METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* IN U.S. HOSPITALS, 1975-1991

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ABSTRACT

OBJECTIVES: **Analyze changes that have occurred among U.S. hospitals over a 17-year period, 1975 through 1991, in the percentage of Staphylococcus aureus resistant to b-lactam antibiotics and associated with nosocomial infections.**

DESIGN: **Retrospective review. The percentage of methicillin-resistant S aureus (MRSA) was defined as the number of S aureus isolates resistant to either methicillin, oxacillin, or nafcillin divided by the total number of S aureus isolates for which methicillin, oxacillin, or nafcillin susceptibility test results were reported to the National Nosocomial Infections Surveillance (NNIS) System.**

SETTING: **NNIS System hospitals.**

RESULTS: **Of the 66,132 S aureus isolates that were tested for susceptibility to methicillin, oxacillin, or nafcillin during 1975 through 1991, 6,986 (11%) were resistant to methicillin, oxacillin, or nafcillin. The percentage MRSA among all hospitals rose from 2.4% in 1975 to 29% in 1991, but the rate of increase differed significantly among 3 bed-size categories: <200 beds, 200 to 499 beds, and 2500 beds. In 1991, for hospitals with <200 beds, 14.9% of S aureus isolates were MRSA, for hospitals with 200 to 499 beds, 20.3% were MRSA; and for hospitals with >500 beds, 38.3% were MRSA. The percentage MRSA in each of the bed-size categories rose above 5% at different times: in 1983, for hospitals with 2500 beds; in 1985, for hospitals with 200 to 499 beds; and in 1987, for hospitals with <200 beds.**

CONCLUSIONS: **This study suggests that hospitals of all sizes are facing the problem of MRSA, the problem appears to be increasing regardless of hospital size, and control measures advocated for MRSA appear to require re-evaluation. Further study of MRSA in hospitals would benefit our understanding of this costly pathogen. *(Infect Control Hosp Epidemiol.* 1992; 13:582-586.)**

INTRODUCTION

Staphylococcus aureus remains an important cause of nosocomial infection, especially nosocomial pneumonia, surgical wound infection, and bloodstream infection.[1] Methicillin-resistant *S* aureus (MRSA) first emerged as an important clinical problem in the United Kingdom in the early 1960s, shortly after methicillin came into clinical use.[2,3] Although MRSA

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was first recognized in the United States in 1961, it was not until the late 1960s that reports of outbreak investigations began to appear in the U.S. medical literature.[4-7]

Most of the sources of data on the prevalence and distribution of MRSA in the United States are reports of outbreak investigations and surveys of hospitals and laboratories, including pediatric and Veterans Affairs hospitals.[2-27] MRSA outbreaks have been reported from all U.S. geographic regions, although a wide variation in the geographic distribution of MRSA isolates appears to exist.[14,22,23,25]

Several reports also have suggested an increasing prevalence of MRSA in U.S. hospitals.[17,21,22,25] However, some of these reports provide no information on current trends.[17,21,22] The most recent report by Boyce was based on a questionnaire survey of U.S. hospital epidemiologists during 1987-1989.[25] In addition, all these reports covered relatively limited time periods.

The National Nosocomial Infections Surveillance (NNIS) System, which began in 1970, is the only source of national information on nosocomial infections in the United States. One of the objectives of the NNIS System is to identify changes in nosocomial pathogens and antimicrobial resistance.[28] To determine whether the proportion of S *aureus* resistant to methicillin has increased over a 17-year period, 1975 through 1991, we analyzed NNIS data in which S aureus was associated with a nosocomial infection.

METHODS

The methodology of the NNIS System has been described elsewhere.[29] Standardized definitions for nosocomial infections are used by all participating hospitals.[30] Up to four pathogens can be reported for each site of infection. Multiple isolates of the same species from the same patient are not reported to the NNIS System. The present study examined isolates of S aureus that were associated with nosocomial infections reported to the NNIS System during 1975 through 1991.

Information on hospital characteristics such as medical school affiliation (teaching or nonteaching) and hospital bed size (excluding long-term care or psychiatric beds) was obtained for each hospital. The average hospital bed size over the years of reporting NNIS data was used to stratify the hospitals into three categories: <200 beds, 200 to 499 beds, and 2500 beds.

The percentage MRSA was defined as the number of S *aureus* isolates resistant to either methicillin, oxacillin, or nafcillin divided by the total number of S *aureus* isolates for which methicillin, oxacillin, or nafcillin susceptibility test results were reported to the NNIS System. For each year, the data reported by all hospitals in a given bed-size category were pooled to calculate the percentage MRSA. To better illustrate trends and to reduce the influence of hospitals joining or leaving the NNIS System, we calculated a three-point pooled moving average over consecutive years to smooth the annual percentage MRSA in each bed-size category.

Statistical methods employed in the analysis of these pooled MRSA rates included the use of likelihood ratio chi square tests and various linear models fit to the logarithm of these rates.[31] In addition, other statistical methods were used to confirm the results of these analyses, including an analysis of annual MRSA rates for individual hospitals performed in such a way as to control for changes over time in the composition of the sample of NNIS hospitals.[32]

RESULTS

Susceptibility Testing of S aureus Associated With Nosocomial Infections

Of 80,817 nosocomial S aureus isolates reported to the NNIS System during 1975 through 1991, 66,132 (82%) were tested for methicillin, oxacillin, or nafcillin susceptibility. The percentage tested increased gradually from an estimated 77% in 1975 to 87% in 1991 ($p = .003$, linear model fitting logarithm of annual percentage of S *aureus* tested). The number of S aureus isolates tested for methicillin, oxacillin, or nafcillin susceptibility in a calendar year averaged 3,890 isolates per year (range = 2594-4916).

A total of 182 hospitals reported susceptibility results for at least 1 nosocomial S aureus isolate over the 17-year period, ranging from a low of 56 hospitals in 1984 to a high of 113 hospitals in 1991.

Temporal Trends in Methicillin Resistance Among Nosocomial S aureus Isolates

Of *the* 66,132 S *aureus* isolates that were tested for methicillin, oxacillin, or nafcillin susceptibility during 1975 through 1991, 6,986 (11%) were MRSA. Among all NNIS System hospitals, the pooled percentage MRSA rose from 2.4% in 1975 to 29% in 1991. The percentage of hospitals reporting at least 1 MRSA in a calendar year rose from 47% in 1975 to 79% in 1991.

The rate of increase in percentage MRSA for NNIS System hospitals differed significantly among the 3 bed-size categories (Figure 1) ($p = .004$, linear model fitting logarithm of annual percentage MRSA by bed-size category). The percentage MRSA in each of the bed-size categories mse above 5% at different times: in 1983 for large hospitals (≥500 beds), in 1985 for medium-size hospitals (200 to 499 beds), and in 1987 for smaller hospitals (<200 beds). A hospital's teaching affiliation was not associated with differences

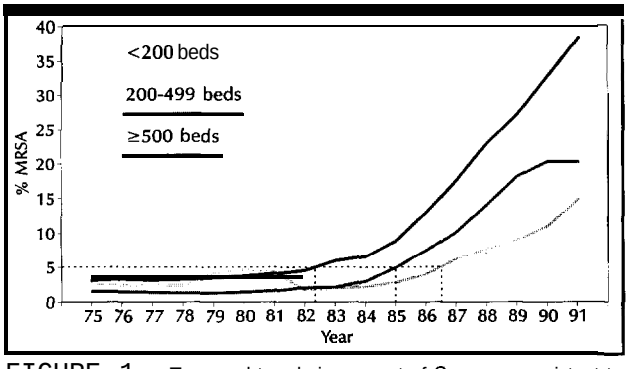

FIGURE 1. Temporal trends in percent of *S aureus* resistant to methicillin, oxacillin, or nafcillin by hospital bed size.

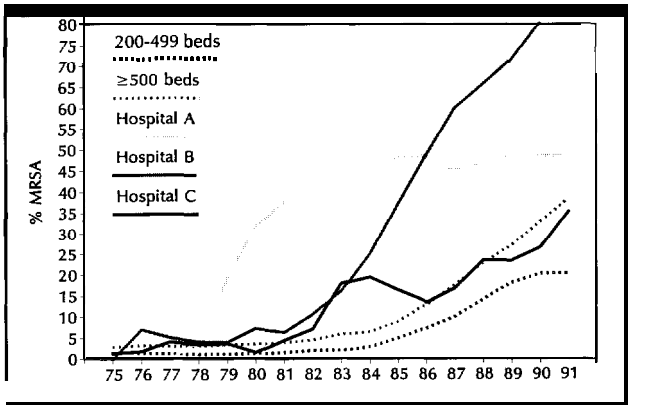

FIGURE 2. Exceptions to temporal trends of percentage MRSA among NNIS System hospitals. The increases in the percentage MRSA for Hospital A (≥500 beds) and Hospitals B and C (between 200 and 499 beds) are exceptions to the general trends and are shown with the solid lines. Trends in the percentage MRSA by hospital bed size for all other hospitals are shown with the dotted lines.

in the percentage MRSA within the bed-size categories ($p = .28$, linear model fitting logarithm of annual percentage MRSA by teaching affiliation, controlling for bed-size category).

Exceptions to Trends of Percentage MRSA Among NNIS System Hospitals

The temporal trends in percentage MRSA for 6 hospitals were dramatic exceptions to the overall trend for NNIS System hospitals shown in Figure 1. These 6 hospitals (3 in the category of 2500 beds and 3 in the category of 200 to 499 beds) experienced a sharp increase in the percentage MRSA that occurred much earlier than for NNIS System hospitals overall. The data from these 6 hospitals were not included in Figure 1. The increase in percentage MRSA for 3 of these hospitals (Hospitals A, B, and C), each of which contributed data over the entire study period, is shown in Figure 2. In addition, Figure 2 also includes the curves for all hospitals in the 200 to 499 and 2500 bed-size categories that were shown in Figure 1 but are represented as dotted lines in Figure 2. The percentage MRSA rose above 5% at nearly the same time (1977 through 1980) for the 3 hospitals in the largest bed-size category (≥500 beds) and at nearly the same time (1982) for the 3 hospitals in the category of 200 to 499 beds.

DISCUSSION

Previous reports have shown both that MRSA prevalence has increased overall and that large tertiary care hospitals are a center of MRSA among U.S. hospitals.[5,7,8,10-13,15-17,21-23,25,27] However, our analysis suggests that MRSA is affecting patients in hospitals of all sizes and appears to be increasing, which was reported in one previous study.[25] The only possible exception to this increase is from 1990 to 1991 in hospitals with 200 to 499 beds. The reason for the one year plateau in this group is unknown.

Our data also suggest that MRSA may have spread from large hospitals, either NNIS System or non-NNIS System hospitals, to the smaller hospitals in the system. This is evident from the years that the percentage MRSA first rose above 5% in each of the three bed-size categories (Figure 1): in 1983, for large hospitals; in 1985, for hospitals with 200 to 499 beds; and in 1987, for hospitals with less than 200 beds. The 5% value may have clinical significance because prescribing practices for empiric therapy of S *aureus* infections may change when the percentage MRSA rises above 5% in a hospital.

Control measures advocated for MRSA appear to require re-evaluation.[15,26,33,34] These measures were either applied or followed inconsistently, or they may be ineffective. As a consequence, empiric vancomycin use in many U.S. hospitals appears to be on the rise.[1] This may lead to the development of vancomycin-resistant enterococci and coagulase-negative staphylococci.[35,36] Although the Centers for Disease Control (CDC) has not received any confirmed reports of vancomycin-resistant S aureus, the isolation and dissemination of a vancomycin-resistant S aureus may occur with disastrous public health consequences since effective antibiotic treatment may not be available in the United States.[37]

Risk factors other than hospital bed size may help to explain some of the observed trend in the percentage of MRSA in NNIS System hospitals. Geographic location may have affected the MRSA rates in Figure 1, as found in surveys of hospitals nationwide.[14,16,17,20-23] We attempted to evaluate the effect of a hospital's location in a particular region. NNIS System hospitals in the midwestern and western regions of the United States tended to have a lower percentage MRSA than those in other regions; five of the six NNIS System hospitals with early and dramatic increases in the percentage MRSA were located in the eastern and

southern regions of the United States (unpublished data). The possible spread of MRSA from these hospitals or other non-NNIS System hospitals with a high percentage MRSA to NNIS System hospitals located in the same area may be responsible for the observed variation in MRSA rates by region. Further analysis is underway to explore this possibility. Other factors such as the size of the metropolitan area, presence of a referring nursing home, and contribution of MRSA from the community of each hospital or a "clustering" of NNIS System hospitals in certain regions may preclude accurate assessment of the percentage MRSA for the region.

The data in our analysis must be interpreted with caution. First, the isolates in our study are from nosocomial infections and may represent a more resistant population of isolates than those from community-acquired S *aureus* infections. Second, there is no standardization or validation of susceptibility testing among NNIS System hospitals, although the methods of susceptibility testing for S *aureus* have not changed significantly since 1985.[38] Frequency of obtaining specimens for culture may have differed in each hospital. Hospitals with MRSA may have been more likely to obtain specimens for culture. Variations in surveillance intensity also could have affected the percentage MRSA. Infections with resistant isolates may have been noted more commonly than infections with susceptible isolates, although the NNIS System has no way to substantiate or control for such selection bias. The NNIS System provides no information on antibiotic use that may profoundly affect antibiotic resistance. Finally, the NNIS System provides no information on outpatient MRSA prevalence that appears to be significant for at least one geographic area of the United States and may have confounded the analysis.[39]

Further examination of the contribution of community-acquired MRSA (including those from nursing homes) to a hospitals MRSA prevalence, the effect of antibiotic use during the 1980s, and predominant modes of transmission of MRSA in hospitals would benefit our understanding of this complex and costly pathogen, which appears to have an increasing etiologic role in nosocomial infections.

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