Antimicrobial Resistance
It's Not Just for Hospitals

Elizabeth A. Bancroft, MD, SM

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) is a well-known hospital pathogen. More than 10% of bloodstream infections in hospitals are due to MRSA, and patients with MRSA have worse outcomes than those with methicillin-sensitive *S aureus*.[1,2] In recent years, identification of MRSA in otherwise healthy individuals in the community (community-associated MRSA) has become increasingly common.

Health care–associated and community-associated MRSA have different clinical and molecular epidemiology. Health care–associated MRSA is associated with invasive disease, health care exposure, and multidrug resistance. Community-associated MRSA has been primarily reported in young, healthy individuals with no recent health care exposure. The strains have generally been sensitive to non–β-lactam antibiotics, although most have had genes for the Panton-Valentine leukocidin and other enterotoxins that may make these strains more virulent.[3-5] Health care–associated MRSA is typified by a USA100 pulse-field electrophoretic pattern, while USA300 is the most commonly reported community-associated MRSA pattern in the United States.[6] Complicating the issue is that patients can unknowingly be colonized with MRSA and therefore have onset of disease away from the source of exposure (hence the terms "community onset" or "health care onset"). Furthermore, molecular studies reveal that either strain can appear in both locations.

Despite an increase in reports of MRSA, traditionally this organism has not been considered of major public health significance. Most community outbreaks have involved skin or soft tissue infections, and little has been reported on invasive infections originating outside health care settings. Few health departments or jurisdictions have systematic surveillance programs for antimicrobial resistance. Of the list of reportable diseases in the United States, only 3 are specifically observed for being caused by antimicrobial-resistant organisms (drug-resistant *Streptococcus pneumoniae*, vancomycin-intermediate *S aureus*, and vancomycin-resistant *S aureus*).

Two reports in this issue of *JAMA*, however, make it clear that antimicrobial resistance is an increasing problem outside of hospitals. Klevens and colleagues[7] used data from the well-described Active Bacterial Core surveillance network to estimate the rate of invasive (bloodstream or other sterile site isolates) MRSA in the United States in 2005. The rate of invasive MRSA was an astounding 31.8 per 100 000. To put this number into context, the estimated rate of invasive MRSA is greater than the combined rate in 2005 for invasive pneumococcal disease (14.1 per 100 000), invasive group A streptococcus (3.6 per 100 000), invasive meningococcal disease (0.35 per 100 000), and invasive *H influenzae* (1.4 per 100 000).[8-11] Furthermore, Klevens et al report that among 5287 patients hospitalized with MRSA during 2005, there were 988 deaths; based on these data, the authors estimate that were 18 650 deaths in patients with invasive MRSA in the United States in 2005. If their projection is accurate, these deaths would exceed the total number of deaths attributable to human immunodeficiency virus/AIDS in the United States in 2005.[12]

Invasive MRSA is only the tip of the drug-resistance iceberg. Another Centers for Disease Control and Prevention study found that 6% of community-associated MRSA was invasive.[13] In another study, 9% of children hospitalized in 2003 for community-associated MRSA had invasive disease.[14] Therefore, it appears that the total burden of MRSA may be much greater than what was estimated in this study.

The report by Pichichero and Casey[15] in this issue of *JAMA* is based on a smaller sample size but nonetheless highlights the importance of surveillance for antibiotic resistance and strain detection in a community setting. Pichichero and Casey documented 9 cases of multidrug-resistant *S pneumoniae* in middle ear fluid samples from children with acute otitis media occurring after the introduction of the 7-valent pneumococcal conjugate vaccine. All cases were due to serotype 19A (a serotype not covered in the vaccine) that was recently reported to increase in Alaskan children after the vaccine was widely used.[16] While it appears that the overall decrease in invasive pneumococcal disease still outweighs the increase in serotype 19A, it is clear that surveillance needs to continue for this important pathogen, both for strain type and antibiotic resistance.

There are important limitations to these 2 studies. In the study by Pichichero and Casey,[15] the total number of cases was small, and the cases identified were those with recurrent or acute otitis media with treatment failure limited to 1 practice in 1 geographic region of the country. Therefore, care must be taken in extrapolating these data beyond the confines of

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Author Affiliation: Los Angeles County Department of Public Health, Los Angeles, California.
Corresponding Author: Elizabeth A. Bancroft, MD, SM, Acute Communicable Disease Control, Los Angeles County Department of Public Health, 313 N Figueroa, Suite 212, Los Angeles, CA 90012 (ebancroft@ph.lacounty.gov).

the cases presented. In the study by Klevens et al,[7] the data are based on a more robust surveillance system, representing approximately 6% of the US population; however, community-associated MRSA rates in skin infections vary considerably by geographic region, and it is unknown whether the surveillance sites in this report represent the distribution of MRSA in the United States. Furthermore, there is likely to be misclassification error in attributing the source of MRSA. The presence of a health care risk factor does not preclude acquisition of a community strain of MRSA from exposure in the community, yet by surveillance definitions those cases would be classified as health care–associated. Moreover, if health care risk factors were not recorded in hospital charts, cases classified as community-associated might have acquired their MRSA from a health care setting or some other unidentified nosocomial source, such as a health care worker in the home. In addition, mortality data were collected from patient charts, and there are no data to firmly establish that MRSA was the actual cause of death.

With aging of the US population and the increase of community-associated MRSA, rates of invasive MRSA will continue to increase unless effective interventions are implemented. Until a successful vaccine is developed (and the study by Pichichero and Casey suggests that vaccines may have unintended consequences), clinicians and public health professionals will have to use the tools now available to control the spread of this organism. Strategies to prevent MRSA infections in hospitals—eg, handwashing, surveillance cultures, judicious antibiotic use, limiting invasive devices, decolonization, and environmental cleaning—are well known but imperfectly practiced. Strategies to prevent sporadic community-associated MRSA are not as well described, although handwashing, not sharing personal items, and keeping wounds clean, dry, and covered are commonly mentioned as methods to control outbreak.

Interestingly, the majority (58%) of MRSA cases were among patients who had health care risk factors but community onset of disease. The majority of these patients had the USA100 genotype, suggesting a health care origin of the organism. It appears that what happens in the hospital does not stay in the hospital. Patients are discharged from health care facilities with MRSA colonization that likely is often unidentified and only later develop invasive MRSA disease. More research is needed to determine the risk factors for developing invasive disease after hospital discharge and the prevention measures necessary to decrease infection. Working vigorously to decrease transmission of MRSA in health care facilities may decrease both nosocomial and community-onset MRSA that occurs in persons with prior health care exposure.

The reports in this issue of *JAMA* reveal that infections with significant antimicrobial-resistant pathogens, the types formerly seen only in hospitals, now have onset in the community. Old diseases have learned new tricks. Consequently, new collaborations between the public health and medical communities are needed to identify and control antimicrobial resistance. It is not practical for public health departments to perform surveillance for MRSA or other highly prevalent resistant organisms without a robust system of electronic laboratory reporting. In the meantime, population surveillance can be achieved by public health personnel working with hospitals and laboratories in their jurisdictions to develop aggregate antibiograms. Clinicians also should be encouraged to report to the health department any new trends in antibiotic resistance that they identify.

Collaborative research is needed to determine how to control health care–associated, community-onset MRSA and how to prevent community-associated MRSA from entering the hospital. Public health personnel and clinicians should combine efforts to ensure judicious antibiotic use. Additional resources may be needed to monitor and enforce infection control in health care facilities. For instance, in California, restaurants are routinely inspected more frequently (once per year) than nursing homes (once every 2 years), hospitals (once every 3 years), or physicians' offices (never). To be serious about controlling nosocomial disease and antibiotic resistance will require cleaning up the source.

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