Are Active Microbiological Surveillance and Subsequent Isolation Needed to Prevent the Spread of Methicillin-Resistant *Staphylococcus aureus*?

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**Background.** Infection-control strategies usually combine several interventions. The relative value of individual interventions, however, is rarely determined. We assessed the effect of daily microbiological surveillance alone (e.g., without report of culture results or isolating colonized patients) as an infection-control measure on the spread of methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) in a medical intensive care unit (MICU).

**Methods.** Colonization of patients with MSSA and MRSA was assessed by cultures of nasal swabs obtained daily and, if a patient was intubated, by cultures of additional endotracheal aspirates. Pulsed-field gel electrophoresis was used to determine relatedness between MSSA or MRSA isolates in surveillance cultures (i.e., cultures of nasal swab specimens obtained daily) and those in clinical cultures (i.e., any other culture performed for clinical purposes). Adherence to infection-control measures by health care workers (HCWs) was determined by observations of HCW-patient interaction.

**Results.** During a 10-week period, surveillance cultures were performed for 158 patients. Fifty-five patients (34.8%) were colonized with MSSA, and 9 (5.7%) were colonized with MRSA. Sixty-two patients were colonized before admission to the hospital (53 had MSSA, and 9 had MRSA). Two patients appeared to have acquired MSSA in the MICU, but, on the basis of genotyping analysis, we determined that this was not the result of cross-acquisition.

**Conclusion.** Surveillance cultures and genotyping of MRSA and MSSA isolates demonstrated the absence of cross-transmission among patients in the MICU, despite ongoing introduction of these pathogens. Reporting culture results and isolating colonized patients, as suggested by some guidelines, would have falsely suggested the success of such infection-control policies.

Antibiotic-resistance is increasingly problematic in the treatment of critically ill patients, and colonization with antibiotic-resistant pathogens has become endemic in many intensive care units (ICUs). Transmission of pathogens from patient to patient via the hands of health care workers (HCWs) is a common route of colonization. Important variables for transmission are the degree of nursing staff cohorting, rates of contact between HCWs and patients, adherence to hand hygiene by HCWs, and pathogen colonization pressure [1].

Many different infection-control strategies have been used to reduce transmission of pathogens in the ICU. In nearly all cases, >1 infection-control strategy has been implemented in addition to preexisting (standard) infection-control programs, which complicates interpretation of the value of any specific intervention [2, 3]. Active microbiological surveillance, including reporting culture results to staff and isolating colonized patients, has been advised as an essential measure to limit the spread of antibiotic-resistant pathogens [4]. However, the number of interventions reported in studies of active surveillance is usually >5 (e.g., educate staff, perform surveillance cultures, increase the number of infection-control nurses in unit, report surveillance culture results, isolate colonized patients on the basis of...
results of surveillance cultures, increase environmental cleaning, and increase adherence to hand hygiene protocols).

To assess the value of surveillance cultures (i.e., cultures of nasal swab specimens obtained daily) alone, without use of additional measures (such as reporting results to staff and isolating colonized patients), we studied colonization and transmission of methicillin-susceptible Staphylococcus aureus (MSSA) and methicillin-resistant S. aureus (MRSA) by means of unreported microbiological surveillance. Unobtrusive observations of patient-HCW interaction were used to determine variables influencing transmission dynamics.

**METHODS**

**Setting.** Cook County Hospital is a public teaching hospital in Chicago with beds for 600 patients. The medical ICU (MICU) has 16 beds, 12 in single rooms and 4 in double rooms. The study was commissioned by the infection-control committee and approved by the institutional review board at Cook County Hospital. This study was conducted from 25 September through 12 December 2000.

**Microbiological surveillance.** Microbiological surveillance of colonization with MSSA or MRSA was performed in the MICU for 10 weeks. All patients admitted to the MICU were included. Nasal swab specimens (for all patients) and endotracheal aspirates (for patients who underwent ventilation) were obtained within 12 h after admission to the hospital and daily throughout the MICU stay. All specimens were plated directly on mannitol salt agar (BD Diagnostic Systems). Colonies that grew on mannitol salt agar were plated on trypticase soy agar with 5% sheep blood (BD Diagnostic Systems) to determine the hemolytic status of isolates and to test colonies using latex agglutination (Staphaurex; Abbott Laboratories Diagnostics). Colonies on mannitol salt agar plates were replicated on Oxacillin Screen Agar (BD Diagnostic Systems) to screen the entire bacterial population for oxacillin resistance. All isolates were tested for oxacillin resistance according to NCCLS guidelines [5]. Data on the number of clinical isolates of MRSA recovered in the ICU were derived from the hospitals’ microbiology laboratory. When colonization was identified \( \leq 48 \) h after ICU admission, it was considered as having been introduced into the MICU. When colonization was identified \( >48 \) h after ICU admission, PFGE was used to discriminate between endogenous colonization (due to selection of preexisting resistant flora by antibiotic pressure) and cross-transmission, by means of Smal-generated restriction fragment–length polymorphism patterns. All serial surveillance and clinical isolates were typed by PFGE. Criteria described by Tenover et al. [6] were used to analyze results of PFGE typing.

**Data on infection control and infection rates.** For 7 weeks of the study period, the degree of nursing staff cohorting, the rates of contact between patients and nurses, and nursing staff adherence to hand hygiene were determined by observation of patients and HCWs, as described elsewhere [7]. Experienced infection-control nurses performed unobtrusive observations daily (during the day or evening, according to a predetermined schedule), and the MICU staff was unaware of the schedule of observations. Nurses were observed randomly during 30-min periods to assess contact rates and the degree of cohorting. The degree of cohorting expresses the likelihood that, after a first contact, the second contact will be with the same patient. Patients were observed randomly during 15-min periods to assess contact rates with HCWs, and during the same interval, these HCWs were monitored for adherence to hand hygiene. As part of the standard infection-prevention program, infection-control nurses had monitored adherence to hand hygiene during an 18-month period that overlapped that of the current study. These observations were performed using comparable definitions but were less frequent (twice monthly) than observations performed for study purposes, and they did not include contact rates and degrees of cohorting. The long-term observations of adherence to hand hygiene prescriptions were used to evaluate whether infection-control compliance had changed over time.

The numbers of patients in MICU with MRSA isolated from clinical cultures (i.e., any other cultures performed for clinical purposes) were obtained from infection-control records from January 1999 to January 2003. The incidence was expressed as the number of positive MRSA cultures per 3-month period. Other infection-control measures were not performed, and feedback of results was not provided to MICU staff during the study.

**Statistical analysis.** Continuous variables were compared using Student’s *t* test or the Mann-Whitney *U* test, when appropriate. Categorical variables were studied with \( \chi^2 \) analysis. Potential correlations were studied using Pearson’s correlation. Data are expressed as mean values ± SD, unless otherwise indicated. Analyses were performed with SPSS software (SPSS).

**RESULTS**

**Colonization.** During the 10-week study period, 160 patients were admitted to the MICU. A total of 1216 surveillance cultures were obtained from 158 patients; 2 patients refused to participate. We were not able to collect specimens from 1 patient on one day; however, specimens were obtained from this patient on the days adjacent to this day. The daily rate of bed occupancy in the MICU was 81% ± 11% (range, 56%–100%). The numbers of patients colonized with MSSA and MRSA during this period were 55 (34.8%) and 9 (5.7%), respectively. Colonization was imported into the MICU by 62 patients (53 were colonized with MSSA, and 9 were colonized with MRSA). Two patients appeared to have acquired MSSA in the MICU, but on the basis of PFGE results, we determined that colonization was not due to cross-acquisition and, therefore, that
acquisition of MSSA was endogenous. PFGE of introduced MSSA and MRSA isolates revealed almost as many different genotypes as patients from whom these strains were recovered. Few similar genotypes were found among MSSA isolates. Because these strains were introduced to the MICU at the time of admission and these patients did not share an overlapping time period in the ICU, cross-transmission is unlikely to have occurred. The daily endemic prevalence of staphylococcal colonization was 22.8% ± 12.5% (range, 0%–46.7%) for MSSA and MRSA, 12.2% ± 10.2% (range, 0%–37.5%) for MSSA only, and 10.5% ± 6.8% (range, 0%–25%) for MRSA only (figure 1). Patients colonized with MRSA had a longer length of stay in the ICU than did patients colonized with MSSA (14.4 ± 20.9 vs. 3.3 ± 4.6 days; P = .006, by the Mann-Whitney U test).

Infection-control variables. Patients and HCWs were observed for a period of 361.5 h, during which 1133 contacts between HCWs and patients were recorded. Nurses had a mean of 1.9 patient-contacts/h, and patients had a mean of 4.2 HCW-contacts/h. The mean rate of adherence to glove use was 68%, to hand hygiene was 53%, and to glove use and/or hand hygiene was 78%. The mean degree of cohorting of MICU nurses was 77%. Alcoholic hand rub was used by HCWs in 15% of all hand hygiene opportunities and was highest among physicians, compared with nurses (32% vs. 8%; P = .01, by χ² analysis).

Historical infection rates and infection control. The number of patients who had MRSA isolated from clinical cultures per 3-month period varied from 3 to 10 (figure 2). During our study period (which overlapped parts of the third and fourth quarter of 2000), 11 patients had a total of 14 positive clinical cultures (9 yielded MSSA, and 5 yielded MRSA). Five of 9 patients for whom surveillance cultures yielded MRSA had clinical cultures that yielded MRSA. Six patients for whom surveillance cultures were positive for MSSA had clinical cultures that were positive for MSSA. Typing of each clinical isolate revealed a genotype identical to the patient’s surveillance isolate. There was no discernible trend of changing incidence of colonization with MRSA or MSSA over the 3-year period. In addition, the rate of adherence to hand hygiene, as determined by infection-control nurses, varied from 32% to 48% and did not change dramatically in the 18-month observation period.

DISCUSSION

S. aureus is a pathogen that is well adapted for patient-to-patient spread. Staphylococcal infections are associated with considerable morbidity and often with attributable mortality (especially when caused by methicillin-resistant strains) [8, 9]. However, whether and how infection prevention should be performed is a matter of debate, especially when colonization with MRSA is endemic. Some have argued that active surveillance should be performed to identify and isolate the iceberg of colonized patients (i.e., the majority of colonized but usually unidentified patients) [4]. Such a strategy has been successful for 20 years in The Netherlands, where the proportion of staphylococcal infections caused by MRSA is <1% [10]. Importantly, in such a circumstance, patients at high risk for colonization with MRSA (e.g., patients who were transferred from foreign hospitals where MRSA is endemic) can be easily identified, and introduction of MRSA from other hospitals in The Netherlands or from the community can be neglected.
The dynamics of colonization with *S. aureus* in ICUs in hospitals where MRSA is endemic are more complicated, and the potential for active surveillance–based isolation to be a successful infection-control strategy in such a setting is contentious. Using detailed microbiological surveillance—without reporting results or isolating colonized patients—in a busy, urban MICU where 6% of all patients were colonized with MRSA at admission and the mean daily prevalence of MRSA was 10%, we found that cross-transmission of MRSA did not occur during a 10-week study period; these results were confirmed by genotyping. Importantly, the period of study appeared not to be an outlier when considering the number of patients with MRSA isolated from clinical cultures or the daily practice of HCWs regarding adherence to hand hygiene. Therefore, the data suggest that cross-transmission did not occur and that if active surveillance cultures for MRSA would have been combined with reporting of results and isolation of colonized patients, these would have appeared to be successful interventions, although, in fact, they were not necessary. These findings were supported further by the absence of cross-transmission of MSSA. We do not recommend that all institutions perform active surveillance and bacterial genotyping as part of their prevention strategies. But we do want to emphasize that recommendations should be based on sound data. This study questions the necessity of screening and isolating patients colonized with MRSA in a high-risk environment. For an evidence-based recommendation, however, prospective comparative trials with relevant end points should be performed.

In addition, the negative effects of isolating individuals on patient care should be considered. In an observational study, HCWs were one-half as likely to enter the rooms of patients in contact isolation [11], and patients may even suffer psychologically from isolation [12].

The risks of pathogen transmission depend on several HCW-related variables, such as contact rates, level of cohorting, and adherence to hand hygiene measures [13]. Data from our MICU during this study period showed 4.2 HCW-contacts/h for patients, a mean degree of nurse cohorting of 77%, and a mean level of adherence to hand hygiene or gloving of 78%, which apparently were sufficient in aggregate to prevent cross-transmission [7]. The degree of cohorting of nurses has been determined in only a few studies. The relevance of this measure emerged from theoretical models of pathogen transmission, in which cohorting was expressed as the likelihood that, after a patient contact, the next contact would be with the same patient [13]. If cohorting was 100%, there would be no opportunity to transmit pathogens to other patients. In our MICU, the mean degree of nurse cohorting was 77%, with weekly means of 67%–90% [7]. Because ICU physicians usually care for all patients in the unit, their level of cohorting is much lower than for nurses, and as a result, their chance to transmit pathogens is much higher than that for nurses [7].

Many health care–related variables are ward-specific and may not be constant over time. For example, understaffing can lead to decreased degrees of cohorting, increased contact rates, and decreased adherence to infection-control measures [14]. The possible effects of these changes were demonstrated by Grundmann et al. [15], who reported that periods with lower staffing levels were associated with clustered spread of MRSA in their

![Figure 2](cid://image.png)
ICU. Several other studies have also identified understaffing as a risk factor for MRSA infection [2], as well as for catheter-related bloodstream infections [16] and prolonged duration of ICU stay [17,18].

Improved adherence to infection-control measures, fixing staff deficits, or identification and isolation of carriers, theoretically, could have prevented the spread of MRSA in periods of understaffing. Because isolation procedures usually increase the workload for HCWs, it is uncertain whether such a strategy can be implemented without providing additional staff, especially when a problem emerges because of understaffing. In fact, the greatest benefit of the multiple interventions included in programs of active microbiological surveillance and isolation may derive from the allocation of extra staff required by increased numbers of patients for whom there are contact precautions and/or from reduced entry of HCWs into isolation rooms [11].

Our results need to be interpreted in light of study limitations. Control of MRSA may reflect improved HCW adherence, because of the presence of an individual who obtained cultures, although hand hygiene adherence did not appear to change markedly (figure 2). Infection-control effects for patients colonized with MRSA may have been better by chance, but our data do not indicate this. Lack of MRSA and MSSA transmission may also have been chance phenomena, although this seems unlikely for a period of 3 months. Finally, most (12 of 16) of the beds in the MICU were single rooms, which may not apply to other settings.

The emerging picture of these studies is that general recommendations for targeted infection-control measures, such as performance of active surveillance cultures and subsequent isolation of colonized patients, require a greater understanding of the epidemiology of nosocomial pathogens in general and of hospital factors in particular, such as relative importance of acquisition routes (endogenous or cross-transmission), colonization pressure, cohorting, adherence to hand hygiene, and staffing levels. These factors are rarely assessed in studies of infection-control interventions but should greatly influence the choice of infection-control measures [19].

Acknowledgments

We thank the Chicago Infectious Diseases Research Institute, Catherine Nathan, Tom Rice, Robert Hayes, Mary O’Flaherty, Camiel Wielders, and all nurses in the medical intensive care unit and those in the infection-control program at Cook County Hospital (Chicago) for their assistance and support.


Potential conflicts of interest. All authors: no conflicts.

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