

Duration of Colonization with Methicillin-Resistant *Staphylococcus aureus*

Ari Robicsek,^{1,3} Jennifer L. Beaumont,⁵ and Lance R. Peterson^{2,4}

Departments of ¹Medicine and ²Pathology, Northwestern University's Feinberg School of Medicine; and ³Department of Medicine, Division of Infectious Diseases, ⁴Department of Pathology and Laboratory Medicine, Division of Microbiology, and ⁵Center on Outcomes, Research, and Education, NorthShore University HealthSystem, Evanston, Illinois

The duration of colonization with methicillin-resistant *Staphylococcus aureus* is not well defined. During 1564 admissions after a clinical culture or surveillance test positive for methicillin-resistant *Staphylococcus aureus*, we retested patients for methicillin-resistant *Staphylococcus aureus* colonization. During the first year after the positive culture result was obtained, 48.8% of the patients (95% confidence interval, 45.8%–51.7%) remained colonized; at 4 years, 21.2% of the patients (95% confidence interval, 13.1%–31.4%) remained colonized.

It is commonly presumed that patients with a history of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization or disease are likely to still be colonized when they are readmitted to the hospital. This assumption underlies the hospital practice of maintaining lists that flag MRSA-positive patients so that, at hospital admission, they can be placed in contact isolation [1] and, when necessary, given appropriate empirical therapy and antibiotic prophylaxis. It is not known for how long after an episode of MRSA colonization or disease a patient should be flagged as an infection-control risk. Prior studies that examined the duration of MRSA colonization have been small and limited to specialized patient populations [2–8], and clear guidelines have not been set [9].

NorthShore University HealthSystem is a 3-hospital health care organization in suburban Chicago in which universal admission surveillance for MRSA is practiced [10]. In this retrospective

study, we determined the duration of MRSA colonization in a large population of patients who were retested at hospital admission after a prior episode for which a MRSA test yielded a positive result.

Methods. All nonneonatal patients hospitalized overnight at any of the 3 participating hospitals from 1 November 2006 through 31 December 2007 were included if both of the following conditions were true: (1) they had a past clinical (not surveillance) culture positive for MRSA at any time from 1 January 2002 through the day prior to hospital admission or a positive result of a surveillance test (and no positive result of a past clinical culture) for MRSA at any point from 1 November 2006 through the day prior to hospital admission, and (2) they were tested for MRSA colonization within 2 days after hospital admission.

Double-headed premoistened swabs (BBL CultureSwab; Becton Dickinson) were used to obtain bilateral anterior nares samples from all included patients. Swab samples were processed using the BD-GeneOhm real-time PCR test (Becton Dickinson); processing was modified to accommodate high-volume testing [11]. Positive results were confirmed with culture on colistin-nalidixic acid agar with 5% sheep blood (Remel), followed by a Staphaurex latex agglutination test (Murex Biotech) and PCR testing for the presence of the *mecA* gene. A true-positive result of a PCR test was defined as the recovery of MRSA on culture or, if no MRSA grew on culture, a positive PCR test result in the presence of a culture positive for MRSA in the previous 12 months [11]. Any other positive PCR result was considered to be a false-positive result. Patients with a history of a positive MRSA test result were considered to be persistently colonized if they had a true-positive surveillance test result at hospital admission or a positive clinical culture result within 2 days after hospital admission.

For all study patients, the laboratory information system (which includes all inpatient and outpatient laboratory tests), the hospital administrative databases, and the electronic medical record were used to determine individual patient details. The method of Elixhauser et al. [12] was used to determine certain comorbidities from *International Classification of Diseases, Ninth Revision* codes. Long-term care facility residence was determined through review of nursing admission notes and the home addresses of all patients. Institutional review board approval was obtained for data collection.

Backward stepwise logistic regression modeling was used to evaluate the utility of hospital admission and demographic characteristics, the presence of comorbidities, the time since

Received 25 July 2008; accepted 26 November 2008; electronically published 20 February 2009.

Reprints or correspondence: Dr. Ari Robicsek, Northwestern University's Feinberg School of Medicine, 2650 Ridge Ave., Burch 124, Evanston, IL 60201 (arobicsek@enh.org).

Clinical Infectious Diseases 2009;48:910–3

© 2009 by the Infectious Diseases Society of America. All rights reserved.

1058-4838/2009/4807-0010\$15.00

DOI: 10.1086/597296

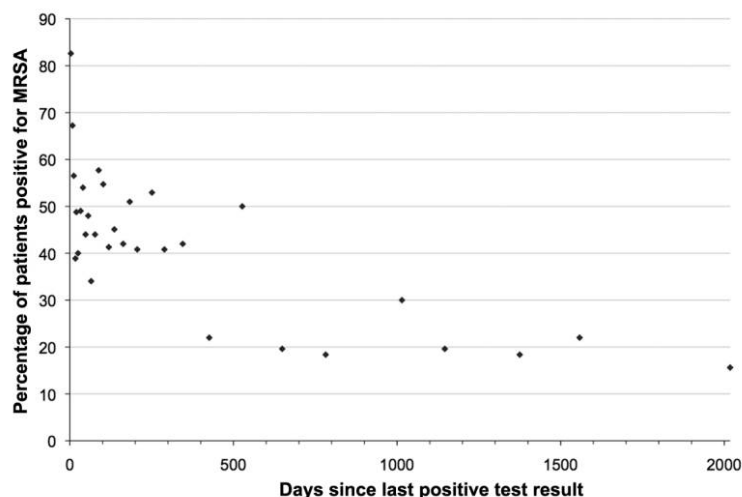


Figure 1. Decrease in the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) over time. There were 1564 hospital admissions of patients with a history of MRSA colonization. Each point represents ~50 admissions.

the last positive MRSA test result, and whether the last test was a clinical or surveillance test as predictors of continued colonization with MRSA. All variables that were statistically significant ($P = .1$) in univariate models were entered into the multivariable model. Statistically nonsignificant predictors were then removed one at a time until only variables with $P < .05$ remained. The final model was then fit using generalized estimating equation methodology, to adjust for the nonindependence introduced by repeat hospital admissions for some patients [13]. We elected not to use Kaplan-Meier survival estimates because, for previous MRSA carriers who were not colonized at the time of hospital admission, the true time at which they became uncolonized was unknown. Kaplan-Meier estimates would assume that they remained colonized until the date of the study admission, which would lead to an overestimate of colonization duration. Statistical analyses were performed using SAS, version 9.1 (SAS Institute).

Results. Of 48,203 overnight admissions to the hospital during the study period, surveillance testing was performed in 43,504 (90.3%). In 1564 hospital admissions (involving 824 patients), there was a prior clinical culture positive for MRSA; 996 of these occurred after a clinical culture for MRSA, and the remainder occurred after only a positive surveillance test result. The hospital admissions after a clinical culture occurred a mean of 518.7 days (median, 296 days) after the most recent positive clinical culture result. Because universal surveillance data were only available from November 2006 onwards (as opposed to January 2002 onwards for culture data), the mean and median times to hospital admission after only a positive surveillance test result were shorter—80.3 and 56 days, respectively.

For all hospital admissions included in our study, the mean

age of the patients was 71.3 years (median, 77 years). Of the patients represented by the 1564 admissions, 787 (50.3%) were female, 1342 (85.8%) were white, 774 (49.5%) had spent time in a long-term care facility after their positive MRSA test results prior to the current admission, 712 (45.5%) had diabetes mellitus, 683 (43.7%) had congestive heart failure, 557 (35.6%) had chronic lung disease, and 458 (29.3%) had pressure ulcers. The percentage of hospital admissions in which the patient was admitted under the care of the internal medicine ward was 88.9%, and 11.6% of admitted patients went directly to an intensive care unit.

Of the 1564 admissions of previously colonized patients, 648 (41.4%) involved patients who were still colonized, according to the results of either a clinical culture or a surveillance test. After a positive culture result, the rate of persistent colonization during year 1 was 48.8% (95% CI, 45.8%–51.7%), during year 2 was 28.2% (95% CI, 21.6%–35.5%), during year 3 was 23.0% (95% CI, 15.2%–32.5%), and during year 4 was 21.2% (95% CI, 13.1%–31.4%) (figure 1). Predictors of continued colonization are presented in table 1.

Discussion. It is widely assumed that MRSA colonization persists for a long time, although the duration of colonization has not been well established. Although it is common practice for hospitals to maintain lists of MRSA-colonized patients so that, at hospital admission, these patients can be rapidly identified and placed in contact isolation, it is not known how long patients should remain on such a list [9].

A number of previous studies of colonization duration have focused on specialized patient populations (e.g., neonates [2] or rehabilitation patients [3]) and are not clearly applicable to general inpatients. Other small studies have evaluated duration of colonization in patients admitted to a general hospital [4–

Table 1. Predictors of continued colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in patients with positive results of previous clinical or surveillance tests for MRSA.

Characteristic	Percentage of patients colonized at hospital admission	Univariate model		Multivariable model	
		OR (95% CI)	P	OR (95% CI)	P
Admission location					
Internal medicine (vs. other units)	42.4	1.48 (1.06–2.07)	.023	1.48 (1.04–2.10)	.028
ICU	49.4	1.41 (1.04–1.92)	.028	1.39 (1.00–1.94)	.047
Demographic characteristic					
Male sex	41.8	1.12 (0.88–1.42)	.368		
Age, years					
0–50	35.0	1.00 (reference)	.207		
51–70	38.9	1.14 (0.75–1.72)			
>70	43.7	1.34 (0.94–1.91)			
Race					
White	42.7	1.00 (reference)	.033	1.00 (reference)	.128
Black	30.4	0.57 (0.36–0.88)		0.63 (0.40–1.00)	
Other	42.2	0.97 (0.57–1.65)		1.01 (0.59–1.72)	
Long-term care facility residence	41.2	0.94 (0.74–1.19)	.592		
Presence of comorbidities					
Cancer	37.0	0.78 (0.55–1.10)	.154		
Chronic lung disease	43.8	1.11 (0.87–1.40)	.406		
Congestive heart failure	42.0	1.02 (0.80–1.29)	.891		
Diabetes mellitus	39.5	0.96 (0.76–1.21)	.742		
Pressure ulcer	45.8	1.37 (1.07–1.77)	.013	1.29 (1.00–1.67)	.048
Renal disease	36.2	0.91 (0.70–1.19)	.487		
Characteristic of colonization					
Time since last positive test result, 30-day units	...	0.97 (0.96–0.98)	<.001	0.97 (0.96–0.98)	<.001
Type of test that yielded last positive result: culture (vs. surveillance)	38.0	0.64 (0.51–0.82)	<.001	0.95 (0.73–1.25)	.73

NOTE. Overall, 41.4% of patients remained colonized at hospital admission. ICU, intensive care unit.

8]. The patients included in these investigations (range, 52–135 participants) were identified as MRSA colonized through both targeted surveillance and incidental positive clinical culture results. In these studies, estimates of colonization half-life ranged from 7.4 months [8] to 40 months [4]. Because of the relatively small sample sizes, the potentially biased method of detecting colonized patients (i.e., targeted surveillance of populations at high risk of colonization), and the widely varying results, these studies are not clearly applicable to general inpatients, either.

We examined 1564 consecutive admissions of previously colonized patients at 3 general hospitals. In this population, a reduction to a 50% rate of colonization occurred rapidly (in <1 month). However, the colonization rate thereafter decreased slowly, remaining close to 50% for ~300 days and never decreasing to much below 20%. These results may represent the fact that our cohort likely comprised 2 separate groups of individuals: intermittent carriers, who became decolonized quickly, and chronic carriers, who required months or years for decolonization [14].

In contrast to the high rate of continued colonization in this group, the overall rate of MRSA colonization among the 43,504 hospital admissions included in this study was 4.1%. This suggests that, even in the fourth year after a positive clinical culture result, the risk of MRSA colonization does not subside to that of the general inpatient population. Previously colonized patients, even at this point, had a colonization risk of 21%, which is ~5 times the colonization risk of an inpatient who has not been colonized. The risk of continued colonization remained high in this group, even among patients who lacked other traditional risk factors for colonization (e.g., long-term care facility residence [15] or recent hospitalization [16]). However, as noted by other investigators [5, 7], the presence of a break in the skin—in our study, a pressure ulcer—predicted continued colonization. Of interest, MRSA-colonized patients detected through a universal surveillance program had the same risk of continued colonization as did patients with positive clinical culture results.

This study has a number of limitations. First, patients were only routinely tested for nasal colonization; culture of samples

from other sites occurred only as clinically indicated. The sensitivity of nasal-only PCR in comparison with multiple-site culture has not been well tested [17], but it is reasonable to assume that $\geq 10\%$ of colonized patients were not detected. Second, some of the colonized patients had received systemic or topical antimicrobial agents active against MRSA as part of their therapeutic or decolonization regimen. Both these limitations could have led to underestimates of the continued colonization rate. Third, although this study included a large number of patients, there are some cautions with regard to generalizability. A large proportion of patients were white, and all were retested in the context of hospital readmission. Different colonization dynamics may apply to MRSA-colonized patient populations with a different racial composition and populations of patients who are never readmitted to the hospital.

In conclusion, we have found in a large population of MRSA carriers that, after an initial rapid decrease in colonization prevalence, rates of continued colonization remained high for prolonged periods. Previously colonized patients should be considered to be at high risk of continued carriage for at least 4 years.

Acknowledgments

Financial support. NorthShore University HealthSystem Research Institute Research Career Development Award (to A.R.) and Ortho-McNeil-Janssen Pharmaceuticals/Johnson & Johnson (to A.R.).

Potential conflicts of interest. A.R. and L.R.P. have received funding from Becton Dickinson. J.L.B.: no conflicts.

References

1. Siegel JD, Rhinehart E, Jackson M, Chiarello L; Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in healthcare settings, 2006. Available at: <http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroGuideline2006.pdf>. Accessed 15 November 2008.
2. Mitsuda T, Arai K, Fujita S, Yokota S. Epidemiological analysis of strains of methicillin-resistant *Staphylococcus aureus* (MRSA) infection in the nursery: prognosis of MRSA carrier infants. *J Hosp Infect* **1995**;31:123–34.
3. Aeilts GD, Sapico FL, Canawati HN, Malik GM, Montgomerie JZ. Methicillin-resistant *Staphylococcus aureus* colonization and infection in a rehabilitation facility. *J Clin Microbiol* **1982**;16:218–23.
4. Sanford MD, Widmer AF, Bale MJ, Jones RN, Wenzel RP. Efficient detection and long-term persistence of the carriage of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* **1994**;19:1123–8.
5. Scanvic A, Denic L, Gaillon S, Giry P, Andremont A, Lucet JC. Duration of colonization by methicillin-resistant *Staphylococcus aureus* after hospital discharge and risk factors for prolonged carriage. *Clin Infect Dis* **2001**;32:1393–8.
6. Vriens MR, Blok HE, Gigengack-Baars AC, et al. Methicillin-resistant *Staphylococcus aureus* carriage among patients after hospital discharge. *Infect Control Hosp Epidemiol* **2005**;26:629–33.
7. MacKinnon MM, Allen KD. Long-term MRSA carriage in hospital patients. *J Hosp Infect* **2000**;46:216–21.
8. Marshall J, Muhlemann K. Duration of methicillin-resistant *Staphylococcus aureus* carriage, according to risk factors for acquisition. *Infect Control Hosp Epidemiol* **2006**;27:1206–12.
9. Siegel JD, Rhinehart E, Jackson M, Chiarello L; Healthcare Infection Control Practices Advisory Committee. Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings 2007. Available at: http://www.cdc.gov/ncidod/dhqp/gl_isolation.html. Accessed 15 November 2008.
10. Robicsek A, Beaumont JL, Paule SM, et al. Universal surveillance for methicillin-resistant *Staphylococcus aureus* in 3 affiliated hospitals. *Ann Intern Med* **2008**;148:409–18.
11. Paule SM, Hacek D, Kufner B, et al. Performance of the BD GeneOhm methicillin-resistant *Staphylococcus aureus* test before and during high-volume clinical use. *J Clin Microbiol* **2007**;45:2993–8.
12. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* **1998**;36:8–27.
13. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* **1986**;73:13–22.
14. Wertheim HF, Melles DC, Vos MC, et al. The role of nasal carriage in *Staphylococcus aureus* infections. *Lancet Infect Dis* **2005**;5:751–62.
15. Jernigan JA, Pullen AL, Flowers L, Bell M, Jarvis WR. Prevalence of and risk factors for colonization with methicillin-resistant *Staphylococcus aureus* at the time of hospital admission. *Infect Control Hosp Epidemiol* **2003**;24:409–14.
16. Furuno JP, McGregor JC, Harris AD, et al. Identifying groups at high risk for carriage of antibiotic-resistant bacteria. *Arch Intern Med* **2006**;166:580–5.
17. Singh K, Gavin P, Vescio T, et al. Microbiologic surveillance using nasal cultures alone is sufficient for detection of methicillin-resistant *Staphylococcus aureus* isolates in neonates. *J Clin Microbiol* **2003**;41:2755–7.