Eradication or Decolonization of Methicillin-Resistant Staphylococcus aureus Carriage: What Are We Doing and Why Are We Doing It?

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(See the article by Simor et al. on pages 178–85)

In the United States and, more recently, in parts of Canada, rates of health care–associated methicillin-resistant Staphylococcus aureus (MRSA) infection have continued to increase despite intensive infection-control efforts; in some series, 30% of isolates are methicillin resistant [1–3]. Some groups have advocated “search and destroy” policies that recommend routine screening for MRSA to identify, isolate, and treat carriers, with the ultimate goal of eradicating the pathogen from health care facilities [4]. The article by Simor et al. [5] in this issue of Clinical Infectious Diseases describes a randomized controlled study of an MRSA eradication strategy in health care facilities from a major metropolitan area in Canada.

Evaluation of the efficacy of infection-control strategies is difficult, particularly during outbreaks. Typically, several uncontrolled interventions are performed at once and analyzed in retrospect [6–8]. This study reflects the unique opportunity to prospectively plan, implement, and evaluate a randomized and controlled infection-control intervention to eradicate MRSA.

All MRSA carriers are not the same; carriage may be transient, intermittent, or persistent for months to years [9, 10]. Persistent carriers are more heavily colonized (frequently at multiple sites), are more likely to transmit to others, and are more likely to become infected than transient carriers [10]. Interpretation of results might be confounded if transient MRSA carriers spontaneously clear their colonization, even in the absence of effective treatment. In this study, use of a standard definition of persistent carriage ensures that most patients will remain persistently colonized unless they are treated with an effective agent [11].

What sites of MRSA colonization should be targeted for surveillance screening and eradication? The anterior nares have been thought to be the most frequent site of MRSA carriage, and effective treatment has been associated with a reduction in skin colonization in healthy health care workers [9, 12]. However, nasal colonization has not been not universally found among MRSA-positive patients with implanted devices, and the rectum may be an important reservoir among those with community-acquired MRSA [13, 14]. Therefore, if the goal of an intervention is true eradication of MRSA carriage, then routine surveillance by culture or molecular methods must involve 1 site to detect all colonized patients. In the study of Simor et al. [5], anterior nares, perianal skin, wounds, and device-insertion sites were cultured before and after therapy.

What treatment modalities should be used in an MRSA eradication strategy? Methods to eradicate MRSA have included the use of oral antibiotics plus rifampin. The use of rifampin ensures excellent penetration into secretions and tissues. The use of combination therapy has been effective in treating MRSA in the nares and at other sites [8, 15–17]. However, the wide-scale use of systemic antibiotics has been associated with the development of drug resistance and the loss of valuable therapeutic agents for subsequent treatment of infection.

As a result of this drug-resistance issue, topical antibacterial agents and germicides have been the preferred intervention for MRSA eradication programs [8]. Mupirocin has no structural similarities with existing systemic antibiotics that might lead to the development of cross-resistance, and in its topical form, it has minimal toxicity [7, 18, 19]. Mupirocin is ap-
proved for the prevention of MRSA outbreaks [7, 8, 18, 19]. The rate of eradication of nasal colonization after initial treatment with mupirocin has been reported to be 95%–100% for patients undergoing hemodialysis or peritoneal dialysis, 88% for patients infected with HIV, 85% for nursing home residents, and 87% for candidates for liver transplantation [7, 20].

Chlorhexidine baths have been used in combination with intranasal mupirocin in uncontrolled trials and during outbreaks [21, 22]. In one study, the mean rate of MRSA eradication from nares with combined therapy was 72% over several years [22]. In the study of Simor et al. [5], a topical germicide and antibiotic plus oral agents and rifampin achieved 92% eradication of MRSA. Knowing the baseline rates of colonization at the various sites would help to justify the use of combination therapy for all patients.

How long should the initial eradication regimen be continued? There is no consensus on the optimal duration of systemic antibiotic treatment to eradicate MRSA carriage; regimens of 7–14 days have been used. For mupirocin treatment of nares, treatment for 5–7 days has been effective. If wounds are treated, a duration of 14 days has been suggested [23]. It would seem that use of the shortest duration of effective treatment would be necessary to minimize the likelihood of drug resistance.

Eradication of MRSA carriage is not guaranteed or permanent. Thus, “decolonization” rather than “eradication” may be a more appropriate term. The effect of any eradication or decolonization strategy seems to last 90 days at most, although more prolonged follow-up has been infrequent. Most studies with prolonged follow-up have been of methicillin-susceptible S. aureus carriers. Recolonization rates at 12 months after treatment have approached 50% and 75% for healthy health care workers and patients undergoing peritoneal dialysis, respectively; the recolonization rate at 4 months in patients undergoing hemodialysis is 56%; and the recolonization rate is 71% at 2.5 months in HIV-infected patients [24–27].

In a blinded, randomized, controlled trial of nursing home residents, 61% remained decolonized for up to 90 days, with a trend of up to 6 months following mupirocin treatment predominantly in nares [20]. These results were similar to those seen for Simor et al. [5], who achieved decolonization for up to 8 months. In both trials, chronic debility and the presence of medical device wounds at baseline did not appear to affect response to initial decolonization therapy. We do not know in what ways baseline characteristics, discharge status, or duration of stay changed by 90 days that might have predisposed the patient to recolonization following treatment.

MRSA decolonization has not necessarily led to a reduction in infection in all patient populations. Most studies of decolonization have not been randomized controlled trials; in many instances, the pretreatment carrier status of the populations studied was not determined [6, 24, 28]. Risk of subsequent MRSA infection may be dependent on the virulence of the strain, the clinical care setting, and the severity of the patient’s illness. MRSA infection rates vary from 51% in intensive care units to 39% in non-intensive care unit inpatient wards and to 24% in outpatient settings [7]. Observational studies of intranasal mupirocin and chlorhexidine baths in an intensive care unit have shown a significant reduction in incidence of nosocomial MRSA infection [22]. The study by Simor et al. [5] was not specifically designed to assess the effect of eradication of colonization on infection. We do not know what proportion of patients had intensive care unit, hospital, or chronic care stays that might have influenced risk of MRSA infection. To assess the impact of eradication of MRSA colonization on infection, interventions should be studied in settings in which patients are at great risk of MRSA infection, such as intensive care units.

There may be a role for decolonization strategies that benefit the individual as well as the institution. MRSA colonization has been associated with reinfection, debility, or death [8, 9]. One-third of hospitalized patients who acquire MRSA infection will be readmitted to the hospital within 18 months; 80% will have MRSA infection at a new site, and 56% of those infections will be severe [9]. In patients with bacteremia or endocarditis, 10% became reinfected over 6–36 months [8]. In the patient with known infection, a decolonization strategy might prevent reinfection.

Might routine MRSA decolonization be detrimental? Increased mupirocin use has been associated with increased drug resistance and failure to clear the organism. In this study, drug resistance was commonly noted in 24% of isolates, and 19% had high-level drug resistance, suggesting that mupirocin use was already common in the community. After treatment, an additional 5% of patients had a strain exhibiting high-level drug resistance, and the presence of drug resistance was associated with microbiological failure. The gene for high-level mupirocin resistance, mupA, has been found on a plasmid in USA300 MRSA clones, suggesting that the future usefulness of this drug might limited [29].

Increased resistance of MRSA to systemic antibiotics following decolonization regimen has also been an issue in this study and others. Resistance to other germicides in MRSA has been reported following wide-scale use; whether resistance to chlorhexidine will become an issue is not known [30]. In addition, the frequency of adverse effects as a result of systemic antibiotic use is not trivial. In this study, 25% of the patients developed gastrointestinal adverse reactions and 5% discontinued treatment. The potential for drug interactions is likely, especially with rifampin-based strategies. If routine use of eradication strategies is to be applied to patients in general, then attention to adverse effects and drug interactions will be critical.
Finally, could eradication of the patient’s initial MRSA colonizing strain allow for acquisition of a more virulent strain, such as a community-acquired MRSA strain? Fortunately, this study and others have shown that most patients undergo relapse with their baseline strain. However, we must be vigilant that our attempts to eradicate old strains do not facilitate the acquisition of strains that contain virulence determinants.

I have raised more questions than I have answered. As Simor et al. [5] point out, it remains to be seen whether combination therapy is superior to therapy with mupirocin alone for decolonization of MRSA. Will the same regimen be necessary for all patients regardless of the number of sites colonized? If eradication of MRSA carriage is the goal, will long-term surveillance and intermittent therapy be required to prevent recurrences? Should decolonization of patients be limited just to health care facilities or extended to patients at the highest risk of infection who reside in the community? The negative impact of any intervention on antibiotic resistance, drug interactions, side effects, recolonization, and cost should carefully be assessed. Ultimately, the success or failure of this approach will be judged by our ability to prevent MRSA infection. It will be essential to study populations that have rates of MRSA infection sufficiently high to prove that eradication or decolonization actually works.

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References


