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A U.S. Population-Based Survey of *Staphylococcus aureus* Colonization

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Background: The epidemiology of staphylococcal colonization and community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) is changing, and little is known from the national perspective.

Objective: To describe the U.S. epidemiology of *S. aureus* nasal colonization, compare risk factors for colonization with methicillin-sensitive *S. aureus* (MSSA) versus MRSA, and compare antibiotic resistance patterns and genetic factors of colonizing strains of *S. aureus*.

Design: Secondary analysis of data from the National Health and Nutrition Examination Survey (NHANES), a stratified, multistage probability sample.

Setting: United States.

Participants: 2001–2002 NHANES participants older than 1 year of age.

Measurements: Colonization of MSSA and MRSA, risk factors for colonization, antimicrobial resistance, and percentage of isolates with selected genetic factors.

Results: The prevalence of colonization with *S. aureus* and with MRSA was 31.6% and 0.84%, respectively, in the noninstitutionalized U.S. population. People younger than 65 years of age, men, persons with less education, and persons with asthma were more likely to acquire *S. aureus*. Persons of black race and those of Mexican birth had lower risk for *S. aureus* colonization. Persons 65 years of age or older, women, persons with diabetes, and those who were in long-term care in the past year were more likely to have MRSA colonization. Hispanic persons had statistically significantly less risk than white persons. Isolates of MRSA with staphylococcal chromosomal cassette *mec* type IV (which is often associated with community-associated MRSA) were statistically significantly more likely to be sensitive to erythromycin, clindamycin, and ciprofloxacin.

Limitations: Colonizing isolates may be different from isolates associated with infection. Risk factors identified may differ from those associated with invasive disease. The 2001–2002 NHANES data are several years old and may not reflect the most recent changes in epidemiology, but they are the only national data available.

Conclusions: Characteristics of persons with MSSA and MRSA seem to differ. These findings may be useful for differentiating those who may be at risk for MRSA.

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Although *Staphylococcus aureus* is one of the most common causes of community- and health care–associated infections, little is known about its effects on the U.S. population as a whole. We analyzed newly available data from the 2001–2002 National Health and Nutrition Examination Survey (NHANES) to expand our understanding of the national epidemiology of *S. aureus* colonization. This most recent version of the survey is the first to contain information about *S. aureus* nasal colonization. We aimed to describe the U.S. population epidemiology of *S. aureus* colonization, compare risk factors for colonization with methicillin-sensitive *S. aureus* (MSSA) versus methicillin-resistant *S. aureus* (MRSA), and compare genetic factors and toxin production genes in colonizing strains of both MSSA and MRSA and antibiotic resistance patterns for staphylococcal chromosomal cassette *mec* (SCC*mec*) type II (a methicillin resistance gene locus commonly seen in health care–associated MRSA) versus SCC*mec* type IV (a methicillin resistance gene locus commonly seen in community-associated MRSA).

METHODS

Data Sources

We undertook a secondary analysis of NHANES, 2001–2002 (1). Since the early 1960s, the National Center for Health Statistics has conducted NHANES to obtain representative information on the health and nutritional status of the U.S. population. The survey used a stratified, multistage probability design to sample the civilian, noninstitutionalized U.S. population. The sampling design allows calculation of estimates of the U.S. population (2). Beginning in 1999, NHANES became a continuous annual survey rather than a periodic survey. The data are released on public use data files every 2 years. The 2001–2002 NHANES is the most recent release of this cross-sectional national survey, which included in-home interview data, examination data from a mobile examination center, and laboratory data. Furthermore, NHANES included data on *S. aureus* colonization for the first time in this version.

Study Sample

Of 11 039 persons interviewed, 10 477 (94.9%) had physical examination data. Among them, 9622 (91.8%)

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had a nasal swab for *S. aureus* obtained, and we included these participants in our analysis. We compared the demographic characteristics (age, sex, and race or ethnicity) of those who were interviewed with those who had nasal swabs obtained. We found that they were essentially the same, and therefore, we considered patients who had swabs obtained to be representative of the national sample.

Study Variables

Microbiological Analysis

Nasal swabs were first examined for proper labeling and integrity. They were then plated on mannitol salt agar (MSA), a selective medium for the isolation of *S. aureus*. The MSA plates were incubated at 37 °C for 48 hours. Mannitol-fermenting colonies were selected from the MSA plates and subcultured to trypticase soy agar and 5% sheep blood agar plates (BAPs) and incubated at 37 °C overnight. The MSA plates with little or no growth were reincubated at 37 °C overnight, and plates with non–mannitol-fermenting growth were held at room temperature. These plates were reexamined the next day, and any yellow or gold colonies were subcultured to BAPs. Overnight cultures on BAPs were first screened by using Staphaurex (Remel, Lenexa, Kansas), a rapid latex kit for identifying *S. aureus*. A tube coagulase test using rabbit plasma with EDTA was then performed on Staphaurex-negative isolates from BAPs with structure consistent with that of *S. aureus* and on Staphaurex-positive isolates with structure inconsistent with that of *S. aureus* (nonhemolytic). Staphaurex-positive isolates and Staphaurex-negative, tube coagulase–positive isolates were identified as *S. aureus* and were saved for further testing. Staphaurex-positive, tube coagulase–negative isolates were discarded.

Staphylococcus aureus isolates were screened for methicillin resistance following the National Committee for Clinical Laboratory Standards (NCCLS) disk-diffusion method. Overnight cultures from BAP were plated on Mueller–Hinton agar, and a 1-μg oxacillin disk was placed on the inoculated plate. Zone diameters were measured and recorded after 24-hour incubation at 37 °C as sensitive ($\geq$13 mm), intermediate (11 mm to 12 mm), or resistant ($\leq$10 mm). Isolates that were resistant to oxacillin (MRSA), those that were intermediate to oxacillin (MSSA), and every tenth isolate that was sensitive to oxacillin (MSSA) by disk diffusion were saved for additional testing of organism characteristics. These tests included antibiotic susceptibility testing (minimal inhibitory concentration [MIC]) using broth microdilution according to NCCLS reference methods; strain typing by pulsed-field gel electrophoresis using *Sma*I enzyme; singleplex polymerase chain reaction (PCR) for detection of genes encoding enterotoxins, toxic shock syndrome toxin-1, and Panton–Valentine leukocidin toxin; and SCC*mec* typing by PCR (3).

The NHANES quality control and quality assurance protocols meet the 1988 Clinical Laboratory Improvement Act mandates. Detailed quality control and quality assurance instructions are discussed in the NHANES Laboratory Procedures Manual (4).

Context

Epidemiology and risk factors for colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) in the U.S. population are poorly understood.

Contribution

Extrapolation of 2001–2002 National Health and Nutrition Examination Survey (NHANES) data indicates that 84 million noninstitutionalized persons in the U.S. population are colonized with MSSA and 2 million are colonized with MRSA. Long-term care facility residence, diabetes, and age 65 years or older are associated with MRSA colonization. Men are at greater risk for MSSA colonization, and women are at greater risk for MRSA colonization. Black persons and those of Mexican birth are at decreased risk for colonization.

Implications

Risk for MRSA colonization differs according to previously unrecognized population characteristics.

—The Editors

Risk Factors

We examined potential risk factors associated with MSSA and MRSA available in the NHANES data set. These were demographic variables (age, sex, race or ethnicity, education, and birthplace), insurance coverage, health or disease status, and hospitalization or long-term care. We expected that older people would have more chronic conditions and more exposure to antibiotic therapy and hospitalization and, therefore, could be at higher risk for acquiring MRSA. We arbitrarily defined older age groups as age 65 years or older and all other age groups as age less than 65 years.

Statistical Analysis

We estimated the prevalence of MRSA and MSSA colonization in the U.S. population by using appropriate weighting variables provided with the data set (2). We estimated the prevalence of *S. aureus* and MRSA, categorized by risk factor, by using weighted samples. We first performed bivariate analyses to examine the association of each individual risk factor with *S. aureus* and with MRSA. Then, we performed logistic regression analyses to examine risk factors for *S. aureus* and MRSA, respectively. The multivariate models allowed us to examine the effect of each potential risk factor while controlling for other variables. We ran a series of stepwise regressions, and the final models only included the statistically significant independent variables. We used Wald statistics to test the statistical significance of each independent variable. We calculated odds

Table 1. **Colonization with *Staphylococcus aureus* (Methicillin-Sensitive and Methicillin-Resistant) by Risk Factor among the U.S. Population**

Characteristic	Total Participants, *n* (%)*	*S. aureus* Present, *n* (% [95% CI])
Total	9622 (100)	2964 (100)
Age		
<65 y	8429 (89.1)	2672 (33.0 [31.3–34.7])
≥65 y	1193 (10.9)	292 (26.0 [22.9–29.1])
Sex		
Male	4685 (48.7)	1582 (37.0 [34.2–39.8])
Female	4937 (51.3)	1382 (28.0 [26.3–29.7])
Race or ethnicity		
Non-Hispanic white	4032 (68.8)	1296 (32.9 [31.2–34.6])
Non-Hispanic black	2446 (12.0)	694 (26.8 [24.6–29])
Mexican American or Hispanic	2862 (15.1)	886 (34.2 [31.9–36.5])
Other race or multiracial group	282 (4.1)	88 (33.9 [28.2–39.6])
Education		
<High school	4690 (33.1)	1577 (35.8 [33.6–38.0])
High school diploma	1336 (19.3)	399 (31.3 [28.8–33.8])
>High school	2355 (40.5)	700 (31.5 [29.2–33.8])
Not applicable (age < 7 y)	1241 (7.1)	288 (24.8 [21.3–28.3])
Country of birth		
United States	8146 (88.4)	2533 (32.4 [30.9–33.9])
Mexico	917 (3.9)	243 (27.3 [23.5–31.1])
Other	544 (7.6)	184 (35.0 [31.3–38.7])
Covered by health insurance†		
Yes	7748 (83.7)	2412 (32.5 [30.8–34.2])
No	1737 (16.3)	518 (32.6 [30.3–34.9])
Health or disease status		
Has diabetes†		
Yes	461 (4.9)	139 (30.2 [23.6–36.8])
No	9087 (95.1)	2804 (32.4 [30.7–34.1])
Has asthma		
Yes	1208 (12.2)	423 (36.3 [33.4–39.2])
No	8406 (87.8)	2539 (31.9 [30.1–33.7])
Hospitalization and long-term care use		
Overnight hospital stay in last year		
Yes	822 (9.0)	243 (30.0 [24.8–35.2])
No	8800 (91.0)	2721 (32.6 [30.9–34.3])
Long-term care facility in last 12 mo		
Yes	50 (0.5)	12 (17.9 [1.9–33.9])
No	9571 (99.5)	2952 (32.5 [31.0–34.0])

* The study sample size is presented as an absolute number. The percentages were generated by using weighted samples and therefore do not correspond exactly.
† Approximately 1% of data not available.

ratios and 95% CIs. We used weighted samples in chi-square tests and logistic regressions.

We compared antimicrobial resistance profiles and genes for toxin production in a subset of MSSA versus MRSA and in a subset of SCC*mec* type II versus SCC*mec* type IV by using chi-square tests. We used unweighted samples because of the small size of these subsamples. We performed data analyses by using SUDAAN-callable SAS, version 9 (Research Triangle Institute, Research Triangle Park, North Carolina), which is often used to analyze data collected from surveys with complex sampling designs.

Role of the Funding Sources

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RESULTS

Population Epidemiology

A total of 9622 participants had cultures for *S. aureus* obtained. Of these participants, 2889 (31.6% [95% CI, 29.8% to 33.4%]) and 75 (0.84% [CI, 0.4% to 1.2%]) were colonized with MSSA and with MRSA, respectively. On the basis of these data, approximately 84 million and 2 million noninstitutionalized persons in the U.S. population are colonized with MSSA and MRSA, respectively. Prevalence of *S. aureus* was as low as 26.8% among black persons and was as high as 38% among men (**Table 1**). The highest prevalence of MRSA was among people who had been in a long-term care facility in the past 12 months (30.9%), people with diabetes (8.5%), and people 65 years of age or older (8.3%) (**Table 2**). Of persons with MRSA, half are estimated to be colonized with SCC*mec* type II and half with SCC*mec* type IV.

Staphylococcal Colonization Risks

In a multivariate logistic regression model, persons younger than 65 years of age, men, those with less than a high school education, and those with asthma were more likely to have acquired staphylococcal colonization. Black persons and those of Mexican birth were at lower risk than white persons and than those born in the United States, respectively (**Table 3**).

MRSA Colonization Risks

Among persons colonized with *S. aureus*, those 65 years of age or older, women, those with diabetes, and those who resided in a long-term care facility in the past 12 months were more likely to have MRSA colonization. Hispanic persons were less likely to have MRSA than white persons (**Table 4**).

Antimicrobial Resistance in Toxin Genes

Table 5 shows the differences in genes for toxin production between MSSA and MRSA. Enterotoxin A and the toxic shock syndrome toxin-1 were more likely to be detected in MSSA isolates, whereas enterotoxin D and

Panton–Valentine leukocidin were more likely be found in MRSA.

Of the 75 MRSA isolates, 38 were SCC*mec* type II and 37 were SCC*mec* type IV. **Table 6** summarizes the toxin production genes and antibiotic resistance profiles categorized by SCC*mec* type. Enterotoxin D was more likely to be found in SCC*mec* type II isolates, and enterotoxin B and Panton–Valentine leukocidin were statistically significantly more likely to be found in SCC*mec* type IV isolates.

All MRSA isolates were sensitive to trimethoprim–sulfamethoxazole and vancomycin. The SCC*mec* type IV MRSA isolates were statistically significantly more likely to be sensitive to erythromycin, clindamycin, and ciprofloxacin than SCC*mec* type II MRSA isolates.

Discussion

Population Epidemiology

Staphylococcus aureus is one of the most common causes of both community- and hospital-acquired infections of skin, surgical sites, blood, and the lower respiratory tract (5). The anterior nares are the most consistent location from which *S. aureus* can be isolated. Although this colonization is a normal process, it may be a source for invasive infection.

The relationship between colonization and infection is not completely understood, but it is associated with factors intrinsic to the host, as well as to the strain of *S. aureus*. Using molecular typing, investigators have shown that more than 80% of bloodstream infections caused by *S. aureus* in hospitalized adults were preceded by colonization of the anterior nares with the same strain (6). Using the NHANES database, we calculated what we believe to be the first national population prevalence estimates of *S. aureus* colonization. The finding that 31.6% of the U.S. population was colonized with *S. aureus* provides a more reliable national estimate than that previously available, which ranged from 20% to 60% but used sampling that was not representative of the U.S. population (7–9).

Staphylococcal Colonization Risks

Populations previously reported to have increased rates of staphylococcal colonization include persons with type 1 diabetes mellitus, persons receiving hemodialysis or peritoneal dialysis, intravenous drug users, persons with rheumatoid arthritis and chronic sinusitis, those receiving repeated injections for allergies, those infected with HIV, and older individuals (5, 9). Our findings differ from those previously reported. For example, why younger people (<65 years) and men would be at higher risk and black people would be at lower risk for staphylococcal colonization is not known. Why lower levels of educational achievement would be a risk factor is also difficult to speculate, unless this is a surrogate for lower socioeconomic status and, therefore, crowded living conditions. A diagnosis of asthma may be a marker of contact with the health care system and, therefore, may be a risk, as noted in our study. The finding that persons of Mexican birth are at lower risk for staphylococcal colonization is newly described and parallels our finding, which is discussed later, that Hispanic persons have a lower risk for MRSA colonization.

Table 2. **Methicillin Resistance among Persons Colonized with *Staphylococcus aureus* by Risk Factor**

Characteristic	Total Participants, *n (%)**	MRSA Present, *n (% [95% CI])*
Total	2964 (100)	75 (100)
Age		
<65 y	2672 (91.2)	49 (2.0 [0.5–3.5])
≥65 y	292 (8.8)	26 (8.3 [4.1–12.5])
Sex		
Male	1582 (55.6)	30 (1.3 [0.4–2.2])
Female	1382 (44.4)	45 (4.1 [2.0–6.2])
Race or ethnicity		
Non-Hispanic white	1296 (69.9)	36 (2.7 [1.3–4.1])
Non-Hispanic black	694 (9.9)	25 (4.1 [1.8–6.4])
Mexican American or Hispanic	886 (15.9)	11 (0.8 [0.2–1.4])
Other race or multiracial group	88 (4.3)	3 (3.6 [0.0–7.8])
Education		
<High school	1577 (36.6)	35 (2.4 [1.2–3.6])
High school diploma	399 (18.6)	10 (2.9 [0.4–5.4])
>High school	700 (39.3)	19 (2.5 [0.9–4.1])
Not applicable (age < 7 y)	288 (5.4)	11 (3.1 [0.0–6.7])
Country of birth		
United States	2533 (88.4)	68 (2.7 [1.3–4.1])
Mexico	243 (3.3)	3 (0.9 [0.0–2.1])
Other	184 (8.3)	4 (2.4 [0.0–4.9])
Covered by health insurance†		
Yes	2412 (83.7)	65 (2.2 [1.3–3.1])
No	518 (16.3)	10 (4.5 [0.0–9.2])
Health or disease status		
Has diabetes†		
Yes	139 (4.6)	11 (8.5 [4.1–12.9])
No	2804 (95.4)	64 (2.3 [0.9–3.7])
Has asthma		
Yes	423 (13.7)	14 (3.9 [0.1–7.7])
No	2539 (86.3)	61 (2.4 [1.2–3.6])
Hospitalization and long-term care use		
Overnight hospital stay in last year		
Yes	243 (8.3)	15 (5.1 [0.7–9.5])
No	2721 (91.7)	60 (2.3 [0.8–3.8])
In long-term care facility in last 12 mo		
Yes	12 (0.3)	5 (30.9 [13.0–48.8])
No	2952 (99.7)	70 (2.5 [1.1–3.9])

* The study sample size is presented as an absolute number. The percentages were generated by using weighted samples and therefore do not correspond exactly.
† Approximately 1% of data not available.

Table 3. **Risk Factors for Colonization with *Staphylococcus aureus* (Methicillin-Sensitive and Methicillin-Resistant): Logistic Regression**

Characteristic	Odds Ratio (95% CI)	*P* Value
Age < 65 y	1.4 (1.2–1.7)	0.002
Men	1.5 (1.3–1.8)	<0.001
Race		<0.001
Non-Hispanic white (reference)	1.0	
Non-Hispanic black	0.7 (0.6–0.8)	
Mexican American or Hispanic	1.1 (0.9–1.3)	
Other race or multiracial group	1.0 (0.7–1.4)	
Education		<0.001
<High school (reference)	1.0	
High school diploma	0.8 (0.7–0.9)	
>High school	0.8 (0.7–0.9)	
Not applicable (age < 7 y)	0.5 (0.4–0.7)	
Country of birth		<0.001
United States (reference)	1.0	
Mexico	0.6 (0.5–0.7)	
Other	1.1 (0.9–1.4)	
Has asthma	1.2 (1.0–1.4)	0.040

MRSA Colonization Risks

For several decades, MRSA has caused infections in patients with well-described risk factors, including hospitalization, surgery, residence in long-term care facilities, dialysis, or intravenous drug abuse (5). The prevalence of health care–associated MRSA may be surmised from the National Nosocomial Infections Surveillance system, which reported in 2003 that 57.1% of *S. aureus* clinical isolates were methicillin-resistant (10).

In recent years, MRSA has caused infections in patients without traditional risk factors (11–14). Many infections have occurred in the community and have affected children and young adults, and some infections have been associated with substantial morbidity. These community-associated MRSA strains have distinct genotypes, phenotypes, and epidemiologic features when compared with health care–associated MRSA. Unlike multidrug-resistant, health care–associated MRSA, for which treatment options are limited, community-associated MRSA strains have generally been reported as susceptible to several antimicrobial agents, including clindamycin, fluoroquinolones, and trimethoprim–sulfamethoxazole (15, 16). Most community-associated MRSA strains have caused skin and soft-tissue infections, and Panton–Valentine leukocidin has been implicated as a possible virulence factor (17). The sequenced prototype community-associated MRSA strain MW2 was isolated from a pediatric case of fatal septicemia in North Dakota in 1998 (12) and was shown to harbor SCC*mec* type IV (18). No definition of community-associated MRSA is universally accepted. Several authors have posited that SCC*mec* type IV is characteristic of community-associated MRSA, although a complete definition of community-associated MRSA probably needs a combination of *mec* type and epidemiologic analysis (19, 20).

Several publications have examined the epidemiology of MRSA at the community and city level. Within the Centers for Disease Control and Prevention's Active Bacterial Core Surveillance Program are population-based surveillance in Baltimore and Atlanta and laboratory-based surveillance in 12 hospitals in Minnesota. In the survey, 8% to 20% of clinical MRSA isolates were not associated with traditional risk factors and, therefore, were classified as community-associated MRSA (16). Similarly, in a hospital-based study, up to 40% of MRSA infections in adults were acquired before hospitalization (21). Jernigan and colleagues (22) found that among healthy adults presenting to a primary care clinic for routine care, 24.7% were colonized with *S. aureus* and 3% were colonized with MRSA. All of these MRSA isolates had an antibiotic resistance pattern typical of community-associated MRSA (that is, sensitivity to several non–β-lactam antibiotics). However, the MRSA colonization was associated with previous admission to a nursing home or hospital and presence of underlying illness (22). These findings highlight the difficulties in characterizing the epidemiology of MRSA in the community.

Charlebois and colleagues (23) attempted to determine the prevalence and risk factors for nasal colonization with *S. aureus* and methicillin resistance among the urban poor population in San Francisco. They found that 22.8% were colonized with *S. aureus* and 12.0% of *S. aureus* isolates were methicillin-resistant. The overall prevalence of MRSA was 2.8%. They noted that all but 2 individuals (0.24%) with MRSA had known risk factors (23). In contrast, some communities have a vastly higher prevalence. The Texas Children's Hospital reported in 2002 that 35% to 51% of their community-associated clinical isolates of *S. aureus* were methicillin-resistant (24). The wide variety of results from these studies clearly suggest that while the epidemiology of *S. aureus* and MRSA colonization and infection is well-characterized in several local communities, the burden of staphylococcal disease on the U.S. population as a whole merits further analysis.

Our investigation of the NHANES data demonstrates

Table 4. **Risk Factors for Methicillin Resistance among Persons Colonized with *Staphylococcus aureus*: Logistic Regression**

Characteristic	Odds Ratio (95% CI)	*P* Value
Age < 65 y	0.3 (0.1–0.9)	0.030
Men	0.4 (0.2–0.6)	<0.001
Race		0.010
Non-Hispanic white (reference)	1.0	
Non-Hispanic black	1.5 (0.8–2.9)	
Mexican American or Hispanic	0.3 (0.2–0.6)	
Other race or multiracial group	1.4 (0.4–5.2)	
Has diabetes	2.6 (1.1–6.1)	0.030
In long-term care facility in last 12 mo	7.4 (2.5–21.8)	0.001

Table 5. **Differences in Genes Encoding Toxin Production between Methicillin-Sensitive *Staphylococcus aureus* and Methicillin-Resistant *Staphylococcus aureus****

Toxin	MSSA (*n* = 297), *n* (%)	MRSA (*n* = 75), *n* (%)	*P* Value
Panton–Valentine leukocidin	3 (1.0)	6 (8.0)	<0.001
Enterotoxin A	64 (21.6)	6 (8.0)	0.007
Enterotoxin B	16 (5.4)	7 (9.3)	0.2
Enterotoxin C	17 (5.7)	2 (2.7)	0.3
Enterotoxin D	15 (5.1)	43 (57.3)	<0.001
Enterotoxin H	16 (5.4)	1 (1.3)	0.100
Toxic shock syndrome toxin-1	90 (30.3)	5 (6.7)	<0.001

* MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *Staphylococcus aureus*.

that MRSA colonization in noninstitutionalized persons is rare (0.84% of the population and 2.5% of those colonized with *S. aureus*). Several risk factors shown in **Table 4** for MRSA versus MSSA colonization probably reflect traditional risk factors for health care–associated MRSA (age > 65 years, diabetes, and long-term care facility use). Why men would be at risk for MSSA colonization and women would be at risk for MRSA is unclear. We initially hypothesized that women confounded the relationship between long-term care exposure and MRSA colonization because women tend to live longer than men and, therefore, a larger percentage may live in long-term care facilities. However, multivariate logistic regression demonstrated the independent effect of sex and long-term care exposure on MRSA colonization.

We found that Hispanic people had a lower risk for MRSA colonization than white people. This, combined with our findings that those born in Mexico had less MSSA colonization, argue for further exploration of the link between ethnicity and staphylococcal colonization and disease. Given that antimicrobial agent use is a risk factor for colonization and for infection with resistant bacteria in general, our findings are intriguing and, perhaps, are counterintuitive since use of antibiotics without prescription has been reported more frequently among persons from Central and South America (25–27). Furthermore, certain bacterial species have been shown to have higher levels of antimicrobial resistance among Hispanic populations. For example, Hispanic persons were at highest risk during an outbreak of antimicrobial-resistant shigellosis (28), and being foreign-born was a substantial risk factor for drug-resistant tuberculosis along the Mexico–Texas border (29). If antimicrobial agent use does not explain the relationship between Hispanic ethnicity and staphylococcal colonization, genetic or other unrecognized factors may play a role.

Antimicrobial Resistance

Our comparison of antimicrobial resistance profiles from MRSA with SCC*mec* type II versus SCC*mec* type IV demonstrates the unique profile of the latter (**Table 6**). The SCC*mec* type IV gene, often associated with community-associated MRSA, is smaller than the other *mec* types and is less likely to carry several resistance genes.

Toxin Genes

Some strains of staphylococci produce 1 or more exoproteins, which include toxic shock syndrome toxin-1 and the staphylococcal enterotoxins (staphylococcal enterotoxins A, B, C, D, E, H, and I [SEA, SEB, SEC, SED, SEE, SEH, and SEI, respectively]). These toxins share the properties of pyrogenicity and superantigenicity and the capacity to enhance the lethality of endotoxin in animal models (30). The enterotoxins also are highly emetogenic and cause staphylococcal food poisoning. Patterns of the presence of toxin genes may be helpful in epidemiologic investigations. These data indicate that enterotoxin D may be a marker for health care–associated MRSA since it was present statistically significantly more often in MRSA than in MSSA and in SCC*mec* type II MRSA than in SCC*mec* type IV MRSA.

The Panton–Valentine leukocidin gene encodes an exotoxin that has been associated with skin and soft-tissue infections, as well as severe necrotizing pneumonia (31). This gene, especially in combination with the presence of the SCC*mec* type IV gene, may be a genetic marker for community-associated MRSA (32). The Panton–Valentine leukocidin gene was detected in 1% of MSSA isolates and 8% of MRSA isolates in this data set. Most published data on the prevalence of Panton–Valentine leukocidin production are in isolates of community-associated MRSA that have been associated with clinical disease. Among persons

Table 6. **Genes Encoding Toxin Production and Antimicrobial Resistance in Methicillin-Resistant *Staphylococcus aureus* Staphylococcal Chromosomal Cassette *mec* Types II and IV***

Variable	SCC*mec* Type II (*n* = 38), *n* (%)	SCC*mec* Type IV (*n* = 37), *n* (%)	*P* Value
Toxin			
Panton–Valentine leukocidin	0 (0)	6 (16.2)	0.010
Enterotoxin A	3 (7.9)	3 (8.1)	0.97
Enterotoxin B	1 (2.6)	6 (16.2)	0.040
Enterotoxin C	0 (0)	2 (5.4)	0.100
Enterotoxin D	32 (84.2)	11 (29.7)	<0.001
Enterotoxin H	0 (0)	1 (2.7)	0.3
Toxic shock syndrome toxin-1	2 (5.3)	3 (8.1)	0.6
Resistance			
Clindamycin	24 (63.2)	0 (0)	<0.001
Erythromycin	36 (94.7)	20 (54.1)	0.030
Ciprofloxacin	35 (92.1)	6 (16.2)	<0.001
Trimethoprim–sulfamethoxazole	0 (0)	0 (0)	NA
Vancomycin	0 (0)	0 (0)	NA

* NA = not applicable; SCC*mec* = staphylococcal chromosomal cassette *mec*.

with clinical infection, Panton–Valentine leukocidin rates of up to 93% have been reported (32). While the NHANES data demonstrate higher rates of Panton–Valentine leukocidin detection in SCC*mec* type IV isolates than in SCC*mec* type II isolates (16.2% vs. 0%), the overall rates are less than those previously reported. This may reflect the differences in virulence between colonizing and infecting flora.

Limitations

We analyzed the 2001–2002 NHANES data, which are the most recent data available and are the only national data available describing *S. aureus* colonization; however, the data are now several years old and may not reflect the most recent changes in epidemiology. Limitations to conclusions can be drawn from our secondary analysis. The emergence of community-associated MRSA varies regionally, and local epidemiology must always be considered in clinical decision making. The data set does not contain information about where study participants currently reside or if they live in urban, suburban, or rural environments. Whether race and ethnicity or the geographic variation of racial or ethnic groups accounts for the risk factors described should be further investigated. Although all staphylococcal disease starts with colonization and the vast majority of colonization can be detected by culturing the anterior nares, colonizing isolates may be different from isolates associated with infection on a population basis. Differences in virulence factors are likely, which make some colonizing isolates more likely to cause invasive disease. Thus, while our study provides U.S. population estimates of *S. aureus* colonization, risk factors for colonization identified in NHANES may not be the same as those associated with invasive infections. The relatively few MRSA isolates ($n = 75$) may have limited our power to identify certain risk factors. We did not compare the risk factors between SCC*mec* type IV isolates ($n = 37$) and SCC*mec* type II isolates ($n = 38$) because there were so few; however, future studies with larger sample sizes should consider performing this analysis. If the MRSA isolates were a combination of health care–associated MRSA and community-associated MRSA (as suggested by *mec* type), then the risk factor analysis of the group of all MRSA may have been influenced by 2 unique sets of epidemiologic risk factors.

Conclusions

The NHANES data allow for an accurate estimation of the population prevalence of *S. aureus*, MRSA, and the subtypes of MRSA that are thought to be community- and health care–acquired. Despite several reports of high rates of methicillin resistance emerging in community settings, these data demonstrate a fairly low national prevalence of MRSA colonization. Further research is needed to examine the basis of our findings that those of Mexican birth and Hispanic ethnicity have a lower risk for MSSA and MRSA colonization, respectively. Analysis of this large data set confirms observations made in smaller clinical series: MRSA with SCC*mec* type II tends to be resistant to several classes of antibiotics, while MRSA with SCC*mec* type IV tends to be resistant only to the β-lactams. Hence, use of trimethoprim–sulfamethoxazole or ciprofloxacin rather than vancomycin for infections caused by MRSA SCC*mec* type IV may be reasonable. While vancomycin therapy could be avoided in less serious SCC*mec* type IV infections, increased use of quinolones poses its own risks for both emerging resistance and adverse drug events. Continuing studies defining the epidemiology of MRSA of different *mec* types are warranted because clinical prediction tools would be beneficial in choosing empirical therapy. The observation that most type IV staphylococci carry the Panton–Valentine leukocidin gene is not borne out in colonizing isolates; however, the gene is substantially more common in this subgroup of MRSA. Analysis of future NHANES data will be important to track national trends in *S. aureus* colonization.

Note added in proof: An article based on the NHANES data set was published in the *Journal of Infectious Diseases*: Kuehnert MJ, Kruszon-Moran D, Hill HA, McQuillan G, McAllister SK, Fosheim G, et al. Prevalence of *Staphylococcus aureus* nasal colonization in the United States, 2001-2002. J Infect Dis. 2006;193:172-9. [PMID: 16362880]. Our analyses were completed independently. The results of the 2 papers vary somewhat because of different analytic strategies.

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