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CONFERENCIA

THE CHANGING EPIDEMIOLOGY OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

JOHN A. JERNIGAN

Hospital Infections Program, Centers for Disease Control and Prevention. Atlanta, Georgia, USA

Background and Need

Since its first appearance in the early 1960's, methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as an important pathogen in hospitals worldwide[1]. In the last 15 years, endemic and epidemic MRSA infections have become increasingly common, and are now present in nearly every US hospital. Data from the National Nosocomial Infection Surveillance System (NNIS) show that 47% of all *S. aureus* isolates from US intensive care units in 1998 were methicillin-resistant[2].

A growing body of literature suggests that MRSA, while once considered to be exclusively a nosocomial pathogen, may be emerging as an important cause of infection among low-risk community populations. MRSA in non-hospitalized populations was first noted in the early 1980's when Saravolatz et. al. described an outbreak of community-acquired MRSA infections in Detroit, primarily among intravenous drug users[3]. Since that time isolated cases or sporadic clusters of MRSA infection have been reported among populations with little or no documented contact with health care facilities, and such reports may be occurring with greater frequency[4-13a].

Whether or not these community MRSA infections are truly community-acquired or are the result of carriage of MRSA acquired during previous contact with healthcare facilities, however, is not known. Retrospective studies examining characteristics of hospitalized patients with "community-acquired" MRSA colonization or infection have produced conflicting results, some finding that MRSA colonization is associated with previous contact with health care institutions, others finding no such association[14-17]. A potential flaw in such retrospective investigations is susceptibility to misclassification of "community-acquired" MRSA infection or colonization. Patients found to be colonized or infected with MRSA early in their hospitalization (e.g. within 48 hours of admission) are often assumed to have acquired it in the community. However, because MRSA colonization can persist for months or years, it can be very difficult to determine exactly when colonization took place[18], and therefore difficult to distinguish true community- acquired MRSA colonizations and infections from those which may have been acquired during a health care facility encounter months or years earlier. Two recent prospective studies confirmed that MRSA colonization at the time of admission is not rare. However, both studies found that colonization occurred almost exclusively among patients with significant previous encounters with the health care system[19-21].

There is evidence, however, suggesting that at least some community isolates of MRSA may in fact have origins completely unrelated to healthcare. Unlike most nosocomial MRSA isolates, some recently reported community-acquired isolates from patients with out known MRSA risk factors have been multidrug susceptible (except to beta-lactams)and have distinctive molecular characteristics, suggesting that their origin may not have been from a healthcare setting[13a].

These conflicting study results illustrate how little is known about the epidemiology of MRSA outside of health care institutions. The data clearly indicate that there is a growing population of patients who are MRSA-colonized or infected at the time of hospital admission, but it remains unclear how many of these patients acquired the organism through transmission among low-risk persons in the community and how many acquired it during a previous encounter with a health care facility. Larger community-based studies are needed to answer this question[22].

A better understanding of the epidemiology of MRSA in the community may hold important implications for the approach to both the treatment and prevention of *S. aureus* infections. First, if the prevalence of MRSA colonization in the community is significant, empiric therapeutic choices for selected patients with community-acquired *S. aureus* infections may need to be altered to include agents with activity against MRSA. Identification of risk factors associated with community-acquired MRSA infection might provide important guidance to physicians treating such patients.

Estimating the incidence of MRSA infection within the community may also have an important impact on infection control strategies. Identifying significant community-acquired MRSA infection would imply the existence of significant reservoirs of MRSA colonization within the community. If this were the case, one might predict that many patients admitted to health care facilities will have unrecognized MRSA colonization and serve as reservoirs of transmission, thereby undermining traditional MRSA control measures which depend upon early identification of colonized patients in order that appropriate preventive measures can be applied. If a large community MRSA reservoir exists, MRSA control programs might require modification, either by adopting a more universal approach to preventing transmission based on an assumption that every patient is potentially colonized, or by implementing a surveillance system designed to identify MRSA-colonized patients at or near the time of admission.

Defining the incidence of MRSA infection in the community might also hold important implications for efforts to control the emergence of glycopeptide resistance among staphylococci. If MRSA has, in fact, escaped the confines of its association with health care settings, then a similar epidemiologic fate might be expected for glycopeptide-resistant *S. aureus* (GRSA) or glycopeptide-intermediate *S. aureus* (GISA). Recognizing the emergence of community-acquired MRSA might therefore serve as a valuable warning: MRSA control measures have failed, and therefore alternative approaches will likely be required to control and contain GISA and GRSA.

A proposed research project funded by the Centers for Disease Control and Prevention seeks to better define the epidemiology of MRSA in low-risk community populations by utilizing the Active Bacterial Core Surveillance (ABCs) component of the Emerging Infections Program (EIP) to determine the incidence of and risk factors for community-acquired MRSA infection in several different geographic areas of the United States.

In addition to helping define the epidemiology of community-acquired MRSA, this and similar projects may provide an opportunity for population-based surveillance for the emergence of GISA. Recent studies suggest that MRSA strains with vancomycin-resistant subpopulations may be more common and more geographically widespread than was initially appreciated, emphasizing the need for intensified surveillance for GISA[23, 24]. All clinical isolates of GISA described to date have been methicillin-resistant, suggesting that GISA isolates will be most likely found by examining MRSA isolates. As this future projects involve identification of all invasive MRSA infections in the targeted surveillance areas, they may provide a unique opportunity for population-based surveillance for infection with GISA.

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