To investigate persistent carriage of methicillin-resistant *Staphylococcus aureus* (MRSA), we conducted a prospective 10-month study of MRSA carriage in previous carriers who were readmitted to our hospital. Four screening specimens, 2 from the skin and 2 from the nares, were obtained within 3 days after admission, in addition to diagnostic specimens requested by physicians. Of the 78 patients included in our study, 31 (40%) were persistent carriers of MRSA, with an estimated median time of 8.5 months to MRSA clearance. In the multivariate analysis, the only factor significantly associated with persistent carriage was the presence of a break in the skin at readmission (odds ratio, 4.34; \( P = .004 \)); however, a trend was found for admission from a chronic-care institution (odds ratio, 3.65; \( P = .06 \)). Our data confirm that prolonged carriage of MRSA can occur after hospital discharge, support routine screening for MRSA at readmission of previously MRSA-positive patients, and suggest that a particularly high index of suspicion for MRSA carriage should be maintained if these patients have a break in the skin.

Methicillin-resistant *Staphylococcus aureus* (MRSA) has become a major threat worldwide, and the incidence of infection with MRSA is increasing in many countries despite the institution of infection control programs [1–3]. The major contribution of hospitalized MRSA carriers to the spread and persistence of nosocomial MRSA infection or colonization is well documented [4, 5]. In addition, it has recently been shown that hospital discharge of MRSA carriers can result in the spread of MRSA within the community [6, 7].

The few available studies of the duration of MRSA carriage after hospital discharge have produced conflicting results [8, 9]. We have developed an automatic alert system that identifies previous MRSA carriers at the time of readmission to our hospital, which is in an area of high MRSA endemity. Using this system, we prospectively assessed the duration of and factors associated with persistent MRSA carriage.

**METHODS**

**Background.** The Bichat–Claude Bernard Hospital is a 1200-bed hospital in Paris that serves as both a primary and a tertiary referral center, with approximately 35,000 hospitalizations of longer than 24 hours' duration per year.

A program for limiting the spread of MRSA was started in 1995 in several wards, primarily in the intensive care units, and then was extended to the rest of the hospital in early 1997. As part of this program, all patients with MRSA colonization or infection are prospectively followed until their discharge from the hospital. The following information is collected: demographic characteristics, residence before admission...
(home or other health care institution), date(s) and ward(s) of admission and transfer(s) within the hospital, ward at first identification of MRSA, date(s) and site(s) of colonization or infection, outcome, date of hospital discharge, and destination after discharge.

On the basis of the findings from surveillance cultures and cultures of clinical specimens, cases of MRSA colonization or infection are classified as either acquired in or imported to the hospital. Imported cases are those meeting any of the following criteria: MRSA recovered from any site within 48 h after admission, MRSA recovered from an infected site within 72 h after admission, or a history of MRSA colonization and/or infection. Other cases are classified as acquired in the hospital.

**Patients and study design.** In addition to this surveillance program, we started an automatic alert system in 1998 to identify readmitted patients who have a history of MRSA colonization or infection during a previous stay in our hospital. This readmission alert involves automatic comparison, 3 times a day, of the list of newly admitted patients with the computerized database of the bacteriology laboratory. When a newly admitted patient is identified as having been colonized or infected by an MRSA strain during a previous hospitalization, an alert is automatically sent to the infection control unit, where the personnel promptly notify the ward of the patient’s admission, assist in the institution of contact-isolation precautions, and recommend that the patient be screened for MRSA if necessary. During the study period, our program did not attempt to eradicate MRSA carriage, either with use of topical antimicrobials or with use of antiseptics.

The present study was conducted during a 10-month period, from 1 January through 30 October 1998. Since preliminary data from our hospital suggested that MRSA carriage persisted at least 3 months after hospital discharge, use of contact-isolation precautions without readmission screening was routinely recommended for patients readmitted within 3 months after hospital discharge. Both contact-isolation precautions and readmission screening were recommended for patients readmitted >3 months after discharge. These patients formed the study population.

The following information about patients in the study population was collected: time since discharge from our hospital; antibiotic therapy received within 3 months before readmission; age at readmission; sex; residence before admission (home or other health care institution); immunodeficiency status; severity of underlying diseases, as defined by the McCabe and Jackson score [10] and chronic health evaluation score [11]; types of any breaks in the skin; and any surgery or invasive procedures performed prior to readmission.

**Microbiological techniques.** Four specimens for MRSA screening, 2 from the skin and 2 from the nares, were obtained within 72 h after readmission of the patient (Culturette EZ; Becton Dickinson). Samples were taken from all breaks in the skin; if the skin was intact, a single swab was used to sample 4 different skin sites (the axilla and groin on both sides). A single swab was used to sample both nares. Clinical specimens were obtained as requested by the physicians in charge of the patient.

Screening swabs were plated on Chapman agar and incubated for 48 h at 37°C. *S. aureus* was identified as gram-positive cocci producing DNase (DNase test medium; bioMérieux) and free coagulate (as determined by the tube coagulate test with reconstituted citrate rabbit plasma [bioMérieux]). Resistance to methicillin was determined by means of the standard disk method, on Mueller-Hinton agar plates. The disks contained 5 μg of oxacillin. Inhibition of growth was interpreted in accordance with standard recommendations [12].

To compare isolates recovered from each patient during the previous and current hospitalizations, we used antibiotic susceptibility pattern (ASP) determinations and pulsed-field gel electrophoresis (PFGE) typing. ASPs were determined by the disk-diffusion method, as defined by the French Committee for Antimicrobial Susceptibility Testing of the French Society for Microbiology [10]. The following antibiotics were tested: gentamicin, tobramycin, fosfomycin, rifampin, fusidic acid, and pefloxacin. Strains were considered to have different ASPs if the ASPs differed for at least 1 of the antibiotics tested. After restriction of genomic staphylococcal DNA with *Sma*I (Boehringer), separation of the DNA macrorestriction fragments was achieved by PFGE (Pulsaphor system; Pharmacia-Biotech) as previously described. Macrogenomic patterns were considered to be similar if the number of fragment differences was 0 or 1; otherwise, they were considered to be different [13, 14].

**Statistical methods.** The time until clearance of MRSA was estimated from the date of hospital discharge on the basis of Kaplan–Meier estimates and actuarial life-table methods [15]. To evaluate factors potentially associated with persistent MRSA carriage on readmission, continuous variables were compared using the nonparametric Wilcoxon rank-sum test, and categorical variables were compared using the χ² test or Fisher’s exact test, as appropriate. ORs and 95% CIs were calculated. Next, we performed a multivariate analysis, using a conditional logistic regression model in which we included the variables suggested by the univariate analysis (P < .20). All tests were 2-sided, and P values <.05 were considered significant. Statistical analysis was performed with use of Epi Info (version 6.0; Centers for Disease Control and Prevention) and SPSS software (version 8.0; SPSS).

**RESULTS**

During the study period, MRSA was found in 424 admitted patients. The incidence of MRSA positivity (in imported or hospital-acquired cases, excluding screening specimens and du-
plicates) per 100 admissions was 1%. Of the 424 hospitalized patients, MRSA was considered to be imported in 222 (52%). Ninety-nine (45%) of the 222 imported cases involved patients with a history of MRSA colonization or infection during a previous stay in our hospital. These patients were identified through the automatic alert system, and their screening and/ or clinical specimens were positive for MRSA at readmission.

During the same period, the automatic alert system identified 146 readmitted patients who previously had been carriers of MRSA. Of these 146 patients, 78 were readmitted >3 months after the end of the previous stay, and those patients formed the population for the present study. Fifteen (19%) of the 78 patients were admitted from long-term care institutions or rehabilitation units, 38 (49%) had rapidly or ultimately fatal disease, 24 (31%) were in poor general health, and 34 (44%) had a break in the skin. Sixty (76.9%) of the 78 patients had at least 1 of these features.

At readmission, results of cultures for MRSA were negative for 47 (60%) of the 78 patients and positive for 31 others (40%). The median time to a negative MRSA screening result, based on the Kaplan-Meier estimate, was 8.5 months (figure 1).

Microbiological surveillance. MRSA was identified in the first set of routine screening specimens from 23 of the 26 screened patients (5 other patients had MRSA in clinical specimens). MRSA was detected in the nasal swab specimens of 21 (91%) of those 23 patients and in the skin specimens of 10 (43%). Therefore, the sensitivity of the testing of the first set of routine screening specimens, combined with clinical specimens, was 90% (28 of 31 patients). For 3 patients, both the first set of routine screening specimens and the clinical specimens were negative for MRSA, but MRSA was identified in the second set of routine screening specimens. For the 47 patients classified as MRSA free, all 4 routine screening specimens were negative for MRSA.

In 17 (55%) of the 31 persistent carriers of MRSA, ASPs of the strains isolated during the previous and current hospitalizations were similar. Six other patients were carriers of at least 2 different MRSA strains during the previous hospitalization, within 15 days before discharge; in all 6, at least 1 of these strains was found at readmission. Strains in 6 other patients had different ASPs during the previous and the current hospitalization. The ASP was not available for strains in the remaining 2 persistent carriers of MRSA.

PFGE patterns of isolates recovered during the previous and current hospitalizations were compared. In 12 of the 31 persistent carriers of MRSA, subcultures of MRSA isolates were not available. For 19 persistent carriers of MRSA, pairs of MRSA isolates from the 2 hospitalization periods were available. In 15 pairs (79%), the PFGE patterns were similar. They were different in the remaining 4 pairs (there were at least 7 fragment differences among the 4 pairs). These 4 pairs were from patients readmitted to our hospital from long-term care institutions or rehabilitation units. Of the 23 PFGE patterns (15 patterns of isolates from patients with similar strains during the previous and current hospitalizations and 8 patterns of isolates from patients with different strains), 4 were similar (for isolates from 4 different patients).

Factors associated with persistent MRSA carriage. Two factors were associated significantly with persistent MRSA carriage: admission from another health care institution and pres-
Table 1. Variables associated with persistent MRSA carriage (by univariate analysis) in a study of 78 patients readmitted >3 months after a previous hospitalization at Bichat–Claude Bernard Hospital, Paris, in 1998.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Persistent MRSA carriage (n = 31)</th>
<th>No persistent MRSA carriage (n = 47)</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>21 (68)</td>
<td>31 (66)</td>
<td>1.05 (0.58–1.89)</td>
<td>&gt;.25</td>
</tr>
<tr>
<td>Age, mean y ± SD (median)</td>
<td>63 ± 17 (67)</td>
<td>59 ± 21 (63)</td>
<td>&gt;.25</td>
<td></td>
</tr>
<tr>
<td>Age &gt;60 y</td>
<td>20 (65)</td>
<td>25 (53)</td>
<td>1.33 (0.74–2.39)</td>
<td>&gt;.25</td>
</tr>
<tr>
<td>Time since hospital discharge, mean d ± SD (median)</td>
<td>252 ± 176 (183)</td>
<td>241 ± 154 (228)</td>
<td>&gt;.25</td>
<td></td>
</tr>
<tr>
<td>Readmission within 6 mo of discharge</td>
<td>15 (48)</td>
<td>18 (38)</td>
<td>1.28 (0.74–2.20)</td>
<td>&gt;.25</td>
</tr>
<tr>
<td>Residence before readmission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Another health care institution</td>
<td>10 (32)</td>
<td>5 (11)</td>
<td>2.00 (1.21–3.30)</td>
<td>.02</td>
</tr>
<tr>
<td>Home</td>
<td>21 (68)</td>
<td>42 (89)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>7 (23)</td>
<td>13 (28)</td>
<td>0.85 (0.42–1.65)</td>
<td>&gt;.25</td>
</tr>
<tr>
<td>McCabe score &gt;0</td>
<td>12 (35)</td>
<td>26 (55)</td>
<td>0.70 (0.42–1.17)</td>
<td>&gt;.25</td>
</tr>
<tr>
<td>Chronic health evaluation score &gt;2</td>
<td>11 (35)</td>
<td>13 (28)</td>
<td>1.28 (0.66–2.49)</td>
<td>&gt;.25</td>
</tr>
<tr>
<td>Break in skin</td>
<td>21 (67.7)</td>
<td>13 (28)</td>
<td>2.72 (1.48–4.98)</td>
<td>.0005</td>
</tr>
<tr>
<td>Surgery after initial hospital discharge</td>
<td>7 (23)</td>
<td>7 (15)</td>
<td>1.67 (0.45–6.23)</td>
<td>&gt;.25</td>
</tr>
<tr>
<td>Antibiotics taken within past 3 mo</td>
<td>19 (61)</td>
<td>24 (51)</td>
<td>1.33 (0.72–2.46)</td>
<td>&gt;.25</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) of patients, unless otherwise indicated. MRSA, methicillin-resistant Staphylococcus aureus.

* Nursing facility or rehabilitation unit.

ence of a break in the skin (table 1). All 15 patients admitted from another health care institution came from a nursing facility or a rehabilitation unit. Forty breaks in the skin were noted in 33 (42%) of the 78 study patients; these included ulcers (n = 10), tracheostomy wounds (n = 10), jejunostomy or colostomy (n = 4), psoriasis lesions (n = 4), surgical wounds (n = 4), bedsores (n = 3), and other breaks (n = 5). Similar proportions of patients in the MRSA-positive and MRSA-negative groups had undergone an invasive procedure (data not shown). In the multivariate analysis, only the presence of a break in the skin remained significantly associated with persistent MRSA carriage (OR, 4.34; 95% CI, 1.60–11.8; P = .004); a trend was observed toward a higher risk of persistent MRSA carriage in patients coming from another health care institution (OR, 3.65; 95% CI, 0.95–12.0; P = .06).

**DISCUSSION**

Against a backdrop of increasing prevalence of MRSA worldwide, the admission of MRSA-positive patients has become a major mode of introduction and dissemination of MRSA within health care institutions. Recent reports have indicated that 20%–60% of MRSA-positive patients were identified within 48–72 h after admission to a health care facility [16, 17]. MRSA is highly endemic in France. In a recent French multicenter survey, MRSA was considered to be imported in 43% of patients from whom a clinical MRSA isolate was recovered [4]. This is consistent with our finding that 52% of cases were imported in our study. Because admission screening is not performed in all the wards of our hospital, this proportion is probably an underestimation of the true prevalence of imported cases among hospitalized MRSA carriers.

Some imported cases involve patients with a documented history of MRSA infection or colonization during a previous stay in the same hospital. This has prompted some hospitals, including ours, to develop readmission alert systems [16] aimed at identifying, at the time of readmission, patients who previously tested positive for MRSA, thus allowing prompt institution of barrier precautions. During our study period, 45% of imported MRSA cases (99 of 222) involved patients who were found to have MRSA-positive specimens during a previous stay in our hospital.

Forty percent (31 of 78) of the patients in our study who were identified by the readmission alert system as having a history of MRSA-positive specimens during a previous stay in our hospital tested positive for MRSA during the current stay. It is noteworthy that the yield of the first set of screening specimens (from skin and nasal swabs), combined with clinical specimens, was 90%. This suggests that 1 set is adequate to detect most persistent carriers of MRSA. From most of the persistent carriers, the same MRSA strain was recovered during the 2 hospitalizations, as evaluated with a reference molecular method. In 4 cases, however, isolates recovered during the previous and the current hospitalization were different; all 4 pa-
tients had been readmitted from long-term care or rehabilitation facilities. This confirms that acquisition of another MRSA strain in this setting frequently occurs [9, 18].

The persistence of MRSA carriage has been diversely estimated in the literature. In one study, the prevalence of MRSA carriage was 67%–70% at 30 months after hospital discharge, with a half-life of MRSA carriage of ~40 months among readmitted patients [9]. In another study, the prevalence of MRSA carriage in neonates who were discharged to home decreased rapidly, dropping to 36% after 3 months [8]. In our study, the median time to MRSA clearance was 8.5 months. However, MRSA carriers were not sampled at regular intervals for MRSA persistence; they were screened only at readmission to our hospital. Had regular sampling been performed after hospital discharge, reversal to a negative screening result would perhaps have been detected more rapidly in some patients. If so, we may have overestimated the median time to MRSA clearance in our study.

Several factors may explain the differences in results across these studies [8, 9]. In the study by Sanford et al. [9], many persistent carriers of MRSA seem to have been admitted from chronic-care institutions, and many had wounds. By contrast, the neonates studied by Mitsuuda et al. [8] were usually free of skin lesions and were discharged to home. Factors associated with MRSA persistence in our study were the presence of a break in the skin and, to a lesser extent, admission from a chronic-care institution. The differences between the populations in the 2 earlier studies may explain the differences in time to MRSA clearance.

The presence of a break in the skin was the only factor significantly associated with persistent MRSA carriage at readmission in our multivariate analysis. Although this factor has not been evaluated as a risk factor for MRSA persistence in hospitalized patients, it is well known to increase the likelihood of persistent MRSA carriage in health care providers [19]. Observational data from recently hospitalized patients also showed higher rates of persistent MRSA carriage in patients with a break in the skin [20]. In other recent publications, one factor associated with MRSA carriage at admission was the presence of open wounds [21, 22]. In addition, surgical wounds and skin lesions are 2 major sites of hospital-acquired MRSA infections [23]. Our findings are therefore concordant with earlier data and support the theory that breaks in the skin have a major role as persistent reservoirs of MRSA.

There was a nonsignificant trend toward an association between admission from a chronic-care institution and persistent MRSA carriage. The fact that this factor was not significant in our study may be ascribed to the small size of our patient population, particularly the small number of patients admitted from chronic-care facilities. The prevalence of MRSA is frequently high among long-term care patients, who often carry MRSA for years [18]. Our results are in keeping with these data.

In conclusion, we found that prolonged MRSA carriage is common after hospital discharge, with the main risk factor being the presence of a break in the skin. Therefore, patients known to have tested positive for MRSA during an earlier hospital stay and those with a break in the skin should be screened routinely for MRSA at readmission, and isolation precautions should be taken for these patients until the screening results are available.

References