Community-Associated Methicillin-Resistant *Staphylococcus aureus* Skin and Soft Tissue Infections at a Public Hospital

Do Public Housing and Incarceration Amplify Transmission?

Bala Hota, MD, MPH; Charlotte Ellenbogen, MD; Mary K. Hayden, MD; Alla Aroutcheva, MD, PhD; Thomas W. Rice, PhD; Robert A. Weinstein, MD

**Background:** Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections have emerged among patients without health care–associated risk factors. Understanding the epidemiology of CA-MRSA is critical for developing control measures.

**Methods:** At a 464-bed public hospital in Chicago and its more than 100 associated clinics, surveillance of soft tissue, abscess fluid, joint fluid, and bone cultures for *S aureus* was performed. We estimated rates of infection and geographic and other risks for CA-MRSA through laboratory-based surveillance and a case-control study.

**Results:** The incidence of CA-MRSA skin and soft tissue infections increased from 24.0 cases per 100 000 people in 2000 to 164.2 cases per 100 000 people in 2005 (relative risk, 6.84 [2005 vs 2000]). Risk factors were incarceration (odds ratio [OR], 1.92; 95% confidence interval [CI], 1.00-3.67), African American race/ethnicity (OR, 1.91; 95% CI, 1.28-2.87), and residence at a group of geographically proximate public housing complexes (OR, 2.50; 95% CI, 1.25-4.98); older age was inversely related (OR, 0.89; 95% CI, 0.82-0.96 [for each decade increase]). Of 73 strains tested, 79% were pulsed-field gel electrophoresis type USA300.

**Conclusions:** Clonal CA-MRSA infection has emerged among Chicago’s urban poor. It has occurred in addition to, not in place of, methicillin-susceptible *S aureus* infection. Epidemiological analysis suggests that control measures could focus initially on core groups that have contributed disproportionately to risk, although CA-MRSA becomes endemic as it disseminates within communities.

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**METHODS**

**SETTING**

The study was performed at John H. Stroger, Jr Hospital of Cook County (CCH), a 464-bed public hospital in Chicago, Ill, and its more than 100 associated clinics; CCH primarily serves the urban poor (ie, uninsured or indigent individuals) in Cook County. The mean annual patient care volumes from 2001 through
2004 were 749,992 clinic visits, 146,316 emergency department visits, and 23,041 hospital admissions.

The study was reviewed by our institutional review board. The need for informed consent was waived.

CASE DEFINITION
Using a previously validated electronic case definition (κ statistic, 0.97 [100% sensitive and 97% specific for community-associated infection compared with medical record review]), we identified individuals without health care exposures with community-onset S aureus infections. Individual’s older than 1 year with MRSA or methicillin-susceptible S aureus (MSSA) growing from microbiological cultures of soft tissue, abscess fluid, joint fluid, or bone with (1) culture obtained while an outpatient or within the first 3 days of a hospitalization, (2) no clinical isolate of MRSA in the last 6 months, (3) no hospitalization or surgery within 1 year, and (4) no hemodialysis were designated as having community-associated infection; all other infections were defined as health care–associated infection. Only the first isolate from a patient within 6 months was counted as CA-MRSA or CA-MSSA.

STUDY DESIGN
Using the electronic case definition, we conducted surveillance from January 1, 2000, through August 31, 2005, among a cohort of individuals infected with community-associated S aureus in clinical cultures of soft tissue, abscess fluid, joint fluid, or bone specimens. Isolates were obtained from patients seen at the CCH emergency department, at affiliated clinics, or on CCH inpatient wards. These clinical infection sites were selected because they account for more than 90% of infections and have a low likelihood of attribution to nosocomial acquisition (ie, from intravenous catheters).

A nested case-control study was conducted using CA-MRSA cases compared with CA-MSSA controls. Cases and controls were identified from September 1, 2001, through August 31, 2004, to ensure complete data for all covariates.

DATA COLLECTION
Data were collected from our clinical data repository. Electronic records were queried for presence of diabetes mellitus, human immunodeficiency virus, chronic renal insufficiency, and infection relapses within 1 year. Prior antimicrobial use was determined from antimicrobial prescriptions from inpatient or outpatient pharmacies and were categorized as having been given within 1 week or within 1 year to 1 week before the culture date. Exposures to the Cook County Jail within 1 year before positive culture results were obtained from arrest records of the Cook County Department of Corrections. Home addresses were obtained from electronic data; if multiple addresses were available for a patient, the address historically closest to the culture results was used.

MICROBIOLOGICAL ANALYSIS
Clinical isolates were identified as S aureus using routine methods. Antimicrobial resistance was determined by automated broth microdilution (MicroScan; Dade Behring, West Sacramento, Calif). Isolates were considered resistant to methicillin if the oxacillin minimum inhibitory concentration was at least 4 µg/mL. Clindamycin resistance was determined in all periods by automated broth microdilution. Inducible clindamycin resistance was determined by D test when requested by clinicians.

Community-associated methicillin-resistant S aureus isolates from patients with cultures performed on or after January 1, 2004, were available for further analysis. Isolates from patients with recent incarceration, with cultures performed in July 2004, or with residence within the borders of 2 specific geographic clusters were studied for pulsed-field gel electrophoresis (PFGE), staphylococcal chromosome cassette mec type, and presence of the Panton-Valentine leukocidin gene to assess clonality among isolates clustered geographically, temporally, and with a common exposure (eg, incarceration). Antibiogram data were used to examine isolates before January 1, 2004.

STATISTICAL ANALYSIS
Prevalence (the number of positive culture results divided by the number of cultured patients) and incidence (the number of positive culture results among Cook County patients seen at CCH divided by the CCH catchment population residing in Cook County) of infection with CA-MRSA or CA-MSSA were calculated. The CCH catchment population was calculated from an estimation of the proportion of all Cook County residents who seek care at CCH. This proportion was determined by dividing the number of Cook County residents hospitalized at CCH in 2004 for infections of skin or subcutaneous tissue or erysipelas (International Classification of Diseases, Ninth Revision code 035 or 680-686) by the number with these diagnoses hospitalized at all Cook County hospitals in that year, stratified by ZIP code of residence. Data for all Cook County hospitalizations were obtained from the Illinois Hospital Association; 2004 was chosen because it was the first year available with complete data. The proportion for each ZIP code was then multiplied by the total number of residents in each ZIP code as reported in the most recent US census ZIP code tabulation areas from 2000; these values were summed for all ZIP codes in Cook County to produce an unadjusted estimate of the catchment population for CCH. Two hundred nineteen patients with addresses outside of Cook County or without addresses (ie, homeless) were excluded for these calculations.

Addresses were geocoded using commercially available software (Arcview 9.0; ESRI, Redlands, Calif), and these data were entered using SaTScan software version 5.1.33,34 Clusters of cases of CA-MRSA were detected by the Bernoulli method of the spatial scan statistic; this analysis was stratified into 4 periods because of a temporal trend among cases. The periods, chosen a priori to create approximately equal time frames, were period 1 (January 1, 2000, through June 30, 2001), period 2 (July 1, 2001, through December 31, 2002), period 3 (January 1, 2003, through June 30, 2004), and period 4 (July 1, 2004, through August 31, 2005).

To assess the effect of overcrowding on risk of infection with CA-MRSA, we used the Cook County US Census Bureau 2000 occupancy data (percentage of the population living with >1 person per room) for the block group of a patient’s residence. Strata were created based on quartiles of level of overcrowding after examination of the frequency distribution of persons per room in the cohort. Counts of MRSAs cases were compared with counts of MSSAs cases and with counts of all patients who had had cultures performed for each strata of overcrowding. The association of public housing and overcrowding with CA-MRSA infection was assessed using the χ² statistic for univariate analysis. Logistic regression was used to perform multivariate analysis, with presence or absence of CA-MRSA as the outcome variable. Variables were those with P<.15 on univariate analysis and year of culture. Antimicrobial use was excluded from multivariate analysis because differences were only noted within 1 week of culture, which may have reflected therapy for active infections. Interaction was assessed for comorbidities and recent incarceration, as well collinearity. Residence in public
housing regardless of period was used in multivariate analysis, and interaction between period and residence was assessed. Public housing units were categorized based on whether they were contained within clusters detected by SaTScan. Variables were eliminated using backward elimination for $P>0.15$.

Statistical analyses were performed using SAS software version 8 (SAS Institute, Cary, NC).

**RESULTS**

**LABORATORY-BASED SURVEILLANCE**

During 6 years (January 1, 2000, through August 31, 2005), soft tissue, abscess fluid, joint fluid, or bone specimens from 2346 (34.0%) of 6894 patients without health care–associated risk factors grew *S aureus*; 971 (41.4%) and 1375 (58.6%) isolates met our previously defined criteria for CA-MRSA and CA-MSSA, respectively. Community-associated methicillin-resistant *S aureus* isolates were mostly susceptible to aminoglycosides (95%), fluoroquinolones (76%), and trimethoprim-sulfamethoxazole (99%). Erythromycin resistance steadily increased from 51% in 2000 to 87% in 2004; erythromycin-resistant and clindamycin-susceptible strains accounted for most of this increase (25%, 28%, 54%, 69%, 80%, and 81% of CA-MRSA isolates during 2000, 2001, 2002, 2003, 2004, and 2005, respectively). D test results were available for 47 isolates (performed between 2004 and 2005) and were positive in only 2.

Over time, CA-MRSA skin and soft tissue infections increased 6.84-fold (Figure 1). Based on the estimated CCH catchment population of 212,815, CA-MRSA skin and soft tissue infections increased from 24.0 cases per 100,000 people in 2000 to 164.2 cases per 100,000 people in 2005, while the incidence of CA-MSSA skin and soft tissue infections was 90.7 cases per 100,000 people in 2005. During this period, 56% of CA-MRSA infections and 55% of CA-MSSA infections occurred in outpatients or in nonhospitalized emergency department patients, while 44% of CA-MRSA infections and 45% of CA-MSSA infections required hospitalization. There were 5 deaths among CA-MSSA patients and 2 deaths among CA-MRSA patients (mortality rates of 5 per 1000 and 1 per 1000, respectively).

**GEOGRAPHIC ANALYSIS**

Geographic analysis revealed 4 clusters of CA-MRSA infections (Figure 2). Cluster 1 (July 1, 2001, through December 31, 2002) had 15 patients with CA-MRSA (10.7% of that period’s cases). Cluster 2 (January 1, 2003, through June 30, 2004) had 17 patients with CA-MRSA (6.4% of cases). Cluster 3 (January 1, 2003, through June 30, 2004) had 44 patients with CA-MRSA (15.0% of cases). Within the borders of cluster 3 were 5 high-rise public housing complexes; 8 (18.2%) of 44 patients within cluster 3 were residents of this housing. Cluster 4 (July 1, 2004, through August 31, 2005) included a region with its center near CCH and a perimeter that included the geographic area with the highest CCH use in Cook

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**Figure 1.** Counts and incidence of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) and community-associated methicillin-susceptible *S aureus* (CA-MSSA) skin and soft tissue infections among patients at John H. Stroger, Jr Hospital of Cook County (Illinois) from January 1, 2000, through August 31, 2005.
County; 185 patients with CA-MRSA (47.1% of cases) were within this cluster.

RISKS OF PUBLIC HOUSING, INCARCERATION, AND OVERCROWDING

The proportion of community-associated *S aureus* skin and soft tissue isolates that was methicillin resistant was higher among residents who lived in public housing complexes in cluster 3 (55.4%) than among non–public housing residents (41.6%). Public housing residents in cluster 3 had a higher prevalence of CA-MRSA from 2000 through 2005, which was statistically significant in 2005 (*P*<.001) (Figure 3).

We found no association between case status and overcrowding; patients with *S aureus* infections from census block groups that were more overcrowded were not more likely to be infected with CA-MRSA. Similarly, we found no association between high-occupancy block groups and CA-MRSA infection regardless of whether the comparison group was patients with CA-MSSA infections or all patients from whom cultures were obtained, nor did we find an association when occupancy was stratified by race/ethnicity or by year of culture.
NESTED CASE-CONTROL STUDY

On univariate analysis, the following variables were associated with CA-MRSA skin and soft tissue infections: younger age, incarceration within 1 year, African American race/ethnicity, and human immunodeficiency virus infection (Table 1). More patients with CA-MRSA received an antibiotic within 1 week before cultures were performed (9% vs 6%, P=.03), and 44% of patients with CA-MRSA infections received inadequate therapy with a β-lactam antibiotic following culture (no differences in deaths or readmissions were noted as a result of inadequate therapy). Residence in the 5 public housing complexes within cluster 3 during any period was associated with CA-MRSA skin and soft tissue infections on univariate analysis, while residence in public housing developments outside of cluster 3 was not.

MULTIVARIATE ANALYSIS

On multivariate analysis (Table 2), year of culture showed a strong secular trend. Residence in the public housing complexes within cluster 3 was also a risk factor for MRSA skin and soft tissue infections (odds ratio, 2.50; 95% confidence interval, 1.25-4.98) regardless of year of culture, as was recent incarceration (odds ratio, 2.04; 95% confidence interval, 1.13-3.69). Residence in the 5 public housing complexes within cluster 3 during any period was associated with CA-MRSA skin and soft tissue infections. Regardless of pulsed-field gel electrophoresis type, most isolates from all groups were positive for staphylococcal chromosome cassette mec type IV (67 of 73) and Panton-Valentine leukocidin genes. USA400 strains were found in 6 infections. Regardless of pulsed-field gel electrophoresis type, most isolates from all groups were positive for staphylococcal chromosome cassette mec type IV (67 of 73) and Panton-Valentine leukocidin genes (65 of 73).

In the major public safety net health care system of Cook County, we noted a 6.84-fold increase in the risk of skin and soft tissue infections with CA-MRSA from 2000 through 2005. This increase occurred in addition to a stable rate of CA-MSSA infections. Although at the start of the surveillance period our incidence of CA-MRSA infections was similar to that of CA-MSSA infections, the proportion of CA-MRSA infections increased from 4.4% in 2000 to 37.6% in 2005. As noted previously for CA-MSSA, this increase was also due to increased infections in extremely overcrowded public housing developments, including a marked increase in infections in public housing developments in cluster 3.

With the large increase in the proportion of CA-MRSA infections, we had concern about potential inadequate therapy. In our cohort, 26 of 30 (86%) of CA-MRSA infections received inadequate therapy (9% vs 6%, P=.03). Inadequate therapy was defined as either no antibiotics, or if antibiotics were given, the patient had not received an appropriate antibiotic by the time cultures were obtained. Adequate therapy was defined as either the patient received an antibiotic within 1 week before cultures were obtained or received an antibiotic within 24 hours of culture with a subsequent blood culture positive for Staphylococcus aureus. Inadequate therapy was a significant risk factor for CA-MRSA skin and soft tissue infections (odds ratio, 2.50; 95% confidence interval, 1.25-4.98) regardless of year of culture (P=.029). We also noted a strong secular trend of inadequate therapy. Residence in the 5 public housing complexes within cluster 3 was also a risk factor for inadequate therapy (odds ratio, 2.06; 95% confidence interval, 1.03-4.09). Adequate therapy was defined as either the patient received an antibiotic within 1 week before cultures were obtained or received an antibiotic within 24 hours of culture with a subsequent blood culture positive for Staphylococcus aureus.

COMMENT

Community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) infections have become a major public health concern in the United States. In our study, we noted a 6.84-fold increase in the risk of skin and soft tissue infections with CA-MRSA from 2000 through 2005. This increase occurred in addition to a stable rate of Community-Associated Staphylococcus aureus (CA-MSSA) infections. Although at the start of the surveillance period our incidence of CA-MRSA infections was simi-
lar to that found in a recent multicity population-based study, by 2005 it was higher, which may reflect our high-risk patient population (62% African American, 5% recent incarceration, and 6% public housing residents).

African American race/ethnicity and recent incarceration were risk factors for CA-MRSA skin and soft tissue infections; Hispanic race/ethnicity was protective, a finding consistent with the results of prior studies. Residence in specific public housing complexes was also a risk factor and increased the odds of CA-MRSA infection almost 3-fold (Table 2), even after adjustment for the countywide secular increase.

Why CA-MRSA has emerged at such a rapid pace remains unclear. Cross-sectional studies examining other community populations have found MRSA colonization rates far below those of MSSA, generally not exceeding 4% for CA-MRSA compared with 30% for CA-MSSA. Despite the apparently lower prevalence of MRSA colonization, infection rates are approaching or exceeding those of CA-MSSA. Potential host or pathogen explanations for this discordance include CA-MRSA colonization at sites not tested (eg, skin, gastrointestinal tract, or deeper than the anterior nares), greater risk of person-to-person spread from infected patients or of spread from contaminated fomites (eg, towels in locker rooms), virulence factors (eg, Panton-Valentine leukocidin genes) that trump the traditional colonization before infection sequence (ie, “hit-and-run” infections), or yet-to-be-measured increasing rates of CA-MRSA colonization.

An additional explanation for rapid emergence of CA-MRSA is that some community settings may promote cross-transmission. Hospitals and long-term care facilities have long been considered “epicenters” for antimicrobial resistance, housing colonized and noncolonized individuals in close proximity, and offering the opportunity for cross-transmission. Hartley et al suggested that prisons, with their large at-risk populations and long lengths of stay, can be sources of MRSA colonized individuals at rates comparable to those of hospitals. Other community settings such as public housing and halfway houses may amplify CA-MRSA spread; for example, the geographic clusters of CA-MRSA detected in our study that were not related to public housing may represent foci of increased cross-transmission.

The concept of a “core group” of colonized or infected individuals that is responsible for many new infections is basic to the epidemiology of sexually transmitted and some viral infections (eg, severe acute respiratory syndrome); geographically disparate clusters of infection may represent networks of individuals who transmit infection through person-to-person contact, with further spread by individuals who bridge these networks. In the case of CA-MRSA, geographically closed community foci (eg, prisons) may be promoting spread, while other settings or factors (eg, athletics or intravenous drug use) act as bridges for transmission.

Public housing also may represent a bridge between high-risk individuals in Chicago. Since the late 1990s, demolition of high-rise public housing complexes and widespread relocation of public housing residents have occurred as part of the HOPE VI plan. In 2003, 62% of relocated families were moved to other Chicago public housing complexes, potentially contributing to overcrowding not measured by census data. In addition, public housing residents are part of a network associated with inmates; in a 2002 study, 29% of respondents reported that they had been incarcerated or were expecting a resident to arrive from jail or prison. Public housing may also house individuals with severe drug problems, and squatters (or nonlease tenants) may transiently reside in nondemolished public housing between episodes of homelessness. Triangulation of risks for CA-MRSA transmission may occur in the public housing complexes identified in cluster 3, with personal contacts or contaminated fomites promoting cross-transmission among susceptible host populations. However, whether and what interactions among these populations have contributed to CA-MRSA dissemination require further study.

Strain typing by pulse-field gel electrophoresis did not discriminate between the various populations assessed in our study; however, it confirmed that most isolates tested were strain type USA300, whether or not related to incarceration or public housing exposure. These findings are consistent with those of a 3 1⁄2-month laboratory-based survey from Atlanta, Ga, and a cross-sectional study among emergency department patients in which most CA-MRSA skin and soft tissue infections were caused by USA300.

Because of a lack of historical isolates available for typing, we were unable to ascertain if USA300 replaced other CA-MRSA strains in the community. Prior work examining CA-MRSA among Chicago children found clonality in one instance: 69 (78.4%) of 88 clindamycin-susceptible CA-MRSA isolates obtained from 1987 to 2000 were USA400, 70% were erythromycin-susceptible, and D test results were positive in 31 of 33 isolates with dis-
cordant erythromycin and clindamycin susceptibilities. Prior work examining CA-MRSA among Chicago children in one instance found clonality: 69 (78%) of 88 clindamycin-susceptible CA-MRSA isolates obtained from 1987 to 2000 were USA-400, 70% were erythromycin-susceptible, and D-test results were positive for 31 of 33 isolates with discordant erythromycin and clindamycin susceptibilities. In another instance, however, polyclonal infection was described. Given the rapid increases among our patients in prevalence of clindamycin-susceptible, erythromycin-resistant isolates and the low rate of inducible clindamycin-resistance, replacement of another CA-MRSA strain (possibly USA400) by USA300 as the major cause of CA-MRSA infection seems to have occurred between 2000 and 2006 in our patients.

Our data should be interpreted in light of several epidemiological limitations. First, geographic clustering among cases may have been because of the differences between cases and controls in the use of CCH unrelated to infection status. The stability of MSSA rates over time argues against systematic changes in health care use, and Figure 3 shows that public housing complexes in cluster 3 consistently exhibited higher rates of MRSA isolation than other areas, suggesting a true and disproportionate secular trend.

Second, we may be missing data that explain our findings further. For example, the interaction of recent incarceration and human immunodeficiency virus positivity that reduced the risk of CA-MRSA could be explained by prescription of trimethoprim-sulfamethoxazole prophylaxis to patients with AIDS in the jail.

Third, we relied on electronic records for defining health care exposure. In a prospective study by Furuno et al, an electronic rule did not always reliably detect health care exposures. However, a distinction of our data set is that CCH is the county’s largest provider of indigent care and likely sees a “loyal” population of patients. Validation of our rule found only a 3% misclassification rate, in contrast to 29% demonstrated by Furuno et al.

In conclusion, among CCH patients, the rate of CA-MRSA skin and soft tissue infections increased rapidly between 2000 and 2005, adding significantly to the overall burden of staphylococcal disease. Incarceration and residence at some public housing complexes increased the chance of infection with CA-MRSA, perhaps as a consequence of the “epidemiological weight” of these locations. Whether strategies directed at prevention of transmission in these settings will be effective in slowing the emergence of CA-MRSA remains to be determined.

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Correspondence: Bala Hota, MD, MPH, Rush University Medical Center and John H. Stroger, Jr Hospital of Cook County, 637 S Wood St, Chicago, IL 60612 (botta@rush.edu).

Author Contributions: Dr Hota had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Hota, Hayden, Aroucheva, and Weinstein. Acquisition of data: Hota, Ellenbogen, Aroucheva, and Rice. Analysis and interpretation of data: Hota, Rice, and Weinstein. Drafting of the manuscript: Hota and Aroucheva. Critical revision of the manuscript for important intellectual content: Hota, Ellenbogen, Hayden, Rice, and Weinstein. Statistical analysis: Hota. Obtained funding: Weinstein. Administrative, technical, and material support: Ellenbogen, Aroucheva, Rice, and Weinstein. Study supervision: Weinstein.

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REFERENCES


Correction

Error in Figure Key. In the article titled “Community-Associated Methicillin-Resistant Staphylococcus aureus Skin and Soft Tissue Infections at a Public Hospital: Do Public Housing and Incarceration Amplify Transmission?” by Hota et al, published in the May 28 issue of the Archives (2007;167[10]:1026-1033), the symbols for the right side of the key in Figure 1 (page 1028) should have been switched. Therefore, the circles indicate CA-MRSA incidence; squares, the CA-MSSA incidence. The online version of this article was corrected for typographical errors on May 28, 2007.