Concise Communication

Prevalence of Methicillin-Resistant and Methicillin-Susceptible *Staphylococcus aureus* in the Community

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Recent reports indicate that community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) infections are increasing and may now involve persons without risk factors predisposing for acquisition. To estimate the extent of community MRSA in New York City, the prevalence of *S. aureus* and MRSA nasal colonization in a well-patient population of 500 children and guardians was determined. The prevalence of *S. aureus* nasal carriage was 35% for children and 28% for guardians. One person with predisposing risk factors was colonized with an MRSA, which was identified as the predominant clone found in New York City hospitals. A high degree of methicillin-susceptible *S. aureus* strain diversity was noted, with no apparent selection for specific clonal types. Thus, MRSA colonization is not ubiquitous in persons without predisposing risk outside of the health care environment. Bacterial competition and a lack of strong selection may limit the community spread of MRSA and can account for its sporadic distribution.

*Staphylococcus aureus* is the primary cause of nosocomial infection in the United States [1]. In New York City, methicillin-resistant *S. aureus* (MRSA) accounts for ~30% of nosocomial infections and 50% of associated deaths [2]. Although community-acquired *S. aureus* infections are common, recent reports suggest that they may increasingly be caused by MRSA strains [3, 4]. However, findings of community MRSA may not apply to populations from different regions. Thus, the true extent of MRSA in the community is not known.

To estimate community MRSA transmission, we studied the prevalence of *S. aureus* and MRSA colonization of the anterior nares in a well-patient pediatric population and determined whether MRSA carriage occurs in persons lacking risk factors predisposing for acquisition. We chose the study population in light of recent reports indicating an increase in MRSA infections in children lacking risk factors [4]. We also included family members (guardians), because they can serve as reservoirs for asymptomatic MRSA.

Materials and Methods

Study Design and Facility

A cross-sectional study was conducted at the Bellevue Hospital Pediatric Clinic to establish the prevalence of MRSA and methicillin-susceptible *S. aureus* (MSSA) nasal carriage among predominantly healthy children and their guardians visiting the clinic. Of the subjects approached, 500 agreed to the terms of informed consent and allowed nasal swabs. Swabs were collected over a 10-month period. A subject interview queried children and their guardians regarding risk factors for MRSA acquisition. This included previous hospitalization and indicated instrumentation use. In addition, all outpatient clinic visits within the prior year were recorded, both scheduled (indicating possible illness) and routine. Information was also obtained regarding any known antibiotic use within the past year and history of chronic illness or underlying condition (specifically heart disease, cystic fibrosis, diabetes, dialysis, or other long-term medical problems and medications). Household contact with frequently hospitalized persons or health care workers was also considered a predisposing risk.

To compare community *S. aureus* strain types with those found in the hospital, nonconsecutive single patient isolates of MSSA were collected from the Bellevue Clinical Microbiology Laboratory. Medical record information was used to confirm hospital acquisition for these isolates and to ascertain patient infection or colonization. Community isolates were defined as a nasal swab or hospital specimen (obtained within 48 h of admission) from a patient who did not have significant predisposing risk. Infection was determined by clinical criteria and by isolation of *S. aureus* from a normally sterile body site.
Laboratory Methods

**Nasal swabs.** Sterile cotton swabs (CultureSwab Transport System; Difco, Detroit) were used. Swabs were inoculated directly onto mannitol salt agar (Difco) with and without oxacillin (4 μg/mL) within 4 h of sampling. Plates were incubated at 37°C for 48 h and for a limited time at room temperature to stimulate pigment formation. Individual colonies were streaked onto sheep blood agar (5% on trypticase soy agar; Remel, Lenexa, KS) and incubated overnight at 37°C. Morphologically distinct colonies were tested for the production of coagulase (Coagulase Plasma System; Difco). Colonies that grew only on oxacillin-free plates and were both mannitol- and coagulase-positive were considered MSSA. Coagulase-positive organisms that also grew on mannitol salt plates with oxacillin were presumptively identified as MRSA. All isolates were also screened for methicillin resistance on Mueller-Hinton agar (4 μg/mL oxacillin; Remel). The presence of the methicillin-resistance gene was confirmed on all suspected MRSA by polymerase chain reaction analysis of the *mecA* gene [4].

**Susceptibility testing.** Agar disk diffusion testing was done following the guidelines of the National Committee for Clinical Laboratory Standards [5].

**Molecular analysis.** All MSSA and the 1 MRSA isolate were analyzed by pulsed-field gel electrophoresis (PFGE) of Smal-digested chromosomal DNA [2]. Strain typing for the MRSA included Southern blot hybridization with use of the gene probes *mecA* and *Tn554* [2]. Each isolate was also typed by DNA sequencing analysis of the protein A (*spa*) gene hypervariable region as previously described [6]. *spa* typing was used to provide a clonal assessment for MSSA isolates; *mecA* probing is not useful for typing MSSA because the gene is absent.

Statistical Analysis

Fisher’s exact test was used to compare frequencies of categorical variables between *S. aureus*–positive and –negative cases. Binomial and Poisson 95% confidence intervals were calculated for prevalence of MRSA and MSSA as appropriate. Analysis was done with SAS, version 6.12 (SAS Institute, Cary, NC).

**Results**

**Population characteristics.** Five hundred subjects participated in the study; 225 were guardians (86% female), who ranged in age from 18 to 62 years. Children (275 sampled) varied from 1 week to 20 years old; 52% were male. The mean (±SD) ages for children and guardians in the study were 5 ± 4 and 31 ± 9 years, respectively. The study cohort was predominantly Hispanic, as was the clinic population. Persons from each of the 5 New York City boroughs participated in the study (Manhattan, 158; Brooklyn, 181; Queens, 90; Bronx, 64; Staten Island, 2).

Sample characteristics are shown in table 1.

**Community *S. aureus* carriage.** About 32% of the subjects (*n = 160*) were identified as colonized with *S. aureus*. Carriage rates for children and guardians were 35% (*n = 96*) and 28% (*n = 64*) (table 1). The prevalence of MSSA among persons with and without predisposing risk factors was 31.2% (95% confidence interval (CI), 27.0%–36.3%) and 32.2% (95% CI, 23.8%–40.6%), respectively. Subjects colonized with MSSA were not distinguishable from noncarriers in terms of age (child, *P* = .455; guardian, *P* = .058) or ethnicity (not shown), but boys had a significantly greater colonization frequency than did girls (*P* = .022) (table 1). There was no significant association of predisposing risk (see Materials and Methods) between MSSA carriers and noncarriers (table 1).

**Community MRSA carriage.** Only 1 of the 500 subjects sampled was identified as a carrier of MRSA. The carrier was a 5-year-old girl with frequent hospitalization and antibiotic use. The child’s guardian was not an *S. aureus* carrier. The single MRSA isolated in association with potential risk factors indicates a prevalence of 0.26% (95% Poisson CI, 0.007%–1.5%). No community MRSA was found among persons without any risk factors (95% Poisson CI, 0.0–3.1%).

**MRSA isolate,** analyzed by molecular typing, was compared with a large collection of MRSA representative of New York City hospitals [2]. The strain was a member of the most
prevalent clonal type in New York City (figure 1). Antimicrobial susceptibility testing indicated resistance to ampicillin-sulbactam, erythromycin, clindamycin, oxacillin, penicillin, cephalothin, ciprofloxacin, and gentamicin, indicating a multidrug-resistance profile common to New York MRSA [2].

The MRSA-positive child and available family were recultured to assess long-term carriage and familial transmission. Follow-up cultures were obtained 8 months after the initial swab and included the child’s mother (previously swabbed) and father, her twin and younger sisters, and an older brother. On reculturing, only the older brother was culture-positive, and he had an MRSA with a genotype identical to the original isolate (figure 1), indicating familial transmission.

Molecular typing of S. aureus. All MSSA isolated from nasal cultures were strain-typed to identify the spread of successful clones in the community. Sequence analysis of the spa hypervariable locus was used to provide a clonal assessment of the strains [6], and relatedness was confirmed by PFGE. A high degree of MSSA strain diversity was observed, with 59 unique clonal types for 159 isolates. A group of 16 isolates from diverse community sources shared a common strain type (PFGE type “e,” spa type 33; data not shown), and no other strain type was present in >8 isolates.

Molecular typing allowed us to compare strain type and diversity of community-colonizing MSSA from children and guardians with nosocomial MSSA obtained from Bellevue Hospital (not shown; see Materials and Methods). However, similar to community-colonizing MSSA, hospital isolates displayed a high degree of genotypic diversity, with 18 clonal types identified in the 26 isolates collected. Genotypic commonality among the two populations was indicated, because 14 of 18 hospital clonal types were also present among MSSA found in the community.

Discussion

Recent reports suggested that the epidemiology of MRSA might be changing to include significant community transmission and infection for this traditionally nosocomial pathogen [4]. This is not the case for the New York City area. Differences between previous work and the present study may be due to regional variation in community transmission. Previous findings may also stem from the high probability of inadvertently including patients who are readmitted with MRSA colonization or infection, because studies are often based on cases from hospital admissions that include a high percentage of persons with predisposing risk factors [7].

From 500 nasal swabs collected, only 1 MRSA isolate was identified. In contrast, and in agreement with expected results [8], 161 persons (32%) were nasal carriers for MSSA. The person colonized with MRSA had predisposing risk. Similarly, the strain type and antibiogram of the community MRSA identifies it as being the major MRSA clone previously described as endemic in New York City health care facilities [2] and seen in the present study from Bellevue Hospital inpatients (figure 1). Therefore, both strain type and predisposing risk factors implicate hospital acquisition for this community-colonizing isolate.

The low prevalence of MRSA nasal carriage in the healthy population appears to contrast with the diverse dissemination of MSSA. Community strain types were also predominant among hospital MSSA, where these strains are found to be responsible for nosocomial infection.
The lack of community MRSA we observed may reflect the difficulty of clonal spread in the absence of the strong selective advantage of drug resistance, because, without selection, only a small portion of a given population will go on to establish itself in new environments [9]. Thus, lack of selection may account for the observation that methicillin resistance is still mainly nosocomial, in contrast to the community spread of penicillin resistance [10], the determinant of which can escape elimination by rapid, plasmid-mediated horizontal transfer. Inasmuch as MRSA are frequently introduced into the community, they are likely to occasionally become fixed in the population through random drift, explaining the apparent contradiction in the prevalence of community MRSA in different geographic regions. The low prevalence of community MRSA that we observed in New York City could reflect the effect of large population sizes, which minimize the rate of change of gene frequencies due to random drift [11].

Dissemination of MRSA from the hospital may also be reduced by the limited population capable of long-term carriage [8]. To assess transient carriage in our MRSA-positive subject, we reswabbed her and her household contacts 8 months after the initial culture. On reculturing, the subject was no longer colonized with MRSA or MSSA, although familial transmission was indicated, because an older brother without individual risk factors was positive for the same strain as the original isolate.

Populations of chronic carriers are likely to be colonized with MSSA. Therefore, the ability of an MRSA to colonize and replace a pre-existing MSSA strain could be inhibited by bacterial interference. Among staphylococci, a novel form of strain interference based on the secretion of peptides transcribed from the agr operon has been described [12]. Therefore, it is noteworthy that, after loss of MRSA colonization in our community-positive subject, we were able to culture a coagulase-negative staphylococcal strain, which may block invasion of S. aureus strains via inhibition of agr-mediated virulence factor expression [13].

To summarize, in the study population of children and their guardians in New York City, the spread of MRSA to the community is limited and is certainly not ubiquitous beyond high-risk persons. Our conclusions have important implications in that, depending on the region in question, control over the spread of resistant strains may overlook small community clusters and focus on the hospital and health care environment. In areas such as New York City, where community MRSA is not currently prevalent, identification of risk factors for carriage may allow the development of a prediction rule for resistant S. aureus carriage on admission to identify persons who require empirical MRSA coverage. This may help control the use of the glycopeptide vancomycin, the mainstay of MRSA treatment to which resistance is increasingly reported, in patients who are admitted to the hospital with suspected infection [14].

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References