

Nasal Carriage of *Staphylococcus aureus* and Methicillin-Resistant *S aureus* in the United States, 2001-2002

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ABSTRACT

PURPOSE *Staphylococcus aureus* is a common cause of invasive infections, yet most assessments of prevalence are based on health care–based samples. We computed population-based estimates of nasal carriage of *S aureus* and risk factors for carriage, as well as population-based estimates of nasal carriage of methicillin-resistant *S aureus* (MRSA).

METHODS We used the National Health and Nutrition Examination Survey (NHANES) 2001-2002 to estimate carriage of *S aureus* and MRSA for the non-institutionalized US population including children and adults.

RESULTS An estimated 86.9 million persons (32.40% of the population) were colonized with *S aureus*. The prevalence of MRSA among *S aureus* isolates was 2.58%, for an estimated population carriage of MRSA of 0.84% or 2.2 million persons. Among individuals with *S aureus* isolates, individuals aged 65 years or older had the highest MRSA prevalence (8.28%). Among all the racial/ethnic groups studied, Hispanics had the highest prevalence of colonization with *S aureus* but, when colonized, were less likely to have MRSA.

CONCLUSIONS This first nationally representative assessment of carriage of *S aureus* indicates that nearly one third of the population is currently colonized by this organism. Although the prevalence of MRSA remains low, more than 2.2 million people carry this resistant organism; thus, vigilance in promoting appropriate microbial transmission protocols should remain a priority.

Ann Fam Med 2006;4:132-137. DOI: 10.1370/afm.526.

INTRODUCTION

Staphylococcus aureus is one of the most common human pathogens and is capable of causing a wide range of infections. Although primary *S aureus* infections are not common, a great deal of the virulence from this organism occurs through cross-infection by spread from patient to patient in hospitals and other institutional settings. In contrast, healthy individuals have a small risk of contracting an invasive infection caused by *S aureus*, but they can be carriers of the organism.¹ Because its primary habitat is moist squamous epithelium of the anterior nares,² most invasive *S aureus* infections are assumed to arise from nasal carriage.³

The incidence of community-acquired and hospital-acquired *S aureus* infections has been rising with increasing emergence of drug-resistant strains called methicillin-resistant *S aureus* (MRSA).⁴⁻⁸ MRSA is an established pathogen in most health care facilities. Previously limited to hospitals, MRSA infections have been increasingly reported in the community.^{8,9-14} A recent meta-analysis of 27 studies of the prevalence of community-acquired-MRSA among hospital patients that used clinical specimens, as opposed to surveillance cultures conducted at the time of admission, yielded a prevalence of MRSA of 30.2%.¹⁵ The strains of MRSA associated with recent community outbreaks have

Conflicts of interest: none reported

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unique microbiologic and genetic properties that may allow them to spread more easily or cause more skin disease than traditional hospital-based strains.¹⁶

Because many clinical infections arise from spread from a healthy carrier, an understanding of the risk factors for carriage of *S aureus* is crucial to understanding the potential for invasive infections and transmission of MRSA; however, most surveillance of *S aureus* and MRSA has focused on individuals with invasive infections rather than on an entire population.^{10-12,17,18} Focusing on individuals with invasive infections provides a good indication of severe disease but does not provide an accurate assessment of the reservoir of *S aureus* and potential for transmission.

A variety of studies have examined community prevalence of nasal carriage of *S aureus* in diverse subpopulations, such as adult outpatients, health care workers, college students, and injection drug users.¹⁹⁻²⁴ The prevalence of *S aureus* ranges from 20% to 45%, with an estimate of MRSA colonization from 10 community surveillance studies of 1.3%.¹⁵ Few studies, however, have focused on which individuals are most likely to be colonized with *S aureus* and which are most likely to specifically have MRSA. These are issues that may be very useful to clinicians when trying to decide the likelihood that a given patient has a staphylococcal infection and, if so, whether antibiotic coverage should be provided for resistant strains. We undertook this population-based study to produce population-based estimates of nasal carriage of *S aureus* and to identify risk factors for carriage and to determine population-based estimates of nasal carriage of MRSA.

METHODS

The data used for the present study come from the National Health and Nutrition Examination Survey (NHANES) 2001-2002. The NHANES 2001-2002 is a nationally representative sample of the noninstitutionalized US population. The NHANES design includes an oversampling of minorities and allows determination of population estimates. More information on the methods of the 2001-2002 survey including laboratory assessment can be found elsewhere.²⁵

Assessment of *S aureus* was conducted for the entire sample; thus, all participants aged 1 year or older were tested and were included in this study. The number of individuals used in the unweighted sample was 9,622, which represented a weighted population of 268,219,049.

Procedure

Assessment of *S aureus*

The procedure for processing the nasal cultures in the NHANES 2001-2002 began with an inspection of the

nasal swabs for proper labeling and integrity. Nasal swabs were refrigerated and shipped weekly to a contract laboratory. Specimens collected from the nares were plated on mannitol salt agar (MSA), a selective medium for the isolation of *S aureus*. MSA plates were incubated at 37°C for 48 hours. Mannitol-fermenting colonies (ie, those that were yellow or gold) were selected from the MSA plates and subcultured to plates with trypticase soy agar containing 5% sheep blood (ie, blood agar plates [BAPs]) and incubated at 37°C overnight. 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 using Staphaurex, a rapid latex kit for the identification of *S aureus* (Remel, Lenexa, Kan). A tube coagulase test using rabbit plasma with EDTA was then performed on Staphaurex-negative isolates from BAPs with morphology consistent with *S aureus* and on Staphaurex-positive isolates with morphology inconsistent with *S aureus* (ie, nonhemolytic). Staphaurex-positive isolates and Staphaurex-negative, tube coagulase-positive isolates were identified as *S aureus* and saved for further testing. Staphaurex-positive, tube coagulase-negative isolates were discarded.

Assessment of MRSA

S aureus isolates were screened for methicillin resistance by the disk diffusion method of the National Clinical and Laboratory Standards Institute. Overnight cultures from BAPs were plated on Mueller-Hinton agar, and a 1- μ g oxacillin disk was placed on the inoculated plate. Zone diameters were measured and recorded after a 24-hour incubation at 37°C; the results were classified as sensitive (≥ 13 mm), intermediate (11-12 mm), or resistant (≥ 10 mm).

Potential Risk Factors

Several variables were investigated as potential characteristics indicative of carriage of *S aureus*. These factors included the common demographic variables of age, sex, race/ethnicity, and place of birth. We also examined carriage of *S aureus* according to self-reported health status, poverty-income ratio, outpatient health care use in the past 12 months, hospitalization in the past, long-term care admission in the past 12 months, use of antibiotics in the past 30 days, self-report of physician diagnosis of diabetes, self-report of physician diagnosis of asthma, self-reported oral health, and current exposure to cigarette smoke (operationalized as either being a current smoker or living in a house with a current smoker). Given the limited population carriage of MRSA, we

investigated a limited number of characteristics based on whether the unweighted sample size was large enough to make a reliable population estimate (ie, the standard error was less than one third of the parameter estimate).

Analysis

The selection of variables was based on the ability to use the entire population for our estimates. The NHANES limits some questions to certain age-groups (eg, adults) or other population subsets (eg, Hispanics). Consequently, we investigated variables that were available for the entire sample.

We used SUDAAN software (Research Triangle Institute, Research Triangle Park, NC) to account for the complex sample design used in the NHANES in the analysis. Our analysis incorporated both the stratification and clustering aspects of the sampling design. The proper weighting procedures include adjustments for the basic probability of selection and adjustments for nonresponse. Because minorities were oversampled and the sampling design was complex, we used sampling weights provided by the NHANES to compute population estimates based on weighted parameter estimates and standard errors. Chi-square analyses were used for bivariate comparisons. We also conducted a logistic regression analysis of all variables with a bivariate *P* value of $<.10$ and then removed variables that were not significant at this level.

We initially attempted to compute the relationship of several potential risk factors for carriage of *S aureus* and MRSA but found that for some variables, there were too few unweighted individuals in a cell to make a reliable population estimate. Admission to a long-term care facility was one such variable and is therefore not presented.

RESULTS

Carriage of *S aureus*

We found that the prevalence of nasal carriage of *S aureus* in the US population was 32.40% or 86,906,811 persons. Among adults aged 20 and older, nasal carriage of *S aureus* was present in 30.67%. Table 1 provides an indication of the population prevalence of nasal carriage of *S aureus* based on demographic characteristics, age, sex, race/ethnicity, and country of birth were associated with carriage in this community surveillance. In particular, it was noteworthy that non-Hispanic blacks were less likely than non-Hispanic whites or Hispanics to be colonized by *S aureus*.

In addition to looking at demographic characteristics, we also explored the relationship between clinical characteristics and nasal carriage of *S aureus* (Table 2). Among these characteristics, having asthma was positively related to carriage, whereas exposure to cigarette smoke and recent use of antibiotics were negatively associated with carriage.

To account for potential confounding among the demographic and clinical characteristics, we further analyzed the relationship between the potential predictors with a logistic regression model (Table 3). This model shows that even when controlling for the effect of the other characteristics (eg, age, sex, race/ethnicity), the relationships found in the bivariate analyses remain significant.

Carriage of MRSA

We also looked at carriage of MRSA in the same population. The prevalence of MRSA among *S aureus* isolates was 2.58%. This value corresponds to a total population carriage of MRSA of 0.84% or 2,239,888 persons and a carriage of methicillin-susceptible *S aureus* (MSSA) of 31.57% or 84,666,923 persons. Among adults aged 20 years or older, the prevalence of carriage of MRSA was 0.95%. Total population carriage of MRSA was 0.67% for individuals aged 1 to 64 years and 2.16% for individuals aged 65 years or older.

The prevalence of MRSA among *S aureus*

Table 1. Prevalence of *Staphylococcus aureus* Carriage in the US Population Based on Demographic Characteristics

Characteristic	Persons No. (%)	P Value
Age, y		
1-6	5,727,630 (25.62)	<.01
7-19	21,750,247 (41.76)	
20-64	51,795,838 (31.50)	
≥65	7,633,096 (26.02)	
Race/ethnicity		
Non-Hispanic white	60,714,994 (32.91)	<.01
Non-Hispanic black	8,640,926 (26.78)	
Hispanic	13,816,245 (34.19)	
Other	3,734,645 (33.87)	
Sex		
Male	48,339,253 (37.02)	<.01
Female	38,567,558 (28.02)	
Place of birth		
United States	76,736,750 (32.38)	.03
Mexico	2,866,928 (27.26)	
Elsewhere	7,182,631 (35.04)	
Poverty-income ratio*		
<1	12,960,604 (30.86)	.20
≥1	69,309,681 (32.92)	

* In which a score >1.00 indicates the official poverty threshold.

isolates varied by age, race/ethnicity, and sex. Among individuals with *S aureus* isolates, 2.03% of those aged 1 to 64 years were carriers of MRSA, compared with 8.28% of those aged 65 years or older ($P = .01$). Also among individuals with *S aureus* isolates, 2.70% of non-Hispanic whites carried MRSA, compared with 4.14% of non-Hispanic blacks and 0.79% of Hispanics ($P = .01$). In addition, 4.14% of women with *S aureus* isolates carried MRSA, compared with only 1.33% of men ($P = .01$).

DISCUSSION

This study provides the first nationally representative assessment of carriage of *S aureus* in the total US population. The results suggest that nearly one third of the population is currently colonized by *S aureus*. Although the community carriage of MRSA is relatively low at less than 1%, this figure translates to more than 2.2 million people in the United States carrying this resistant organism.

Our prevalence results are similar to those of several previous regional studies focusing on different subgroups of the population in the United States.^{21,24} In

regional estimates that were based on patients, however, even though the patients did not have invasive infections, their MRSA prevalence tended to be substantially higher than that in the more generally representative sample of the NHANES 2001-2002.

Our study extends the previous knowledge in this area by identifying several predictors of nasal *S aureus* carriage. These predictors may help inform clinical decision making when treating community-acquired infections. First, teenagers and male individuals are more likely to be carriers of *S aureus*. When clinicians encounter infections in these 2 groups, especially in body areas where staphylococcal infections are common, such as the skin, treatment should include an antibiotic that is effective against *S aureus*. But while carriage is more common in these groups, the prevalence of MRSA remains low; therefore, clinicians should not be highly suspicious of methicillin resistance in these populations unless the infection is atypical, such as one occurring in a body area that is uncommon for staphylococcal infection (eg, the lungs) or one that is rapidly advancing.

Our study also may be useful in that our findings point out that relative to younger individuals, older adults are less likely to be colonized with *S aureus* but, when colonized, are more likely to have MRSA strains. This finding suggests that older adults with suspected staphylococcal infections may need antibiotic coverage against resistant strains. Because of the higher rates of carriage of resistant organisms in this medically vulnerable population, clinicians may want to initiate vancomycin therapy earlier in the course of a suspected *S aureus* infection in patients older than 65 years.

Whereas studies looking at the risk of carriage of resistant *Streptococcus pneumoniae* indicate that recent beta-lactam use increases the rate of carriage of this organism, our data indicate that recent use of antibiotics is associated with a reduced risk of *S aureus* nasal carriage.²⁶ Unfortunately, because the prevalence of MRSA was low and the number of individuals using antibiotics was small, we were not able to explore whether antibiotic use is related to antibiotic resistance in those who do carry *S aureus*. Among individuals with an *S aureus* isolate who had recently used antibiotics, 4.83% were colonized by MRSA, while only 2.45% of those who had not used antibiotics were colonized by MRSA. This estimate, however, does not meet criteria for reliability in this population-based study because only 6 people had used antibiotics recently and carried MRSA.

Table 2. Prevalence of *Staphylococcus aureus* Carriage in the US Population Based on Clinical Characteristics

Characteristic	Persons No. (%)	P Value
General health status		
Good-excellent	76,339,026 (32.59)	.40
Poor-fair	10,567,785 (31.17)	
Number of outpatient visits in past year		
0	14,873,280 (35.07)	.09
≥1	71,975,850 (31.89)	
Hospitalization in the past		
Yes	7,256,430 (30.04)	.38
No	79,650,380 (32.64)	
Use of antibiotics in past 30 days		
Yes	4,769,010 (24.43)	.01
No	82,137,800 (33.03)	
Oral health		
Good to very good	61,288,546 (32.80)	.78
Poor to fair	25,047,076 (32.22)	
Current smoker or smoker in the household		
Yes	21,806,172 (29.03)	.02
No	64,487,150 (33.83)	
Diabetes		
Yes	3,936,552 (30.22)	.52
No	82,970,259 (32.52)	
Asthma		
Yes	11,918,406 (36.35)	.04
No	74,901,009 (31.86)	

Table 3. Logistic Regression Analysis Predicting Carriage of *Staphylococcus aureus* in the US Population

Characteristic	Odds Ratio (95% CI)
Age, y	
1-6	0.74 (0.63-0.87)
7-19	1.53 (1.36-1.73)
20-64	1.00
≥65	0.73 (0.59-0.91)
Race/ethnicity	
Non-Hispanic white	1.00
Non-Hispanic black	0.71 (0.61-0.83)
Hispanic	1.07 (0.93-1.24)
Other	0.94 (0.64-1.37)
Sex	
Male	1.00
Female	0.66 (0.56-0.78)
Place of birth	
United States	1.00
Mexico	0.67 (0.54-0.82)
Elsewhere	1.11 (0.89-1.39)
Use of antibiotics in past 30 d	
Yes	0.63 (0.45-0.88)
No	1.00
Current smoker or smoker in the household	
Yes	0.78 (0.65-0.95)
No	1.00
Asthma	
Yes	1.24 (1.03-1.51)
No	1.00

CI = confidence interval.

Finally, these data reflect a national sample. Local rates of carriage and resistance may vary considerably. Additionally, data for this study were collected in 2001-2002. Rapid changes in patterns of carriage and resistance are possible. One recent study of children in Nashville, Tenn, for example, showed an MRSA colonization rate similar to that in our study (0.8%) in 2001, but a considerably higher rate when children of the same age-group were sampled just 3 years later.²⁷ Consequently, when clinicians are making therapeutic decisions, they should monitor bacterial carriage rates and resistance patterns for their own hospital and city, as well as take into account the risk patterns found in our study.

This study has several strengths. It provides the first nationally representative community surveillance estimates of *S aureus* and MRSA carriage for the United States. By focusing on nasal carriage within an undifferentiated sample ranging from small children to the elderly, the study provides an estimate of the reservoir

of *S aureus* and MRSA that has not been available in studies focusing on individuals in the health care system or small regional samples.

Even with the aforementioned strengths, our study has some limitations. Because of the small number of individuals colonized with MRSA and the corresponding inability to make reliable population estimates, we were limited in our ability to identify risk factors for community carriage of MRSA; thus, although it is encouraging that the community prevalence of MRSA is less than 1%, our ability to identify characteristics of this group beyond age, race/ethnicity, and sex was limited. A second limitation of the study was that it was restricted to the noninstitutionalized population. Although this population provides for the broadest assessment of the entire population, carriage of *S aureus* and MRSA may differ in other settings.

In conclusion, our study confirms the high prevalence of *S aureus* nasal colonization in the United States; however, it also shows that the rate of MRSA carriage remains low. Few demographic or clinical characteristics are related to either *S aureus* carriage or, more specifically, MRSA carriage. Consequently, clinicians and hospital infection control personnel cannot target specific populations who are at highest risk of transmitting *S aureus* and should remain vigilant in using appropriate protocols for minimizing microbial transmission.

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Key words: *Staphylococcus aureus*; cross infection; drug resistance, bacterial; community-acquired infections

Submitted July 12, 2005; submitted, revised, September 12, 2005; accepted September 21, 2005.

Funding support: This work was supported in part by grant 1D12HP00023-01 from the Health Resources and Services Administration, grant 1 P30AG021677 from the National Institute on Aging, and a Minority Medical Faculty Development Program grant funded by the Robert Wood Johnson Foundation.

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