CONCISE COMMUNICATION

Screening for Carriage of Methicillin-Resistant *Staphylococcus aureus* Shortly After Exposure May Lead to False-Negative Results

John Evison, MD; Kathrin Mühlemann, MD, PhD

We evaluated a double screening strategy for carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) in patients exposed to a newly detected MRSA carrier. If the first screening of the exposed patient yielded negative results, screening was repeated 4 days later. This strategy detected 12 (28%) of the 43 new MRSA carriers identified during the study period. The results suggest that there is an incubation period before MRSA carriage is detectable.

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Screening for carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) has been recommended for patients exposed to a MRSA carrier, for patients with risk factors for MRSA carriage, and for patients admitted to a high-risk unit.[1] It is likely that the process of colonization includes an incubation period during which screening results remain negative because of low colonization density. We evaluated whether a double screening strategy would confirm this hypothesis.

METHODS

Infection control protocols at the University Hospital of Bern (Bern, Switzerland) mandate MRSA screening for patients referred from a foreign hospital or from a Swiss hospital with a high prevalence of MRSA carriage and for patients exposed to a newly detected MRSA carrier in the same room or ward. In August 2002, a policy of double screening was adopted for patients exposed to a newly detected MRSA carrier. Sampling for a second screening was done 4 days after the sampling for the first screening if the first screening yielded negative results. Each screened patient was under preemptive contact precautions until the result of the first screening became available.[2] Screening routinely included culture of swab specimens from both nares, the groin, and any skin lesion, as well as specimens of tracheal secretions for intubated or tracheostomized patients and of urine for patients with urinary catheters. For culture of MRSA, we used an enrichment broth (nutrient broth no. 2 [Oxoid] with 6% sodium chloride) and a biplate with 2 agars (mannitol salt agar 4% [Oxoid] and an oxacillin screening agar containing oxacillin at a concentration of 6 μg/mL [BioMérieux]). Broth cultures were incubated for 18–24 h at 35°C before subculture onto biplates. Biplate cultures were incubated for 48 h at 35°C, and results were read at 24 h and 48 h. Species identification was performed according to standard laboratory procedures. New cases of MRSA carriage were promptly reported to the infection control department by telephone. Typing of MRSA isolates by pulsed-field gel electrophoresis (PFGE) was done as described by Fux et al.[3]

Included in the analysis were all adult patients who underwent a double screening from September 1, 2002, to December 31, 2004, and for whom the first screening yielded a negative result. Patients could be included more than once, provided that previous MRSA screenings had a negative result. Data analysis was based on MRSA exposure episodes.

All analyses were performed in Stata, version 9 (Stata), with statistical significance set at the P value of .05 or less for 2-tailed tests. Differences between mean values were tested by the Student t test or the Mann-Whitney U test, and proportions were compared with the χ^2 or Fisher exact test, as appropriate.

RESULTS

We analyzed a total of 273 MRSA exposure episodes for 249 patients who had a negative result for the first screening. In 12 (4.3%) of the 273 episodes, MRSA carriage was detected by the second screening. The 273 MRSA exposure episodes included in this analysis comprised 13.4% of a total of 2,044 MRSA exposure episodes (for 1,772 patients) for which screening was performed during the study period. The total included screenings for patients referred from hospitals in a foreign country or in a Swiss region with a high prevalence of MRSA carriage. The double screening strategy detected 12 (28%) of a total of 43 new MRSA carriers detected during the study period. (The other 31 new MRSA carriers were detected during diagnostic work-up for infection [2 carriers] or by screening of contacts [29 carriers]). For each of the 12 MRSA carriers detected by double screening, the PFGE banding pattern yielded by the isolate matched the pattern for the isolate from the corresponding source patient. During the study period, 9 different MRSA clones circulated in our hospital, as shown by 9 different PFGE banding patterns.

For the 12 MRSA exposure episodes with a positive second screening result, the median interval from the first to the second sampling for screening was 6 days (range, 3–10 days); for the 261 episodes with a negative second screening result, the median interval was 4 days (range, 1–14 days) (Table, Figure). For the 12 MRSA carriers detected by the second screening, the mean interval from the first day of MRSA exposure to the sampling for the second screening (ie, the longest estimated incubation period) was 11.5 days (range, 9–39 days), and the interval from the first day of contact isolation of the source patient to the sampling for the second screening (ie, the shortest estimated incubation period) was 5 days (range, 1–12 days).

For the 12 MRSA exposure episodes with a positive second screening result, the patient had a longer duration of hospitalization before the first sampling for screening and a slightly higher number of screening samples obtained at the first and

TABLE. Characteristics Associated With 273 Episodes of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Exposure in Which a Double Screening Strategy Was Applied, Stratified by the Results of the Second Screening

Variable	Result of second screening		P
	Positive (n = 12)	Negative (n = 261)	
Patient characteristics			
Age, years	64.4 (16.9–89.4)	62.7 (16.5–91.3)	.5
Male sex	10 (83.3)	161 (61.7)	.1
Risk factors for MRSA carriage			
No. per patient	2 (0–6)	2 (0–6)	
Diabetes mellitus	1 (8.3)	36 (13.8)	.4
Hemodialysis or continuous ambulatory peritoneal dialysis	3 (25.0)	31 (11.9)	.1
Skin lesions	6 (50.0)	87 (33.3)	.1
Tracheostoma	1 (8.3)	13 (5.0)	.4
Urinary catheter	5 (41.7)	100 (38.3)	.5
Injection drug use	0 (0)	5 (1.9)	.7
Immunosuppression[a]	4 (33.3)	57 (21.8)	.4
Screening characteristics			
No. of days from admission to first sampling for screening	17.5 (0–56)	10 (0–100)	.05
No. of days from first to second sampling	6 (3–10)	4 (1–14)	.1
No. of swab samples collected			
At first screening	3.0 (2–6)	2.0 (1–10)	.01
At second screening	3.5 (2–7)	2.0 (1–11)	.05
Patient had screenings prior to this admission	6 (50)	53 (20.3)	.9
No. of days from preadmission screening to current screening	13.5 (1–31)	6 (1–326)	.9
Exposure episode characteristics			
Ward location at time of exposure			.1
Surgery	8 (66.7)	123 (47.1)	
Internal Medicine	2 (16.7)	113 (43.3)	
Intensive Care	2 (16.7)	24 (9.2)	
Unknown	0 (0)	1 (0.4)	
Location of exposure			.9
Patient's room	6 (50.0)	152 (58.2)	
Patient's ward	6 (50.0)	109 (41.8)	
Timing of recent antibiotic use[b]			
Any antibiotic			
Before first screening	10 (83.3)	181 (69.3)	.8
Before second screening	11 (91.7)	179 (68.6)	.6
Anti-MRSA agent			
Before first screening	1 (8.3)	27 (10.3)	.6
Before second screening	3 (25.0)	25 (9.6)	.8

NOTE. Data are no. (%) of exposure episodes or median value (range), unless otherwise indicated.

[a] Immunosuppression defined as steroid treatment equivalent to 7.5 mg or more of prednisone per day, chemotherapy, the use of immunomodulators, or the presence of HIV infection.

[b] Includes antibiotic treatment and prophylaxis during the previous 14 days.

the second samplings for screening than for the 261 MRSA exposure episodes with a negative second screening result. The patients in these 2 groups did not differ in the number of risk factors for MRSA carriage present (Table).

DISCUSSION

The double screening strategy detected 28% of patients with new MRSA carriage, who otherwise would have been missed. The fact that our institution has a low prevalence of MRSA carriage (3%–5%) argues against MRSA transmission from an unknown source during the interval between the 2 screenings. Furthermore, the results of molecular typing argue for transmission of MRSA from the source patients to the respective 12 carriers detected by the double screening strategy.

Our study suggests that MRSA colonization has an incubation period of approximately 5–11 days during which MRSA carriage cannot be detected by conventional screening methods. The study design did not allow for an exact estimation of an incubation period, because, for logistical reasons, exposed patients were not screened at daily intervals.

Interestingly, the interval from admission to an intensive care unit to acquisition of MRSA has been estimated to be 10

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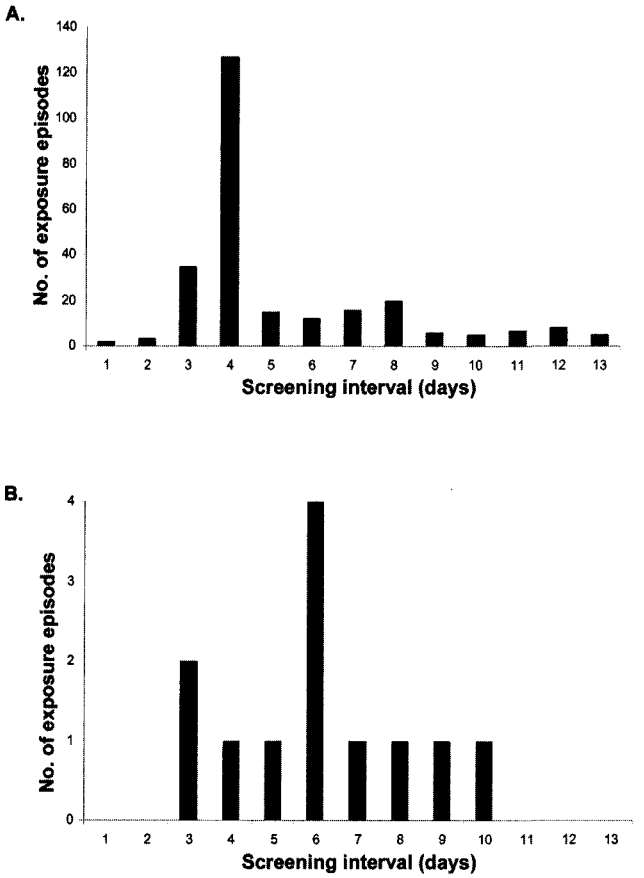

FIGURE. Interval between sampling for the first and for the second screenings for carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) in 273 MRSA exposure episodes. *A*, Episodes with negative results for both sets of screening cultures ($n = 261$); *B*, episodes with negative results for the first screening but positive results for the second screening ($n = 12$).

days,[4] and recommendations for screening for vancomycin-resistant enterococci are based on the assumption that acquisition takes 5–7 days after hospital admission.[5] It may be that these intervals represent incubation periods for colonization, rather than time to acquisition.

Also, selection of antibiotic-resistant microorganisms during antibiotic treatment for lower respiratory tract infection takes a median of 6 days.[6] Therefore, the interval required for bacterial colonization density to reach a detectable level is approximately 1 week both for acquisition of a microorganism from an external site and for selection from among the indigenous flora. It would be interesting to study whether detection methods for MRSA carriage that are more sensitive than our methods, such as polymerase chain reaction assays, would find an incubation period shorter than that in our study.[7]

Whether additional sampling of the throat would have influenced our study results remains unknown. Mertz et al.[8] reported that about one-fourth of MRSA carriers were detected by throat cultures only; however, they compared the sensitivity of screening nares and throat samples to the sensitivity of screening nares samples only. This cannot be compared with our screening algorithm, which routinely included swab specimens of the nares and the groin, as well as additional samples when risk factors were present.

In conclusion, screening culture performed very soon after MRSA acquisition may fail to detect MRSA carriage, because there may be an incubation period for colonization.

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From the Department of Infectious Diseases, University Hospital Bern (J.E., K.M.), and the Institute for Infectious Diseases, University of Bern (K.M.), Bern, Switzerland.

Address reprint requests to Kathrin Mühlemann, MD, PhD, Institute for Infectious Diseases, University of Bern, Friedbühlstrasse 51, 3010 Bern, Switzerland (kathrin.muehlemann@ifik.unibe.ch).

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