Mupirocin-Based Decolonization of *Staphylococcus aureus* Carriers in Residents of 2 Long-Term Care Facilities: A Randomized, Double-Blind, Placebo-Controlled Trial

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Mupirocin has been used in nursing homes to prevent the spread of methicillin-resistant *Staphylococcus aureus* (MRSA), despite the lack of controlled trials. In this double-blind, randomized study, the efficacy of intranasal mupirocin ointment versus that of placebo in reducing colonization and preventing infection was assessed among persistent carriers of *S. aureus*. Twice-daily treatment was given for 2 weeks, with a follow-up period of 6 months. Staphylococcal colonization rates were similar between residents at the Ann Arbor Veterans Affairs (VA) Extended Care Center, Michigan (33%), and residents at a community-based long-term care facility in Ann Arbor (36%), although those at the VA Center carried MRSA more often (58% vs. 35%; *P* = .017). After treatment, mupirocin had eradicated colonization in 93% of residents, whereas 85% of residents who received placebo remained colonized (*P* < .001). At day 90 after study entry, 61% of the residents in the mupirocin group remained decolonized. Four patients did not respond to mupirocin therapy; 3 of the 4 had mupirocin-resistant *S. aureus* strains. Thirteen (86%) of 14 residents who became recolonized had the same pretherapy strain; no strain recovered during relapse was resistant to mupirocin. A trend toward reduction in infections was seen with mupirocin treatment.

Colonization and infection with *Staphylococcus aureus*, which are common in older persons, are perhaps associated with chronic disease and debility [1]. Mortality due to staphylococcal bacteremia is greater among older persons and is >60% among residents of long-term care facilities (LTCFs) and hospitalized older adults [2–4]. For staphylococcal carriers, the risk of infection with *S. aureus* is significantly higher than it is for noncarriers, and infection is usually caused by the colonizing strain [5, 6]. Carriage of methicillin-resistant *S. aureus* (MRSA) has been shown to be a marker for increased risk of infection and mortality among LTCF residents [7–9].

Treatment of persistent staphylococcal carriage with the topical antibiotic mupirocin has been shown to decrease staphylococcal infections among patients undergoing hemodialysis and those who have undergone elective surgery [10–14]. Several noncontrolled studies have shown that mupirocin alone or in combination with other measures decreases *S. aureus* colonization among residents of LTCFs [15–18]. However, there are no controlled trials involving such individuals that have definitively shown that mupirocin decreases *S. aureus* colonization and infection.

This study, which was performed in both community
STUDY PARTICIPANTS AND METHODS

Study population. The Ann Arbor VA Extended Care Center is a 50-bed facility attached to an acute care hospital. Residents are admitted for long-term care (10 beds), rehabilitation (10 beds), and geriatric evaluation (30 beds). Glacier Hills Nursing Center is a 163-bed community LTCF located within a few miles of the VA Medical Center. It has a 127-bed skilled nursing unit and a 36-bed dementia unit.

Eligibility. All residents of the VA and community LTCFs were eligible. Appropriate informed consent was obtained, and guidelines for human experimentation and the conduct of clinical research were followed, as required by the University of Michigan and Veterans Affairs Ann Arbor Healthcare System institutional review boards. After obtaining written informed consent, specimens were obtained from the nares and, when present, wounds of all patients. Residents for whom culture results were positive for \textit{S. aureus} on 2 consecutive cultures performed \(<2\) weeks apart were considered persistent carriers and were enrolled into the treatment trial.

Exclusion criteria. Residents were not enrolled if they were receiving systemic antibiotic therapy or topical antibiotic therapy for wounds, had active \textit{S. aureus} infection, or were judged unable to cooperate with the study. Known hypersensitivity to mupirocin and the presence of large wounds (i.e., a surface area of \(>10 \times 10 \text{ cm}\) and a depth of \(>3 \text{ cm}\)) were also exclusion factors. Residents who were initially found not to be carriers were screened again if they required admission to the hospital and then returned to the LTCF.

Group assignment. Enrolled residents were randomly assigned to study groups by stratification according to LTCF type and presence of wounds. Randomization was performed separately on the basis of residence type and presence of wounds in blocks of 2 to assure that the number of patients assigned to study groups using these strata was equal. Investigators, nursing staff, and study participants were blinded to the treatment group.

Treatment. Mupirocin therapy or placebo was administered twice daily for 14 days by study personnel who wore gloves after appropriate hand disinfection and who were blinded to results of microbiological tests. The study drugs were placed in identical containers labeled “A” or “B” by the study pharmacist. Mupirocin 2% ointment in polyethylene glycol (PEG) base or plain PEG ointment (placebo) was applied to each anterior nares, and the nose was massaged gently. Ointment was applied over wound surfaces in a thin layer.

Samples were obtained from nares and wounds every other day during the treatment period. On day 15 of the study—the day after treatment ended—a sample was obtained. Successive samples were obtained every week during the next 4 weeks, every 2 weeks for 2 months, and monthly for an additional 2.5 months, as long as the patient remained in the facility. Enrolled residents were observed for the development of staphylococcal infection during the same 6-month period, as long as they were residents of the facility.

Permitted local wound care included whirlpool therapy, debridement, and application of hydrogen peroxide, Dakin’s solution (sodium hypochlorite 5.25%), and dressings. Wound therapy was provided before the study drug or placebo was administered. No topical or systemic antibiotic therapy with activity against \textit{S. aureus} was allowed.

Assessment. Demographic characteristics and risk factors for \textit{S. aureus} colonization were assessed at study entry. Dimensions of decubitus or vascular ulcers, other wounds, skin conditions, and devices were recorded. Functional status was measured using a modified Katz scale [19].

Enrolled residents were monitored daily for \textit{S. aureus} infection, on the basis of the Centers for Disease Control and Prevention definitions [20]. All cases were reviewed by a panel of 3 consultants who specialized in infectious diseases and geriatrics, all of whom were blinded to colonization data and treatment regimens.

Outcomes. Outcomes were categorized as cure (i.e., no \textit{S. aureus} was recovered from any site) or failure (i.e., persistence of \textit{S. aureus} at the end of treatment or recolonization after negative culture results on day 15). Recolonization was further defined as relapse (i.e., recolonization by the previously colonizing \textit{S. aureus} strain) or reinfection (i.e., acquisition of a new \textit{S. aureus} strain).

To test the hypothesis that mupirocin therapy led to eradication of \textit{S. aureus} colonization, short-term (15 days after study entry) and long-term (90 days after study entry) responses were assessed, with \textit{S. aureus} colonization being the primary outcome variable. Recolonization, emergence of mupirocin-resistant strains, and reduction in \textit{S. aureus} infections in residents treated with mupirocin were secondary outcomes.

Microbiological methods. Nasal swabs were swabbed with sterile rayon-tipped applicator sticks that were then placed into Stuart’s transport medium. Samples were obtained before daily local wound care and application of mupirocin. Swabs were streaked onto colistin–nalidixic acid agar with 5% sheep blood (BBL; Becton Dickinson) and incubated at 35°C for 24 h. \textit{S. aureus} identification and methicillin-susceptibility testing were performed using standard methods [15, 16]. If a patient was found to have both MRSA and meth-
Table 1. Demographic and clinical characteristics of residents of 2 long-term care facilities (LTCFs) in Ann Arbor, Michigan, who were enrolled into the study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Veterans Affairs hospital</th>
<th>Community-based nursing center</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of residents screened</td>
<td>254</td>
<td>173</td>
<td>…</td>
</tr>
<tr>
<td>Persistent staphylococcal carriers</td>
<td>83 (33)</td>
<td>62 (36)</td>
<td>.5</td>
</tr>
<tr>
<td>No. of residents enrolled</td>
<td>73</td>
<td>54</td>
<td>.6</td>
</tr>
<tr>
<td>Age, mean years ± SD</td>
<td>69 ± 9.9</td>
<td>86 ± 7.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>70 (96)</td>
<td>13 (24)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>26 (37)</td>
<td>14 (26)</td>
<td>.25</td>
</tr>
<tr>
<td>Acute carea</td>
<td>63 (86)</td>
<td>22 (41)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antibiotic usea</td>
<td>43 (59)</td>
<td>13 (24)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ADL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class 1</td>
<td>39 (53)</td>
<td>7 (13)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Class 2</td>
<td>30 (41)</td>
<td>34 (63)</td>
<td>…</td>
</tr>
<tr>
<td>Class 3</td>
<td>4 (6)</td>
<td>13 (24)</td>
<td>…</td>
</tr>
<tr>
<td>Device use</td>
<td>35 (48)</td>
<td>12 (22)</td>
<td>.003</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>11 (15)</td>
<td>5 (9)</td>
<td>.33</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>23 (32)</td>
<td>4 (6)</td>
<td>.001</td>
</tr>
<tr>
<td>Injectable medication use</td>
<td>18 (25)</td>
<td>6 (11)</td>
<td>.05</td>
</tr>
<tr>
<td>Skin disease</td>
<td>9 (12)</td>
<td>1 (2)</td>
<td>.03</td>
</tr>
<tr>
<td>Wounds</td>
<td>7 (10)</td>
<td>1 (2)</td>
<td>.08</td>
</tr>
</tbody>
</table>

NOTE. Data are no. or no. (%) of individuals, unless otherwise indicated. ADL, activities of daily living.

* During the 30-day period before enrollment.

cillin-susceptible *S. aureus* (MSSA), methicillin resistance was verified by a latex agglutination test for penicillin-binding protein 2a (Oxoid). Isolates were stored at −70°C for later analysis.

Each isolate was screened for mupirocin resistance by inoculation onto Mueller-Hinton agar plates containing 2 μg/mL mupirocin. The MICs of mupirocin for isolates that grew on the screening plates were determined by Etest (AB Biodisk) [21]. Mupirocin resistance was defined as an MIC of ≥4 μg/mL, and high-level resistance was defined as an MIC of ≥500 μg/mL [22].

*S. aureus* strains recovered from residents who were re-colonized after therapy and from those who did not respond to therapy were typed by PGFE to determine whether re-colonization or therapy failure was due to the previous colonizing strain or a new strain. Genomic DNA fragments obtained after digestion with *Sma*I (New England BioLabs) were separated by PFGE using a CHEF III system (BioRad) [23, 24]. Gels were stained and photographed, and the banding patterns of different isolates were compared visually. Strain relatedness was determined as described elsewhere [25].

Statistical methods. Data were entered into EpilInfo 6.0 (Centers for Disease Control and Prevention) and analyzed using SAS software. Demographic and clinical characteristics at enrollment that predisposed residents to *S. aureus* colonization were compared between VA and community LTCFs and between treatment groups. Depending on the scale by which variables were measured, the following standard 2-group comparison methods were used: 2-sample Student’s *t* test, for normally distributed variables; Mann-Whitney *U* test, for continuous nonnormally distributed variables; or χ² test, for categorical variables. A *P* value of <.05 was considered to be statistically significant.

The proportion of residents in each treatment arm who were colonized with *S. aureus* was compared after treatment was stopped (i.e., 15 days after study entry) and on day 90 using the standard Cochran-Mantel-Haenszel (CMH) test on day 15 and a modified CMH test on day 90 (because of residents lost to follow-up) [26, 27]. The Andersen-Gill model was used to analyze data on time to decolonization. The model, an extension of the classical Cox regression model, accounts for potential spontaneous clearance and recolonization.

RESULTS

Demographic and clinical characteristics of the study population at enrollment. Of the 427 residents screened for colonization with *S. aureus*, 254 (59%) were from the VA LTCF and 173 (41%) were from the community LTCF (table 1). Overall, 83 (33%) of VA and 62 (36%) of community LTCF residents were persistently colonized with *S. aureus* and eligible
Table 2. Demographic and clinical characteristics of long-term care facility residents randomized to received mupirocin therapy or placebo.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mupirocin group</th>
<th>Placebo group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years ± SD</td>
<td>76.3 ± 12.8</td>
<td>76.0 ± 12.0</td>
<td>.9</td>
</tr>
<tr>
<td>Male sex</td>
<td>43 (67)</td>
<td>40 (63)</td>
<td>.7</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>17 (27)</td>
<td>23 (37)</td>
<td>.2</td>
</tr>
<tr>
<td>Acute carea</td>
<td>42 (66)</td>
<td>43 (68)</td>
<td>.8</td>
</tr>
<tr>
<td>Antibiotic usea</td>
<td>28 (44)</td>
<td>28 (44)</td>
<td>.9</td>
</tr>
<tr>
<td>ADL Class 1</td>
<td>27 (40)</td>
<td>19 (30)</td>
<td>.05</td>
</tr>
<tr>
<td>Class 2</td>
<td>33 (52)</td>
<td>31 (49)</td>
<td>...</td>
</tr>
<tr>
<td>Class 3</td>
<td>4 (8)</td>
<td>13 (21)</td>
<td>...</td>
</tr>
<tr>
<td>Device use</td>
<td>22 (35)</td>
<td>25 (40)</td>
<td>.5</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>7 (11)</td>
<td>9 (14)</td>
<td>.6</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>13 (20)</td>
<td>14 (22)</td>
<td>.8</td>
</tr>
<tr>
<td>Injectable medication use</td>
<td>10 (16)</td>
<td>14 (22)</td>
<td>.3</td>
</tr>
<tr>
<td>Skin disease</td>
<td>7 (11)</td>
<td>3 (5)</td>
<td>.2</td>
</tr>
<tr>
<td>Wounds</td>
<td>5 (8)</td>
<td>3 (5)</td>
<td>.5</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) of study participants, unless otherwise indicated. ADL, activities of daily living.

* During the 30-day period before enrollment.

for enrollment. Of the patients eligible to participate, 127 (85%) were enrolled into the treatment trial; 73 (57%) were from the VA LTCF, and 54 (43%) were from the community LTCF.

A total of 83 enrolled residents (65%) were men, and 44 (35%) were women. The majority of men (84%) were VA LTCF residents, and almost all women (93%) were community LTCF residents. The mean age (± SD) of study participants was 76.2 ± 12.3 years (range, 45–102 years). The VA LTCF study population was significantly younger than community LTCF study population (69 ± 9.9 vs. 86 ± 7.1 years; P < .001).

Among the 73 VA LTCF residents, colonization with MRSA alone occurred in 42 (58%); an additional 2 (3%) were colonized with both MRSA and MSSA at enrollment. Among the 54 community LTCF residents, 19 (35%) were colonized with MRSA only, and 1 (2%) was colonized with both MRSA and MSSA at enrollment; for 2 residents, methicillin susceptibility was not determined because isolates recovered at enrollment were lost. The difference in the prevalence of MRSA carriage was significantly different between the 2 facilities (P = .017).

**Risk factors for colonization with S. aureus.** The most common risk factors for persistent *S. aureus* carriage included recent hospitalization (67% of study participants), antibiotic use in the 30 days before study entry (44%), presence of devices (37%), and diabetes mellitus (32%). Only 8 (6%) of enrolled residents had wounds at enrollment. VA LTCF study participants were significantly more likely to have been hospitalized or to have received antibiotics, to have a device, peripheral vascular disease, or skin disease, and to be functionally more independent than were community LTCF study participants (table 1).

**Response to treatment with study drug.** Sixty-four and 63 LTCF residents were randomized to the mupirocin and placebo groups, respectively (table 2). No significant differences were noted between the groups, with the exception of functional status, which was slightly better in the mupirocin group (P = .05) (table 2). Among study participants who received mupirocin, 36 (56%) were at the VA LTCF, and 28 (44%) were at the community-based LTCF. Colonization with MRSA was noted in 27 (44%) of those in the mupirocin group and in 36 (57%) of those in the placebo group (P = .07).

Of the group of 127 residents who were treated, 102 (80%)
completed 14 days of therapy and were evaluated for treatment efficacy (figure 1). Twenty-two study participants were discharged before completing therapy, and 3 refused to complete therapy. Figure 1 shows data on the number of participants who were evaluated at each of the subsequent time points after study entry.

On day 15 of the study (the day after treatment ended), 51 (93%) of 55 study participants who were randomized to receive mupirocin were no longer colonized with *S. aureus*, compared with 7 (15%) of 47 in the placebo group (*P* < .001) (figure 2). Among 8 study participants with wounds, 3 did not complete 14 days of therapy and could not be evaluated; all 4 who had received mupirocin were no longer colonized with *S. aureus*, and 1 who had received placebo remained colonized.

At 30 days after study entry (2 weeks after treatment was stopped), 35 (88%) of the 40 residents who received mupirocin were free of *S. aureus*, compared with 5 (13%) of 38 of those who had received placebo (*P* < .001). Three residents in the mupirocin group and 1 in the placebo group had become recolonized with *S. aureus*. At day 60, 22 (79%) of 28 of the study participants remained decolonized, and, at day 90, 14 (61%) of 23 who had received mupirocin remained free of *S. aureus*. Among residents in the placebo group, decolonization was uncommon, occurring in 7%–18% at the time points at which samples were obtained. *S. aureus* colonization did not differ between the 2 groups at 180 days, but too few residents remained in the study to draw conclusions about this time period. Over the entire duration of the study, the hazard rate of colonization was 4.12 times higher for the placebo group (95% CI, 2.68–6.31; *P* < .0001).

Four residents in the mupirocin group—all of whom were colonized with MRSA—did not respond to decolonization therapy (table 3). However, decolonization rates did not differ statistically between those with MRSA and those with MSSA (*P* = .08). All 4 remained colonized with the strain recovered at enrollment. One resident each had a low-level and a high-level mupirocin-resistant strain at enrollment that persisted, despite receipt of therapy. Another was colonized with a strain that developed high-level mupirocin resistance during the course of treatment, and the fourth remained colonized with a mupirocin-susceptible strain throughout treatment.

Of the 14 study participants who became recolonized with

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Mupirocin MIC, μg/mL (no. of isolates)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before therapy</td>
</tr>
<tr>
<td>1</td>
<td>&lt;0.98 (2)</td>
</tr>
<tr>
<td>2</td>
<td>16–32 (4)</td>
</tr>
<tr>
<td>3</td>
<td>&lt;0.98 (1)</td>
</tr>
<tr>
<td>&gt;500 (1)</td>
<td>&lt;0.98 (1)</td>
</tr>
</tbody>
</table>

* Isolates recovered on days 1–13.

b Isolates recovered on day 15 and thereafter.
in the mupirocin group had cleared compared with placebo. At the end of therapy, 93% of residents
aureus
in decolonizing persistent S. aureus
In this study of LTCF residents, mupirocin was highly effective
DISCUSSION

patient responded to cephalexin.
not performed for the third, although the infection in this
results for 2 patients were positive for MRSA, and culture was
developed 5–38 days after treatment had stopped; all 3 had
developed infection during treatment and after the regimen was stopped. Cellulitis occurred in 3
study participants, conjunctivitis in 2, a perirectal abscess in 1, and a urinary tract infection in 1. Of the 3 residents in the
mupirocin group who developed infection, all had cellulitis that developed 5–38 days after treatment had stopped; all 3 had
cleared staphylococcal nasal carriage and remained free of S. aureus
in the nares at the time infection occurred. Culture results for 2 patients were positive for MRSA, and culture was
not performed for the third, although the infection in this patient responded to cephalexin.

Infections. Ten (10%) of 102 residents who finished the 14-day treatment course developed laboratory-confirmed or probable infection with S. aureus. Three (5%) of 55 residents treated with mupirocin and 7 (15%) of 47 who received placebo developed infection (P = .10). In the placebo group, 3 and 4 residents, respectively, developed infection during treatment and after the regimen was stopped. Cellulitis occurred in 3 study participants, conjunctivitis in 2, a perirectal abscess in 1, and a urinary tract infection in 1. Of the 3 residents in the mupirocin group who developed infection, all had cellulitis that developed 5–38 days after treatment had stopped; all 3 had cleared staphylococcal nasal carriage and remained free of S. aureus
in the nares as defined by PFGE.

In this study of LTCF residents, mupirocin was highly effective in decolonizing persistent S. aureus colonization in the nares, compared with placebo. At the end of therapy, 93% of residents in the mupirocin group had cleared S. aureus from the nares. Previous studies of mupirocin in LTCFs—although they were not
placebo controlled—showed similar clearance rates [15, 16]. Clearance rates of 90% are similar to those noted for other patient populations [12, 13, 28, 29] and health care workers [30].

Studies to assess decolonization strategies in older persons have been infrequent [15, 16, 18, 31], and some regimens have been less effective in such patients [31–33]. In an older population of hospitalized patients, mupirocin was no more effective than was placebo for clearing MRSA carriage [33]. In an uncontrolled study in which oral antibiotics were administered with or without rifampin, persistent or recurrent colonization within 30 days after treatment completion was demonstrated in 56% of LTCF residents [31], and another study in which oral antibiotics and rifampin were administered noted age as a risk factor for failure to clear MRSA [32].

We found that decolonization due to mupirocin persisted for 45 days after treatment had ended (day 60 after study entry) and that, although the duration of decolonization was still significantly different from that associated with placebo, decolonization efficacy had begun to decrease by day 90 after study entry. Few studies have assessed the effect of decolonization regimens on the persistence of clearance for >30 days after treatment was stopped. An earlier uncontrolled study in our facility noted that 56% of residents remained decolonized for 60 days after mupirocin therapy was stopped [15], and a placebo-controlled study of intranasal bacitracin and oral rifampin demonstrated that 44% of patients who were undergoing hemodialysis remained decolonized for 90 days [34].

In this study, recolonization in 12 (86%) of 14 residents involved the original strain. In contrast, health care workers who were treated with mupirocin were as likely to relapse with a new strain as with their pretherapy strain [35]. Relapse of S. aureus carriage in residents of LTCFs is likely due to persistent risk factors that contribute to initial colonization [9, 36, 37]. Relapse of S. aureus carriage in our study was not associated with the development of mupirocin resistance.

One approach to decrease recolonization is intermittent mupirocin treatment. Thrice-weekly, weekly, and twice-monthly regimens have been used to maintain nasal decolonization in patients undergoing dialysis [38, 39], without development of mupirocin resistance. However, use of a weekly maintenance regimen of mupirocin in MRSA-colonized residents of LTCFs was less efficacious and was associated with mupirocin resistance [16]. On the basis of the results of this study, an alternative approach might be pulse therapy with 14 days of mupirocin every 2–3 months to prevent relapse and decrease the likelihood of resistance. A similar approach has been successful in patients with furunculosis (mupirocin was administered for 5 days each month) [40] and has been suggested for use in patients undergoing hemodialysis [41].

Three of 4 residents who did not respond to therapy were found to carry mupirocin-resistant S. aureus at the end of the

Figure 3. Study participants (n = 14) who were recolonized with Staphylococcus aureus at various time points after initial decolonization. Patients either relapsed with the same pretherapy strain (shaded regions) or acquired a new strain (unshaded regions), as defined by PFGE.

S. aureus after initial decolonization, 12 (86%) relapsed with the same strain and 2 acquired a new strain (figure 3). All recolonizing strains remained mupirocin susceptible. The PEG formulation was well tolerated; failure to complete therapy because of side effects occurred in only 1 placebo recipient, who complained of nasal stuffiness.

Infections. Ten (10%) of 102 residents who finished the 14-day treatment course developed laboratory-confirmed or probable infection with S. aureus. Three (5%) of 55 residents treated with mupirocin and 7 (15%) of 47 who received placebo developed infection (P = .10). In the placebo group, 3 and 4 residents, respectively, developed infection during treatment and after the regimen was stopped. Cellulitis occurred in 3 study participants, conjunctivitis in 2, a perirectal abscess in 1, and a urinary tract infection in 1.

Risk factors that contribute to initial colonization [9, 36, 37]. Relapse of S. aureus carriage in our study was not associated with the development of mupirocin resistance.

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Three of 4 residents who did not respond to therapy were found to carry mupirocin-resistant S. aureus at the end of the

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treatment period, only 1 of whom had a strain that developed resistance. All 4 mupirocin failures in this study occurred in MRSA-colonized residents, but the rate of failure was not statistically different from that for MSSA-colonized residents. MRSA strains are no more likely to harbor or acquire mupirocin resistance elements than are MSSA strains [22]. It is likely that patient factors that select for MRSA—and not only for mupirocin resistance—play a role in failure of decolonization.

Mupirocin PEG ointment has been used extensively for decolonization of staphylococcal carriage [15–17, 42–45]. Different formulations were developed because of concern for nasal side effects and absorption of PEG in neonates and in large burns wounds [14]. In our study, the PEG formulation was well tolerated.

It has been questioned whether data on S. aureus colonization obtained from VA LTCFs are applicable to community LTCFs. As a group, the VA LTCF population is younger, predominantly male, and more functionally independent [8, 36]. We found no differences in colonization rates for S. aureus between the 2 facilities, but the proportion of S. aureus isolates that were methicillin resistant was higher in VA LTCF study participants, confirming previous reports [8]. The colonization rates in the community facility were higher than we anticipated. This could reflect increasing MRSA rates in the community [46, 47] or increasing trends toward transferring sicker patients from the hospital to the LTCF [48].

Approximately 20% of the study participants did not complete the 14-day therapy course; this hampered our ability to detect differences in infection rates. The number of residents in each treatment arm was too small to show a significant difference in infection rates, although a trend toward decreased infection rates was seen in the mupirocin group. Some S. aureus carriers may be at greater risk of infection than others [1, 9, 36]. Mupirocin decolonization might prove more efficacious if residents who were most dependent or who had devices in place, diabetes mellitus, or peripheral vascular occlusive disease were treated.

In conclusion, mupirocin was effective in decolonizing S. aureus in persistent carriers enrolled from 2 LTCF populations. Although recolonization occurred, development of resistance was uncommon. There was a trend towards reduction in infections with mupirocin use. Multicenter trials that focus on persistent S. aureus carriers—who are at greatest risk—are needed to assess the effectiveness of mupirocin in reducing infections in LTCFs.

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References

23. Ramsey MA, Bradley SF, Kauffman CA, Morton TM. Identification of a chromosomal location of the mupA gene encoding low level mu