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Molecular Epidemiology of *Staphylococcus aureus* Colonization in 2 Long-Term Care Facilities

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Abstract

Persistent colonization with *Staphylococcus aureus* was assessed in 22 nursing home residents. Eighteen residents (82%) remained colonized with the same strain found at baseline; 6 (33%) of 18 residents transiently acquired a new strain. Four residents (18%) acquired a new persistent strain. Residents colonized with methicillin-resistant *S. aureus* were more likely to acquire a new strain (67%) than were residents colonized with methicillin-susceptible *S. aureus* (20%) ($P = .04$).

Infection with *Staphylococcus aureus* continues to be a serious problem for residents of long-term care facilities (LTCFs).¹ Asymptomatic carriage is frequently a precursor to infection, and infection is usually caused by the colonizing strain.^{1,2} In one study, one-third of the LTCF population, especially those with chronic disease and debility, were colonized with *S. aureus*.³

S. aureus carriage has been well studied in the general population.⁴ Point-prevalence surveys of *S. aureus* carriage have classified individuals as either carriers or noncarriers. Longitudinal studies of predominantly healthy populations have shown that the duration of carriage can vary.⁵ Persistence of carriage in the LTCF population has been infrequently studied.³ Our study further describes the epidemiological profile of *S. aureus* colonization among LTCF residents. Our specific aim was to characterize *S. aureus* strains in LTCF residents with persistent colonization.

METHODS

Study population

The Ann Arbor Veterans Affairs Extended Care Center is a 50-bed facility attached to an acute care hospital. Glacier Hills Nursing Center is a 163-bed community LTCF located within a few miles of the Veterans Affairs Medical Center. It has a 127-bed skilled nursing unit and a 36-bed dementia unit. All residents at these 2 facilities were eligible for our study. After obtaining written informed consent from the residents or their guardians, specimens were obtained from the nares and, when present, wounds. A total of 127 residents for whom 2 weekly cultures were positive for *S. aureus* were enrolled in a randomized trial of nasal decolonization with either mupirocin or placebo.⁶ We studied isolates from those residents

who were randomized to the placebo arm and who remained persistently colonized with *S. aureus* during the treatment period and for a total of at least 60 days.

Microbiological methods

Nares and wounds were swabbed with sterile rayon-tipped applicator sticks that were then placed into Stuart's transport medium. Swabs were streaked onto colistin-nalidixic acid agar with 5% sheep's blood (BBL; Becton Dickinson) and were incubated at 35°C for 48 hours. Identification and testing of *S. aureus* isolates for susceptibility to methicillin were performed using standard methods.⁶

Pulsed-field gel electrophoresis (PFGE)

Identification and susceptibility testing of *S. aureus* strains, to distinguish methicillin-resistant *S. aureus* (MRSA) strains from methicillin-susceptible *S. aureus* (MSSA) strains, were performed using standard methods.⁶ *S. aureus* isolates were typed by PFGE, to determine the relatedness of strains. Genomic DNA fragments obtained after digestion with *Sma*I (New England BioLabs) were separated by PFGE, using the CHEF DR III system (BioRad). Gels were stained and photographed, and the banding patterns of different isolates were compared visually. Strain relatedness was determined using Tenover criteria.⁷

RESULTS

Of the 127 residents enrolled in the decolonization study, 63 were randomized to the placebo arm. No significant differences were noted between the treatment and placebo groups.⁶ In the placebo group, 36 residents (57%) were discharged before 60 days, 5 residents (8%) cleared their colonization, and 22 residents (35%) remained persistently colonized with *S. aureus* at the end of the study period. The 22 residents who were persistently colonized form the study sample. Nine of these residents were from the Veterans Affairs LTCF, and 13 were from the community-based LTCF. Twelve of the residents were men, and 10 were women.

The mean number ($\pm$ SD) of isolates per resident was 11.7 ± 0.6 ; residents were monitored for a mean of 126 days (range, 60–180 days). A total of 269 isolates obtained from these residents were analyzed by PFGE. There were 136 MRSA isolates (51%) and 133 MSSA isolates (49%) studied.

Eighteen residents (82%) were persistently colonized with the strains found at baseline throughout the study period, including 3 residents who were colonized with 2 separate strains; PFGE results for 1 resident are shown in Figure 1. Six residents (27%) were transiently colonized by different strains that did not persist. Four residents (18%) were colonized by a new strain that replaced the original strain and persisted until the end of the study (Figure 2). Similar patterns of persistence and acquisition occurred at both the Veterans Affairs and community LTCFs.

Colonization with a new strain occurred, on average, 70 days after enrollment in the study. New strains in all of these residents showed a change in susceptibility to methicillin (Figure 2). Eight (67%) of 12 residents colonized with MRSA acquired a transient strain or permanently acquired a new strain, but only 2 (20%) of 10 residents colonized with MSSA acquired a new strain ($P = .04$).

Ten residents received systemic antibiotics during the study period. One resident permanently acquired a new *S. aureus* strain before antibiotic use, and 1 resident permanently acquired a new *S. aureus* strain after antibiotic use. Two residents transiently acquired a new strain before antibiotic use, 2 residents transiently acquired a new strain after antibiotic use, and 4 residents had no change in their colonization pattern.

DISCUSSION

Persistent staphylococcal carriers are of interest, because they typically harbor greater numbers of organisms, are colonized at multiple anatomical sites, and may play a greater role in transmission than do intermittent carriers.⁵ Most longitudinal studies of *S. aureus* colonization have been performed in healthy persons, healthcare personnel, or in patients readmitted to hospital; these studies have ranged in duration from 6 weeks to 8 years. Rates of persistent carriage varied from 9% to 34%.^{5,8,9} Little is known about the epidemiological profile of persistent *S. aureus* carriage in LTCFs. Most studies of *S. aureus* colonization in LTCFs have been based primarily on point-prevalence surveys, rather than longitudinal studies; have been limited to MRSA carriers; and have used molecular methods infrequently.^{10,11}

What constitutes persistent staphylococcal carriage is a subject of debate. In Rotterdam, samples from the nares of healthy elderly patients were cultured weekly for up to 12 weeks; patients with 11 or 12 weekly cultures were considered to be persistent carriers.¹² In a separate validation cohort, 2 cultures performed 1 week apart were 79% predictive of the persistent carrier state, as defined above. In a similar study by the same group, a carrier index greater than 0.80 (ie, the number of cultures positive for *S. aureus* divided by the total number of cultures performed) was used as the definition for persistence.⁵ All *S. aureus* carriers with indices of 1.0 were still positive for *S. aureus* 8 years later.

To be enrolled in the present study, LTCF residents were required to have 2 cultures positive for *S. aureus* 1 week apart and to have a carrier index greater than 0.8. In this way, we believe that only truly persistent carriers, not intermittent carriers, were studied. The results of our study verify that a majority of residents of LTCFs colonized with *S. aureus* remain colonized for months.³ Persistent carriage for prolonged periods has great ramifications for LTCF residents who have resistant staphylococcal strains and who are typically placed in some form of isolation that can interfere with their socialization and rehabilitation and increase costs to their institution.

In the past, it had been thought that the acquisition of new staphylococcal strains would be inhibited by bacterial interference from the colonizing staphylococcal strains that inhabit the specific ecological niche. Therefore, most persistent carriers of *S. aureus* should remain colonized with the same strain. This assumption appears to have been validated by the results of both the present study and our previous study: during 1989–1990, we found by use of phage typing that 82% of persistent carriers harbored the same strain,³ and those findings have been verified in the present study by use of PFGE typing. These findings are similar to those of a study of 19 persistent MRSA carriers who were readmitted to a hospital during a 10-month period; 15 (79%) of the MRSA strains recovered had similar PFGE patterns.⁹ Of note, 4 residents with MRSA strains that had different PFGE types had been transferred to the hospital from LTCFs.

Other studies have not found such consistency in strain colonization.^{5,8} In a smaller study, only 42% of persistent MRSA carriers readmitted to the hospital had MRSA with the same restriction enzyme analysis of plasmid profiles.⁸ After 8 years, only 3 (42%) of 7 healthy healthcare workers with persistent MSSA carriage were colonized by the same strains, as defined by a variety of techniques.⁵

It is unclear why the MRSA carriers seemed to transiently or permanently acquire a new strain during our small study. MRSA-colonized LTCF residents have greater functional impairment.¹¹ MRSA colonization has also been associated with greater use of indwelling devices, such as urinary catheters and feeding tubes, in LTCFs.¹³ Therefore, MRSA-

colonized residents may require more skilled care and may come into contact with the colonized hands of healthcare workers more often than MSSA-colonized residents.

Persistent staphylococcal carriers are at high risk of acquiring infection with their colonizing *S. aureus* strain. Attempts to decolonize carriers and prevent infection have had varying degrees of success.⁶ One concern has been that eradication of the persistent colonizing strain might make the host susceptible to reinfection with new strains. The presence of multiple strains in staphylococcal carriers will add another layer of complexity in interpreting results of decolonization and transmission studies in the LTCF setting.

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FIGURE 1. Pulsed-field gel electrophoresis showing persistent *Staphylococcus aureus* colonization in a nursing home resident (resident 54) for 180 days.

FIGURE 2.

Transient and permanent acquisition of a new *Staphylococcus aureus* strain in nursing home residents with persistent *S. aureus* colonization. MRSA = methicillin-resistant *S. aureus*; MSSA = methicillin-susceptible *S. aureus*.