

Chief Complaint Review

Recurrent MRSA Skin Infections in Atopic Dermatitis

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a frequent cause of recurrent skin and soft tissue infections. For patients with atopic dermatitis, recurrent skin infections with MRSA often lead to eczema exacerbation. There currently is no standard practice in the prevention of recurrent MRSA soft tissue infections in the general and the atopic dermatitis populations. The current article reviews recent data on *S aureus* decolonization treatments for the prevention of recurrent MRSA soft tissue infections in the community setting. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;■:■-■)

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Atopic dermatitis (AD) is a common chronic skin disease that is associated with elevated IgE, food and/or respiratory allergies, and recurrent skin infections. More than 90% of patients with AD are colonized with *Staphylococcus aureus* compared with only 10% in healthy individuals (reviewed in Ong and Leung¹). *S aureus* infection as a trigger of AD has been a well-established clinical observation.² AD severity has consistently been shown to correlate with *S aureus* colonization.¹ Increased *S aureus* colonization and/or infection in AD is due to a combination of factors that include skin barrier defects, immune dysregulation, and *S aureus* virulence. When compared with psoriasis, which also has skin barrier defects, AD lesions have significantly lower antimicrobial peptide expression,³ and this lower antimicrobial peptide expression likely contributes to the increased *S aureus* colonization and/or infection in AD. *S aureus* may trigger AD via various mechanisms. Staphylococcal superantigens are exotoxins that bind to the common variable β chains of T-cell receptors, which result in a polyclonal activation of T cells.¹ These superantigens also induce host production of superantigen-specific IgE, which triggers histamine release from basophils.¹ Analysis of more recent data showed that methicillin-resistant *S aureus* (MRSA) produces more superantigens than methicillin-sensitive *S aureus*.⁴ *S aureus* strains isolated from patients with steroid-resistant AD also produced significantly more superantigen types compared

with those isolated from a general population of AD patients with AD.⁴ Other potential mechanisms by which *S aureus* triggers AD include the production of α - and δ -toxins, which cause keratinocyte toxicity and mast cell activation, respectively.^{1,5}

Community-associated (CA) MRSA skin and soft tissue infections (SSTI) have become a common reason for visits to outpatient clinics and emergency departments in the United States.⁶ These infections have mainly been associated with the emergence of MRSA clone USA300. For patients with AD, eczema exacerbation caused by MRSA SSTI has also become a significant clinical problem in recent years.⁷ The percentage of MRSA in patients with *S aureus*-colonized AD has been reported to range from 11% to 34%.⁸⁻¹¹ Suh et al⁹ reported that 13% of all patients with AD are colonized with MRSA, this is significantly higher than the 1% to 3% of MRSA colonization reported in the general population.⁹ Lo et al¹⁰ also found that patients with AD and with MRSA colonization are more likely to develop SSTI than those with methicillin-sensitive *S aureus* colonization. AD constitutes a risk factor for colonization, recurrent infection, and transmission of MRSA.¹²⁻¹⁴ Infection with MRSA leads to a vicious cycle of AD flare and infection (Figure 1).¹⁵ It also has been observed that patients with AD and with MRSA infections often have an inadequate response to topical anti-inflammatory agents, particularly corticosteroids.¹⁵ The reason for this inadequate response is not fully understood but may be related to corticosteroid resistance induced by staphylococcal superantigen.¹⁶ Continual use of corticosteroids in such a situation may lead to unwanted adverse effects, including skin atrophy and adrenal insufficiency.

The increasing prevalence of CA-MRSA infection and a potential risk of CA-MRSA infection conferred by household contacts have generated considerable interest in strategies in the prevention of CA-MRSA infections. Decolonization remains the primary strategy in the prevention of hospital-associated MRSA infections, which is based on the tenet that infection is preceded by colonization.¹⁷ However, the mechanisms of transmission in CA-MRSA are not completely understood. Nasal colonization may not play as important a role in the pathogenesis of CA-MRSA as skin-to-skin and skin-to-fomite contacts.¹⁷ In addition, analysis of increasing data indicates that the infecting MRSA strains may not be the same as the colonizing strains in the community setting. We previously described 2 illustrative AD cases in which decolonization treatments were successful in preventing recurrent MRSA infection and eczema flare in a patient in one case but not in the other.¹⁸ There currently is a paucity of data on the role of decolonization treatment in the prevention of CA-MRSA infection in both general and AD populations. The current review aims to summarize recent studies that examine the efficacy of MRSA decolonization in the community setting.

MRSA DECOLONIZATION AND STRAIN DISCORDANCE

Miller et al¹⁹ studied the role of decolonization in the prevention of recurrent infections of subjects who have had 2 or

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Abbreviations used

AD- Atopic dermatitis

CA- Community associated

MRSA- Methicillin-resistant *Staphylococcus aureus*

SSTI- Skin and soft tissue infection

more CA-MRSA infections in the past 6 months. Their decolonization regimen consisted of a 10-day course of nasal mupirocin twice daily, topical 3% hexachlorophene body wash daily, and an oral anti-MRSA antibiotic based on investigator choice and antibiotic susceptibility of a prior MRSA isolate (Table I). Their results showed that the mean skin infection rate was significantly lower in the subjects 6 months after decolonization treatment (0.03 infections per month) versus 6 months before the treatment (0.84 infections per month). There was no association between those with recurrent infections after decolonization treatment and MRSA risk factors, including diabetes, hypertension, cancer, recent surgery and/or hospitalization, health care workers, homelessness, or drug use.

Fritz et al²⁰ compared a 5-day decolonization strategy in the index subject versus index subject plus all household members. The decolonization regimen consisted of twice daily application of 0.2% mupirocin ointment to the anterior nares with a sterile cotton applicator and daily use of Hibiclens (4% chlorhexidine gluconate) (Mölnlycke Health Care, Norcross, Ga) in the bath or shower (Table I). The majority of SSTIs (79%) was caused by MRSA. At the 3-, 6-, and 12-month follow-up, self-reported SSTIs were significantly lower in the household-treated group versus the index group (28% vs 47%, 38% vs 61%, and 52% vs 72%, respectively); these results were confirmed by physician-documented SSTI at the 3-, 6-, and 12-month follow-ups (15% vs 34%, 22% vs 43%, and 36% vs 55%, respectively). In addition, household contacts in the household-treated group were less likely to have recurrent SSTI at 1, 3, 6, and 12 months. There was no significant difference in the *S aureus* eradication rate between the 2 treatment groups at these time points.

The efficacy of household decolonization treatment in preventing recurrent SSTI despite no difference in the *S aureus* eradication rate was surprising, given that *S aureus* colonization is a predictor of SSTI.²⁰ A recent large study from Los Angeles and Chicago assessed the risk factors and *S aureus* strain concordance of MRSA SSTI in a community setting.²¹ A total of 350 households each with an index patient who had *S aureus* SSTI and more than 800 household members were enrolled. To assess *S aureus* colonization, culture swabs were taken from the nares, oropharynx, and inguinal folds. *S aureus* strains were assessed by genetic typing. Among the index patients with MRSA SSTI and *S aureus* colonization, only approximately 40% carried a MRSA strain that was concordant with the infecting strain. The majority (60%) was colonized by an *S aureus* strain that was discordant with the infecting MRSA strain. Among the households with an index MRSA infection, only 17% of household contacts carried a concordant MRSA strain. The majority (83%) was colonized with a different MRSA strain. USA300 represented more than half of all infecting strains. Among the index patients, the USA300 MRSA strain was found to be an independent predictor of colonization with the infecting strain. However, only 20% was concordant with the colonizing strain in the household contacts, whereas the majority (80%) was not. The frequent discordance

between the infecting and colonizing MRSA strains seen in this study suggests alternative mechanisms of pathogenesis of CA-MRSA infection that may not involve colonization and transmission from the household contacts. Analysis of these data highlights potential limitations of household decolonization treatment in the prevention of recurrent infection in the majority of patients with CA-MRSA SSTI.

In a follow-up molecular typing study by Rodriguez et al²² based on the culture samples that were obtained from the aforementioned study,²⁰ the investigators found that 67% of index subjects with *S aureus* SSTI had at least one colonizing *S aureus* strain (from anterior nares, axillae, or inguinal folds) that matched the infecting strain.²² The infecting strain from 55% of these index cases was concordant with a colonizing strain from at least one household contact. When compared with index subjects with discordant colonizing and infecting strains, the index subjects with concordant colonizing and infecting strains were more likely to be African American and to have eczema.

A major difference between the studies of Fritz and colleagues^{20,22} and that of Miller et al²¹ was that index patients in the former studies were mostly children, whereas those in the latter study were mostly adults. It is likely that children are in closer contact with other family members, which allows a greater opportunity for transmission.²² However, the relative independence of adults may lead to behaviors and exposures that result in the acquisition of *S aureus* infection in different manners.⁶ Another mode of MRSA transmission may take place via shared objects, such as soap, towels, toilet handles, doorknobs, or kitchen sinks, or via household pets.^{14,23,24}

PRACTICAL CONSIDERATION IN MRSA DECOLONIZATION

Further studies are needed to confirm the role of household decolonization to prevent MRSA SSTI. Even among children, there still is a significant portion of patients with SSTI with no known source of MRSA in their household contacts, which suggests other modes of MRSA acquisition. Decolonization studies that involve patients with well-defined AD as the index subjects also are lacking. The downside of decolonization also should be considered, including the possibility that decolonization of asymptomatic household contacts may lead to more resistant strains of *S aureus*.²¹ Obtaining cultures from different body sites, including the nares, oropharynx, and inguinal folds, of household contacts may be necessary to confirm MRSA colonization. However, it may not be practical to obtain cultures in asymptomatic persons in routine clinical situations. Successful implementation of household decolonization also may depend on providers' willingness to treat other household members, who may not be their patients, or to communicate with their primary physicians about testing and treatment. The latter process can be time consuming. In addition, anti-MRSA antibiotics, for example, linezolid, can have significant adverse effects.¹⁸ Compliance with decolonization treatment in asymptomatic family members may also be a challenge. Optimal and safe use of chlorhexidine is complicated.⁶ The product works best when it is left on for many hours. Users will need to take care not to get the product in open wounds or mucous membranes. Chlorhexidine also will stain clothes or linens if they are rinsed with chlorinated detergents (eg, bleach).

Modifiable risk factors that increase MRSA colonization and infection should be evaluated on a case-by-case basis. These risk



FIGURE 1. AD flare associated with MRSA infection.

TABLE I. Recent MRSA decolonization studies in the community setting and suggested treatment regimen for patients with AD and with MRSA infection and/or colonization

Index adult patient MRSA decolonization treatment by Miller et al ¹⁹
1. Nasal mupirocin twice daily for 10 days.
2. Topical 3% hexachlorophene body wash once daily for 10 days.
3. An oral anti-MRSA antibiotic based on antibiotic susceptibility for 10 days.
Index patient and household decolonization treatment by Fritz et al ²⁰
1. Nasal mupirocin twice daily for 5 days.
2. Hibiclens (4% chlorhexidine gluconate) bath or shower once daily for 5 days; participants (>6 mo of age and not pregnant) were instructed to apply Hibiclens with hands or a clean washcloth and to wash all body parts, except for the face, followed by a thorough rinse with water.
3. Other hygiene practices include the following: not sharing personal hygiene items (eg, razors, brushes, and towels), to use liquid pump or pour soaps and lotion (rather than bar soaps and jars of lotion), and to launder bed linens in hot water at least once weekly, and towels and washcloths after each use.
Suggested treatment regimen for patients with AD and with MRSA infection and/or colonization
1. Nasal mupirocin twice daily for 10 days.
2. Diluted bleach bath (one-fourth cup of 6% sodium hypochlorite per tub of water) 15 minutes daily for 5 days, and then twice weekly; while on bleach bath or routine bath or shower daily, the patient will still apply a topical corticosteroid or calcineurin inhibitor on eczema areas and an emollient on unaffected areas immediately after bath or shower.
3. For patients with signs of skin infections, consider an oral anti-MRSA antibiotic for 10 days based on antibiotic susceptibility.
4. Household hygiene practices according to Fritz et al as outlined above.

factors include household crowding and sharing towels, washcloths, soap, or topical medications.¹⁴ Increased MRSA colonization also has been associated with household contacts who assist with bathing case patients with a history of MRSA infection.¹⁴ This problem directly impacts AD because most patients are young children who require the assistance of their parent or caretaker with bathing. Further studies are needed to address whether intervention may prevent MRSA transmission in assisted bathing practices. Topical corticosteroid ointments for patients with AD have been known to be contaminated with *S aureus*.²⁵ Therefore, care must be taken to avoid *S aureus* contamination of these medications and moisturizers. Host factors in patients with AD, including skin barrier disruption and increased cutaneous inflammation, play a major role in the acquisition of *S aureus*.¹¹ Therefore, it is important to emphasize daily skin care to improve skin barrier function and the appropriate use of topical anti-inflammatory medications, including topical corticosteroids or calcineurin inhibitors.

When patients with AD present with known or suspected MRSA SSTI, the methods of decolonization by Miller et al¹⁹ and Fritz et al²⁰ should be considered (Table I). A culture with susceptibility should be taken from the infected wound. The choice of anti-MRSA antibiotic is best guided by the most recent culture susceptibility from the patient. Empirical use of anti-MRSA antibiotics may vary in different geographic regions and institutions. Some institutions report an increasing trend of resistance to certain anti-MRSA antibiotics, whereas others reported a relatively stable trend with no change in resistance.²⁶ The variation is likely dependent on institutional preference for empirical antibiotic use in MRSA SSTI. We observed a relatively stable trend of 20% and 1% MRSA resistance to clindamycin and trimethoprim-sulfamethoxazole, respectively, in our institution. Therefore, these 2

antibiotics remain our empirical treatment of choice for pediatric patients with suspected MRSA SSTI. Some patients with AD may not tolerate the irritating effects of chlorhexidine.²⁷ We mostly have used a diluted bleach bath for *S aureus* decolonization in patients with AD based on previous studies (Table 1).^{28,29} Although antimicrobial and decolonization treatments are being implemented, daily skin care and topical anti-inflammatory treatment should be emphasized.

In summary, although there is some success in decolonization treatments of index cases and household contacts for prevention of CA-MRSA-associated SSTI, particularly in pediatric subjects, further studies are needed to address other potential sources of infecting strains. These sources may include household pets or shared objects.^{24,30} In addition, variation in AD phenotypes, including severity and atopic status, may be important confounding factors that need to be studied further.

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