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The proportion of Staphylococcus aureus isolates that were methicillin resistant (MRSA) increased from 35.9% in 1992 to 64.4% in 2003 for hospitals in the National Nosocomial Infections Surveillance system. During the same period, there was a decrease in resistance rates for several non–β-lactam drugs among the MRSA isolates.

Infections caused by oxacillin (methicillin)–resistant Staphylococcus aureus (MRSA) are a problem in health care institutions in the United States [1, 2] and worldwide, especially for intensive care unit (ICU) patients [3]. Since the late 1990s, MRSA have been increasingly recognized as a cause of infections among otherwise healthy people outside of health care settings [4]. The infections have predominantly affected the skin and soft tissues, have involved strains that are distinct from health care–associated MRSA strains, and are less resistant to non–β-lactam drugs. In one French hospital, strains of S. aureus that were increasingly susceptible to several antimicrobial agents emerged among hospitalized patients over an 11-year period; these strains had genetic characteristics consistent with strains of S. aureus in the community [5]. The extent to which community strains are replacing the traditional multidrug-resistant MRSA strains as causes of infection in US hospitals is currently unknown, as is the role that such shifts in strains may have in increasing or decreasing rates of resistance to non–β-lactam drugs.

The goals of this study were to describe the changes in the prevalence of MRSA as a cause of health care–associated infections from 1992 to 2003 from National Nosocomial Infections Surveillance (NNIS) hospitals and in the patterns of resistance to other antimicrobial agents. An understanding of the epidemiology of MRSA as a cause of health care–associated infections in ICUs in the United States may help target prevention and control efforts.

Methods. NNIS data were collected using standard methods by hospitals that voluntarily reported health care–associated infections to the Centers for Disease Control and Prevention from 1970 through 2005. In brief, surveillance of infections in participating adult and pediatric ICUs consists of prospective collection of data regarding health care–associated infection at all body sites (i.e., urinary tract infections, surgical site infections, bloodstream infections, pneumonia, and “other”). Data on the patient and the infection are collected. ICUs are classified by the type of care provided. For this analysis, we included burn, coronary, neurosurgical, medical, surgical, combined medical/surgical, and pediatric ICUs. Combined medical/surgical units were the source of most of the data, and these ICUs were further classified into ICUs in hospitals with or without major teaching activities. We grouped patients into 3 age categories: ≤18 years, 19–64 years, and 65–99 years. We grouped hospital size into 3 bed number categories: <200 beds, 200–500 beds, and >500 beds.

We defined the proportion of MRSA isolates as the number of S. aureus isolates tested and reported to be resistant to the semisynthetic penicillins methicillin, nafcillin, or oxacillin of all S. aureus isolates tested against those antimicrobial agents. NNIS hospitals used a variety of automated and nonautomated MIC determination methods and the disk diffusion method; these hospitals have previously been shown to be accurate in their assessment of antimicrobial resistance. Patterns were analyzed to determine the rates of resistance to penicillin, semisynthetic penicillins, and a variety of non–β-lactam antimicrobial agents, including ciprofloxacin, clindamycin, erythromycin, gentamicin, tetracycline, trimethoprim-sulfamethoxazole, and vancomycin. Isolates that were resistant to one of these antimicrobial agents could also have been resistant to >1 of them. Frequencies of 3 common resistance patterns observed in MRSA isolates in the United States were evaluated: resistance to erythromycin, clindamycin, and ciprofloxacin with (associated with strain type...
USA200) or without (associated with strain type USA100) resistance to gentamicin but with susceptibility to other antimicrobials tested; and resistance to erythromycin but susceptibility to other non-β-lactam antimicrobials tested (strain types USA300 and USA400) [6]. Isolates that did not have susceptibility test results for these antimicrobial agents were excluded from analyses.

To quantify changes by characteristics and susceptibility patterns over time, we used least-squares linear regression on the unadjusted annual proportion of resistance. For the overall and stratified proportion of S. aureus isolates that were MRSA, we used the slope to measure the change in the proportion each year and tested whether the slope was significantly different from zero. To evaluate factors associated with MRSA in 2003, we fit a multivariable logistic regression model using generalized estimating equations to control for clustering within hospital units. The model measured the independent effects of patient age, type of ICU, and hospital size in 2003.

Results. Patient data and antimicrobial susceptibility patterns for S. aureus health care–associated infections that met NNIS definitions were obtained from 1268 ICUs in 337 US hospitals. In 1992, a total of 35.9% of the 1838 isolates from patients with S. aureus that were tested for susceptibility to methicillin, nafcillin, or oxacillin were resistant to these agents. In 2003, a total of 64.4% of the 3392 S. aureus isolates tested were MRSA. On the basis of a linear model, the overall increase was 3.1% per year (P < .0001).

Significant increases were observed in the proportion of MRSA from 1992 to 2003 in all strata of age, ICU type, and hospital size. The annual increase in MRSA prevalence was greatest for persons aged ≥65 years (from 39.7% to 72.3%; β = 3.2; P = .001), coronary units (from 22.7% to 62.3%; β = 4.6; P = .001), and hospitals with 200–500 beds (from 30.1% to 61.9%; β = 3.6; P = .001). The best multivariable model included patient age group, type of ICU, and size of hospital; the only significant ORs for MRSA in 2003 were for patients aged ≥65 years (adjusted OR, 3.4; 95% CI, 1.6–7.4; P = .002).

Trends in the proportion of MRSA isolates that were resistant to additional antimicrobial agents were mixed (table 1). A small but statistically significant increase was observed for ciprofloxacin (from 90.5% in 1992 to 92.8% in 2003; β = 0.7; P = .001), whereas no change was observed for erythromycin (from 96.4% in 1992 to 93.5% in 2003; β = 0.13; P = .8). Statistically significant decreases were observed from 1992 to 2003 for clindamycin (from 91.8% to 76.9%; β = −0.7; P = .02), gentamicin (from 67.6% to 16.1%; β = −4.7; P < .0001), tetracycline (from 24.8% to 7.2%; β = −1.5; P < .0001), and trimethoprim-sulfamethoxazole (from 38.5% to 8.5%; β = −2.7; P < .0001).

None of the MRSA isolates were found to be resistant to vancomycin during the study period.

The trends of MRSA resistance to the combination of erythromycin, ciprofloxacin, clindamycin, and gentamicin (consistent with strain type USA200) decreased significantly during 1992–2003 (from 55.1% to 10.2%; β = −4.0; P < .0001). The rate of resistance to the combination of erythromycin, ciprofloxacin, and clindamycin (consistent with strain type USA100) decreased, but the change was not significant (from 82.1% to 71.5%; β = −0.4; P = .2). The percentage of MRSA isolates that were resistant to erythromycin and susceptible to other

### Table 1. Resistance findings for Staphylococcus aureus isolates resistant to methicillin, oxacillin, or nafcillin for select antimicrobials and combinations of antimicrobials with unadjusted linear slopes, National Nosocomial Infections Surveillance system, 1992–2003.

<table>
<thead>
<tr>
<th>Antimicrobial or antimicrobial combination</th>
<th>1992</th>
<th>2003</th>
<th>β</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>391 (90.5)</td>
<td>693 (92.8)</td>
<td>0.7</td>
<td>.001</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>588 (91.8)</td>
<td>1673 (76.9)</td>
<td>−0.7</td>
<td>.017</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>523 (96.4)</td>
<td>1711 (93.5)</td>
<td>...</td>
<td>.8</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>290 (67.6)</td>
<td>1114 (16.1)</td>
<td>−4.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>290 (24.8)</td>
<td>1314 (7.2)</td>
<td>−1.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>499 (38.5)</td>
<td>1584 (8.5)</td>
<td>−2.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>644 (0.0)</td>
<td>2000 (0.0)</td>
<td>...</td>
<td>.4</td>
</tr>
<tr>
<td>Erythromycin, clindamycin, ciprofloxacin, and gentamicin</td>
<td>118 (55.1)</td>
<td>363 (10.2)</td>
<td>−4.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Erythromycin, clindamycin, and ciprofloxacin</td>
<td>262 (82.1)</td>
<td>551 (71.5)</td>
<td>...</td>
<td>.2</td>
</tr>
<tr>
<td>Erythromycin only, susceptible to others tested</td>
<td>523 (4.0)</td>
<td>1748 (14.7)</td>
<td>1.0</td>
<td>.003</td>
</tr>
</tbody>
</table>

* Significant P value indicates that the slope is not equal to zero.
antimicrobials tested (consistent with strain types USA300 and USA400) increased significantly (from 4.0% to 14.7%; β = 1.0; P = .003).

Discussion. In ICUs in the United States, the proportion of MRSA isolates among *S. aureus* isolates increased from 1992 to 2003 by ~3% per year. MRSA have been persistent in health care institutions in the United States for >2 decades [1, 2]. In 1992, burn units were the only ICUs in which MRSA accounted for >50% of all *S. aureus* isolates. In 2003, MRSA accounted for >60% of isolates in most ICUs, among all adult patients, and in all sizes of hospitals. After controlling for type of ICU, we found that patients aged ≥65 years had a greater likelihood of having an MRSA infection than did patients in other age groups.

The observed decrease in multidrug resistance among MRSA isolates in US hospitals that participate in NNIS was also observed in Europe [5, 7], where it was linked with the appearance of a novel strain type containing SCCmec type IV. In the United States, several hospitals have reported MRSA infections associated with community MRSA strains [8, 9]. Our findings of decreasing rates of multidrug resistance are consistent with the appearance of community MRSA strains entering US hospitals. Other factors, including the decreasing use of gentamicin in the late 1990s [10], may have contributed to the apparent shift in strains. Interestingly, the rate of resistance to gentamicin was stable or increased slightly among Enterobacteriaceae during the same time [11]. Thus, the relationship between antimicrobial use and resistance, particularly among *S. aureus* isolates, is likely multifactorial and deserves further study.

Regardless of which MRSA strains are present in hospitals, action is necessary to control further spread. Aggressive programs in several European countries have documented the success of identifying and treating colonized patients quickly. In the United States, the Society for Healthcare Epidemiology of America recommends active surveillance and contact precautions, but it suggests that decolonization is optional [12]. Guidance for screening patients for MRSA colonization may need to be revised if increasing rates of MRSA are associated with community-acquired strains. Individual hospitals should assess whether MRSA is a problem in their facility and customize policies in both infection control and antimicrobial use. The Campaign to Prevent Antimicrobial Resistance in Healthcare Settings (http://www.cdc.gov/drugresistance/healthcare) may be a useful resource for educating providers in both of these areas.

In summary, MRSA infections have become markedly more prevalent in many ICUs in the United States. Shifts in predominant strains are suggested by changing resistance patterns. US hospitals should evaluate the need to implement stricter infection-control and antimicrobial-use practices.

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References