidelines for the management of multidrug-resistant organisms in health care settings [1]. These evidence-based guidelines recommend an aggressive, multifaceted approach to control these organisms. Nonetheless, the guidelines have been fiercely criticized, including in the editorial pages of The New York Times [2] and other media outlets [3, 4]. The major criticism relates to a long-standing dispute in the infection-control community: whether active surveillance cultures for 2 multidrug-resistant organisms (methicillin-resistant Staphylococcus aureus [MRSA] and vancomycin-resistant enterococci [VRE]) should be adopted by all hospitals or whether the use of active surveillance cultures should be incorporated on an institution-by-institution basis, only when other interventions fail to control organism transmission [5]. The CDC guidelines recommend flexibility in the application of active surveillance cultures, considering them to be one of many interventions in a multifactorial approach to control of multidrug-resistant organisms. Critics of these guidelines contend that, given the failure of US hospitals to control the spread of MRSA and VRE, active surveillance cultures should be standard of care in every hospital.

Active surveillance cultures, which are designed to identify all patients colonized with a given multidrug-resistant organism, are performed mainly to detect MRSA and VRE, organisms for which usual reservoirs are established and validated screening tests are available. The 2003 guidelines of the Society for Healthcare Epidemiology of America recommend that all hospitals perform active surveillance cultures for MRSA and VRE, at least among high-risk patient populations [6, 7]. Most proponents of active surveillance cultures, however, propose screening all patients at the time of admission [6, 8]. A 2005 survey by the Emerging Infections Network revealed that only 30% of 463 infectious diseases specialists worked in hospitals that used active surveillance cultures routinely [9].

However, the use of active surveillance cultures is gaining momentum on several fronts. Proponents have partnered with consumer groups to take their message directly to the public. Most notably, the organization Reduce Infection Deaths has taken the position that any hospital that does not perform active surveillance cultures for all patients is not doing all it can to keep patients safe [2]. A new nationwide Veterans Healthcare...
System campaign (“Getting to Zero”) focuses on active surveillance cultures as the key to successful control of MRSA. An Institute for Healthcare Improvement project planned for 2007 also incorporates active surveillance cultures for MRSA as a key component of its intervention package to reduce hospital-acquired infections [10]. Medicolegal factors have also placed new pressure on hospitals to provide evidence that they are aggressively seeking to control MRSA and VRE. Hospitals are increasingly at risk for lawsuits from patients who have acquired MRSA in the hospital, and legislation has already been introduced in Illinois that would mandate screening for MRSA of all persons on admission to the hospital [11]. Finally, the recent development of commercial tests for rapid detection of MRSA and VRE introduces industry partners with an interest in maximizing the use of active surveillance cultures. Industry influence may take a variety of forms, including financial support for consumer groups, funding of national patient safety initiatives, lobbying for legislation, and support of local or national opinion leaders.

Others have summarized the evidence for and against active surveillance cultures as a strategy to control MRSA and VRE [1, 8, 12]. Here, we seek to assist the increasing number of hospitals that plan to use active surveillance cultures. Adequate preparation, including consideration of several preconditions for and unintended consequences of active surveillance cultures, will increase the likelihood that implementation will achieve the goal of improving patient safety.

**PREPARE THE LABORATORY**

Any decision to institute or broaden active surveillance cultures should be made in consultation with the director of the microbiology laboratory. The impact on the laboratory will depend on how broadly the institution plans to implement active surveillance cultures and how often they plan to repeat them during a patient’s hospitalization. If the institution wishes to perform active surveillance cultures on a small subset of high-risk patients, the number of cultures may be manageable with little advance planning. However, if they wish to screen all hospitalized patients, both at the time of admission and weekly during hospitalization, as most propose, the increased laboratory work load will be substantial and may require additional personnel or a change in laboratory work flow. A reasonable approach for hospitals that currently do not perform active surveillance cultures is to begin screening of patients in high-risk units only for one organism (MRSA) and to expand the program gradually. During this “phase-in” period, a variety of other laboratory issues may be addressed.

Once the decision is made to perform active surveillance cultures, which test should one choose? Currently available screening methods for MRSA and VRE include standard culture, several commercially available chromogenic agar media, and PCR-based testing. A complete discussion of the performance characteristics of these tests is beyond the scope of this article. However, in our opinion, any screening test for use in active surveillance culture programs should have a turnaround time of <24 h. Results of active surveillance cultures are designed to guide an intervention—implementation of contact precautions for colonized patients. As recommended in the CDC guidelines for enhanced control of MRSA or VRE, contact precautions should be used for patients for whom active surveillance cultures are performed, pending the result of the screening test [1]. Standard culture methods require 48–72 h to perform, so all screened patients will be subject to the contact precautions intervention for up to 3 days, regardless of whether they are found to have MRSA or VRE (interestingly, this time interval now approximates the ever-decreasing duration of stay at acute care hospitals, amounting to a form of universal contact precautions). Given the negative consequences of contact precautions (see below), continuing this intervention for 48–72 h for patients who do not have MRSA or VRE infection may violate the ethical principle of nonmaleficence, especially when faster screening tests are available.

A turnaround time of <24 h can be achieved using chromogenic agar medium or direct specimen PCR. Rapid screening for MRSA is supported by several commercially available chromogenic agar media (CHROMagar MRSA [BBL], MRSA Select [Bio-Rad], MRSA-ID [bioMérieux], and Chromogenic MRSA agar [Oxoid]), a US Food and Drug Administration (FDA)–approved real-time PCR assay (GeneOhm-MRSA [Becton-Dickinson]) [13], and analyte-specific reagent kits for MRSA PCR. An FDA-approved real-time PCR assay for detection of VRE (the vanA/vanB genes) directly from clinical specimens may soon be available, but “home-brew” assays for VRE are already in use in several centers, including that of one of the authors [14]. Several technical issues have prevented successful development of such assays for MRSA. The most important is distinguishing the presence of MRSA from the presence of mixed flora that include methicillin-resistant coagulase-negative staphylococci and methicillin-susceptible S. aureus [13, 14]. The FDA-approved test has solved this problem by targeting a genetic sequence unique to MRSA, which is close to the SCCmec integration site, providing a crucial link between S. aureus and the mecA gene [13]. The performance characteristics of this assay have been excellent [15], but the risk of emergence of a new SCCmec type that is not detected by this assay will require ongoing surveillance and validation against newly detected clones. Because the FDA-approved real-time PCR assay for MRSA costs $25–$30 per test, the up-front laboratory costs of implementing this assay are very high and may generate significant pressure to demonstrate cost savings in an unrealistically short time frame. Chromogenic agar screening is less costly than the commercially available real-time PCR (~$5 per plate...
vs. $25–$30; costs cited include assay only, not overhead or personnel time), but the turnaround time is also significantly longer (18–24 h vs. 1–4 h), because it requires growth of the organism.

For hospitals with limited availability of molecular diagnostics for infectious diseases, a reasonable starting point for active surveillance cultures would be to use chromogenic agar screening for MRSA. If the active surveillance culture program for MRSA was documented to be effective, an argument could then be made to add resources for further development of rapid diagnostics for both MRSA and VRE.

Other questions defy easy answers. Is one body site sufficient for screening? Who should be charged for the cost of the testing? What will be the response if the patient refuses the test? Available data support the nares as a single site for MRSA testing and either a stool specimen or a sample from a rectal or perirectal site for VRE testing. Although some data suggest increased sensitivity of test results through addition of other body sites for MRSA screening (e.g., the oropharynx, a perirectal site, and the groin) [1, 16], the increased resources required probably outweigh the incremental increase in yield. Although active surveillance cultures are not performed for the diagnosis of individual infections, but rather as part of an effort to provide a safer health care environment, it is our sense that most hospitals performing active surveillance cultures charge the individual patient for the cost of the test. Is it ethical to charge patients, including those without insurance coverage who will pay out of pocket, for a test that will likely play no role in treatment that is necessary for their condition? Some health care centers have chosen to implement contact precautions for those patients who refuse active surveillance culture [17]. We disagree with this approach, because the contact precautions intervention could be construed as punitive, given the potential risks associated with it. Isolation decisions for patients who refuse active surveillance cultures should be made on the basis of risk factors and clinical culture results only.

FOCUS ON ALL ASPECTS OF THE INTERVENTION

Given that active surveillance cultures are performed to guide an intervention (contact precautions) and given the resources associated with implementing active surveillance cultures, it is critical that all aspects of the intervention be evaluated and optimized. If <20% of patients with MRSA or VRE carriage are detected by routine clinical cultures [18], broad institution of active surveillance cultures would be expected to quadruple the use of contact precautions. Because patients for whom contact precautions are implemented should be placed in single-patient rooms [1], it is important to assess the hospital’s capacity for expanding contact precautions to many more patients. If the institution also plans to assign staff to care for cohorts of patients infected or colonized with MRSA or VRE, staffing needs should be evaluated. If availability of single-patient rooms is limited, policies should be developed to outline criteria for other patient placement options (e.g., which patients can be grouped and when they may share a room with a non-infected or colonized patient). Hospitals in which “throughput” problems (prolonged stays in the emergency department, and ambulance diversion because of inadequate bed capacity) are common will need to plan carefully, because an active surveillance culture program will add another level of complexity to the management of beds. For long-range planning, keep in mind that the increasing incidence of community-acquired MRSA will lead to an ever-greater proportion of patients found to be colonized at admission to the hospital.

Once bed availability and staffing needs are reviewed, current adherence of health care workers to contact precautions should be examined. Two observational studies placed baseline adherence to contact precautions at <30% [19, 20]. Obviously, when most health care workers ignore performance of required elements of contact precautions, it makes little sense to seek out more patients for whom contact precautions must be implemented. Cromer et al. [20] reported that adherence to contact precautions increased from <30% to >70% in association with the implementation of an aggressive program of process improvement. We believe that any active surveillance culture program should include monitoring of the adherence of health care workers to all elements of contact precautions. Observation of adherence could be added to the monitoring that all hospitals must now perform for hand hygiene adherence, although this will require additional training and personnel time. The even greater challenge will be to improve adherence to contact precautions to the level at which the intervention is likely to be effective when coupled with an active surveillance culture program.

Contact precautions can lead to several unintended consequences, and these should be carefully evaluated and monitored. The most often cited adverse effect of contact precautions is a reduction in contacts between health care workers and patients. Three studies performed in different health care centers and settings (a medical intensive care unit [21], a surgical intensive care unit and ward [22], and 2 inpatient medical wards [23]) reported remarkably similar findings: the implementation of contact precautions results in an ~50% reduction in contacts between health care workers and patients, including a reduction in the frequency of examination by attending physicians (table 1) [23]. We are unaware of published studies that have attempted to counteract this consequence of contact precautions or that have provided effective solutions to the problem. We recommend performing educational interventions to encourage providing equally attentive care to all patients. During observation of adherence to contact precautions, the frequency with
Table 1. Observational studies of the effect of contact precautions on encounters between health care workers and patients.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study duration</th>
<th>Location</th>
<th>Health care workers observed</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>[21]</td>
<td>7 months</td>
<td>Medical ICU in a university hospital</td>
<td>All</td>
<td>Mean no. of contacts per hour, 2.1 for isolated patients vs. 4.2 for nonisolated patients ($P = .03$)</td>
</tr>
<tr>
<td>[22]</td>
<td>5 weeks</td>
<td>Surgical ICU and surgical wards in a university hospital</td>
<td>All</td>
<td>Mean no. of contacts per hour in ICU, 6.1 for isolated patients vs. 13.8 for nonisolated patients ($P &lt; .001$); mean no. of contacts per hour on ward, 4.2 for isolated patients vs. 7.9 for nonisolated patients ($P &lt; .001$)</td>
</tr>
<tr>
<td>[23]</td>
<td>6 months</td>
<td>Inpatient medical wards at 2 university hospitals</td>
<td>Physicians</td>
<td>Proportion of patients examined during morning rounds by attending physicians, 35% of isolated patients vs. 73% of nonisolated patients ($P &lt; .001$); proportion of patients examined during morning rounds by senior resident physicians, 84% of isolated patients vs. 87% of nonisolated patients ($P = .58$)</td>
</tr>
</tbody>
</table>

**NOTE.** ICU, intensive care unit.

which health care workers entered the rooms of patients for whom contact precautions were implemented, compared with a sample of rooms in which the patients were not subject to contact precautions, could be used to monitor this phenomenon. If contacts between health care workers and patients remain significantly reduced for patients for whom contact precautions are implemented, more aggressive educational efforts (e.g., posters and screensavers) could be introduced.

Another adverse effect of contact precautions is an increase in feelings of isolation and loss of control that can result in anxiety and depression [24]. Tarzi et al. [25], in a cross-sectional study in which 22 geriatric patients for whom contact precautions were implemented for MRSA were compared with control subjects who were matched for age, sex, diagnosis, level of functional independence, and cognitive function, found significantly increased rates of anxiety and depression among patients subject to contact precautions (geriatric depression scale score, >6; 77% vs. 33%). Likewise, Catalano et al. [26] compared Hamilton depression and anxiety rating scales among 27 patients for whom contact precautions were implemented and 24 control subjects. Although patients subject to contact precautions had baseline scores similar to those of control subjects, they had significantly higher depression and anxiety scores after hospitalization for a period of 1–2 weeks [26]. Increasing contacts between health care workers and patients may reduce this effect; other measures include efforts to decrease a sense of isolation and instill a greater sense of control by arranging for increased social contact. Support and consultation from social work, physical and occupational therapy, clinical psychology, or psychiatry departments may also be helpful.

Some hospital departments should be exempted from the active surveillance culture program if the benefits of contact precautions are outweighed by the deleterious effects on the therapeutic plan. This would include the psychiatry department, because isolation could exacerbate psychiatric symptoms and interfere with direct observation of the patient. Inpatient palliative care departments that serve only terminally ill patients should also be exempted. Another problematic department is that of inpatient rehabilitation, because contact precautions have been shown to prolong duration of stay and time to reach rehabilitation goals [27], as well as to increase patient anger [28].

Finally, Stelfox et al. [29] reported an increase in noninfectious adverse events among patients for whom contact precautions were implemented, compared with control subjects. Although the greater dissatisfaction with treatment and reduced documentation of treatment reported by this group are not surprising, given the findings outlined above, the substantial increase in preventable adverse events and failures of supportive care is especially disturbing (table 2) [29]. We hope that increasing contacts between health care workers and patients can reduce the risk for many of these adverse events. Nonetheless, it is imperative that hospitals monitor the incidence of these adverse events among patients for whom contact precautions are implemented, compared with hospital-wide rates of adverse events. Interventions to improve patient safety can then be implemented as indicated by findings of individual institutions.

Patient satisfaction has become increasingly important, and the incorporation of patient satisfaction data into pay-for-performance programs should prompt hospitals to monitor and
manage problems with satisfaction that are caused by the implementation of contact precautions for patients. Both patients and their families require education and counseling regarding the implications of carriage of MRSA or VRE, including future risk for infection and transmission. This task will be shared by nurses, physicians, and infection-control personnel, making it essential that educational materials be available to ensure a consistent message.

Two of the most common questions from patients, families, and health care workers relate to decolonization and duration of implementation of contact precautions. We agree with CDC recommendations against the routine use of decolonization regimens [1]. There is no effective decolonization regimen for VRE, and widespread use of MRSA decolonization regimens is limited by the frequency of recolonization over time and by the emergence of resistance to antimicrobial agents (e.g., mupirocin) [1]. Regarding discontinuation of contact precautions, there are insufficient data to guide policy. Although the CDC makes no formal recommendation, patients with positive test results for MRSA or VRE should generally continue to have contact precautions implemented for the duration of the hospitalization during which results are positive. For subsequent admissions, ≥2 negative test results after the patient has discontinued receiving antibiotic therapy seems to be a reasonable minimum requirement for the discontinuation of contact precautions [1].

Of course, the recommendations above apply to all hospitals that adhere to the CDC guidelines for implementation of contact precautions for patients infected or colonized with multidrug-resistant organisms. However, wide adoption of active surveillance cultures will increase the use of contact precautions dramatically, increasing the urgency of addressing these important issues.

### Table 2. Effects of contact precautions in a retrospective cohort study of patients at 2 university hospitals.

<table>
<thead>
<tr>
<th>Type of measure, measure</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process of care</td>
<td></td>
</tr>
<tr>
<td>Vital signs incompletely recorded</td>
<td>1.92 (1.61–2.30)</td>
</tr>
<tr>
<td>Days with no vital signs recorded</td>
<td>2.55 (1.14–5.69)</td>
</tr>
<tr>
<td>Days with no nursing narrative notes</td>
<td>1.77 (1.40–2.24)</td>
</tr>
<tr>
<td>Days with no physician progress notes</td>
<td>2.91 (1.90–4.47)</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
<td>Adverse events per 1000 days</td>
<td>2.20 (1.47–3.30)</td>
</tr>
<tr>
<td>Supportive care failure (falls, pressure ulcers, and/or fluid or electrolyte disorders)</td>
<td>8.27 (3.09–22.1)</td>
</tr>
<tr>
<td>Patient complaint</td>
<td>23.5 (8.20–66.4)</td>
</tr>
</tbody>
</table>

**NOTE.** Evaluation of 150 isolated patients and 300 matched, nonisolated control subjects. Adapted from [29].

### Table 3. Metrics that could be monitored in table 3.

<table>
<thead>
<tr>
<th>Type of metric, factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process</td>
</tr>
<tr>
<td>Hand hygiene compliance</td>
</tr>
<tr>
<td>Gown and glove compliance</td>
</tr>
<tr>
<td>Chart documentation (vital signs, nursing notes, and physician notes)</td>
</tr>
<tr>
<td>Outcomes</td>
</tr>
<tr>
<td>Colonization conversion rates for the targeted organisms (overall and unit based)</td>
</tr>
<tr>
<td>Nosocomial infection rates</td>
</tr>
<tr>
<td>Nosocomial infection due to targeted organisms</td>
</tr>
<tr>
<td>Patient satisfaction scores stratified by isolation status</td>
</tr>
<tr>
<td>Use of antimicrobial agents typically used to treat targeted organisms (e.g., vancomycin, quinupristin-dalfopristin, linezolid, and daptomycin)</td>
</tr>
<tr>
<td>Hospital throughput measures (duration of patients’ stay, time from decision to admit to transfer to inpatient bed for patients in the emergency department, and ambulance diversion hours)</td>
</tr>
<tr>
<td>Adverse events potentially attributable to contact precautions (e.g., falls, pressure ulcers, and fluid or electrolyte disorders)</td>
</tr>
</tbody>
</table>

### MEASURE MEANINGFUL OUTCOMES

The intervention involving active surveillance cultures and contact precautions is complex, and its effectiveness can be threatened by many factors, including adherence to the contact precautions intervention itself. Regular (biannual) evaluation of the effectiveness of the intervention is, therefore, very important, because failure to note changes in meaningful outcomes should prompt careful review, followed by either reinforcement or reconsideration of the intervention. We outline performance metrics that could be monitored in table 3.

Although one immediate goal of instituting active surveillance cultures and contact precautions is to control spread of MRSA and VRE, the most important patient-safety goal is to reduce infection-related morbidity and mortality. Thus, measures that focus mainly on colonization should be considered secondary to those that focus on infection. To gain the best understanding of the effectiveness of the intervention, appropriate study design and methods should be used that take into account the limitations of quasi-experimental designs (i.e., the “before-after” study designs most commonly used to assess infection-control interventions) [30, 31].

Noninfectious adverse outcomes should also be measured and reported, as we suggest above, and stratified according to contact precautions status. One of the limitations of existing literature concerning active surveillance cultures and contact precautions is that it focuses too narrowly on infection-related outcomes and ignores patients’ overall experience of care, which...
include noninfectious adverse outcomes and patient dissatisfaction, respectively. Measuring these outcomes prospectively allows for early intervention to ameliorate the adverse effects of the active surveillance culture and/or contact precautions intervention or for reconsideration of the intervention itself. Our focus must stay fixed on providing treatment that is not only technically superb and optimally safe, but that is also delivered in the most humanistic manner possible. As Coia et al. [32] recently reminded us, “the bacteria are the problem, not the patients” [p. 355].

IMPACT ON THE INFECTION-CONTROL PROGRAM

Finally, successful implementation of an active surveillance culture and contact precautions program requires additional resources for the infection-control program. The increased demands associated with tracking patients colonized with MRSA and VRE, educating patients and staff, and coordinating the assessment of new processes and outcome measures will require additional personnel in many hospitals.

CONCLUSIONS

Despite the flexibility of recent CDC guidelines for control of multidrug-resistant organisms, hospitals will be under increasing pressure to initiate or expand active surveillance culture programs. Using active surveillance cultures to expand contact precautions and, thereby, decrease transmission of MRSA or VRE is a complex and resource-intensive intervention that has the potential for several unintended adverse consequences. Therefore, careful forethought and preparation should precede the implementation of any active surveillance culture program. In particular, planning should recognize the following needs: preparing the laboratory and reducing the turnaround time for screening tests, monitoring and optimizing the contact precautions intervention, monitoring and ameliorating the known adverse effects of contact precautions, and measuring important outcomes that can evaluate the effectiveness of a program of active surveillance cultures and contact precautions.

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