

Duration of Colonization With Methicillin-Resistant *Staphylococcus aureus*: A Question With Many Answers

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(See the Major Article by Cluzet et al on pages 1489–96.)

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Emergency room visits and hospital admissions for skin and soft tissue infections (SSTIs) have been increasing [1, 2], with a high prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) cultured from the site of infection [3]. By recent estimates, approximately 7% of patients in US hospitals are colonized with MRSA [4]. This includes an increase in colonization with community-acquired strains commonly associated with SSTIs [5, 6].

According to the Society for Healthcare Epidemiology of America, the duration of colonization remains an unresolved issue [7]. Data have shown that individuals remain at increased risk of MRSA infection and death until they are no longer colonized [8]. However, there is a wide range

of estimates for the median time to clearance, ranging from 7 to 9 months [9–11] to well beyond a year [12–14]. Thus, many US hospitals recommend waiting 6 months or more prior to screening for clearance of MRSA colonization [15].

In this issue of *Clinical Infectious Diseases*, the study by Cluzet et al adds to the debate on the duration of MRSA colonization, looking at clearance following diagnosis of an SSTI with a positive MRSA culture [16]. In this longitudinal sampling study, MRSA surveillance cultures were collected from nares, axilla, and groin every 2 weeks for up to 6 months on both index cases and their household members. The first finding of interest was a median duration of MRSA colonization of only 21 days, far less than what has been noted in prior studies [9–14]. I will point out, however, that 92% of the index cases received a systemic anti-MRSA antibiotic as treatment for their SSTI, and around 20% were prescribed topical nasal mupirocin and/or chlorhexidine/bleach baths in the 2 weeks following SSTI diagnosis. The second finding of interest was that SSTI treatment with clindamycin was associated with earlier clearance of MRSA colonization. To my knowledge, this is the first time that this has been suggested in the literature.

In prior studies, longer duration of MRSA colonization has been linked with

older age, need for assistance with activities of daily living, indwelling devices, active skin lesions and wounds, long length of hospital stay and/or residence in a chronic-care facility, and household contacts with MRSA colonization [9–11, 14]. The analysis presented by Cluzet et al continues to show an association between longer duration of MRSA colonization and both older age and number of household members colonized with MRSA. It is important to note, however, that this was a young cohort, with 75% of index cases aged <45 years and 75% of household members aged <37 years. To some degree, this might help to explain the shorter duration of MRSA colonization compared with that found in prior studies.

Differences have been found in MRSA strains isolated from pediatric vs adult patients, with higher percentages of community-associated MRSA (USA300 strains) found in pediatric populations [17]. These USA300 strains of MRSA may more commonly colonize the rectum than the nares [18], with a strong association between rectal colonization and SSTI in pediatric patients [19]. In the study by Cluzet et al, MRSA surveillance cultures were not obtained from the rectum.

It is also useful to relate the finding by Robicsek et al who previously showed that there is a rapid decline (approximately 50%) in MRSA colonization in the first

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month following a positive culture, with a slow decrease in prevalence in those who remain colonized after the first month [20]. In fact, Cluzet et al found a similar trend, reporting a median time to MRSA clearance of 140 days (rather than 21 days) for those participants who remained MRSA colonized at the time of their first study visit (2 weeks after enrollment).

One other possibility that might explain the shorter duration of MRSA colonization in the Cluzet et al study is the issue of inoculum. Prior work has suggested that higher initial inoculums of bacteria may be an important determinant of persistent colonization with MRSA [14]. In the Cluzet et al study, only 6% of the study participants required hospitalization for their SSTI. This suggests a healthier baseline cohort with a possibly lower initial inoculum of bacteria.

Finally, it is important to point out that Cluzet et al censored duration of colonization based on documentation of clearance defined as 2 consecutive sampling periods with no positive MRSA surveillance cultures. This is important as prior studies have suggested that 1 out of 10 MRSA-colonized patients may have 2 or more consecutive negative screenings with a later positive result, at times 6–12 months later [10, 21]. While one study found identical MRSA colonizing strains separated in time by negative results [14], this is an area where more investigation is needed in order to understand whether recurrence of colonization represents recurrence of an old strain or colonization with a new strain.

In terms of the finding that SSTI treatment with clindamycin was associated with earlier clearance, I agree with the authors that the scientific explanation for this finding remains unclear and deserves further study. Prior work has more commonly linked the receipt of antibiotics to MRSA acquisition and longer (rather than shorter) MRSA colonization [5, 10, 22], although one group questioned the link between antibiotics and MRSA acquisition due to confounding by indication

[23]. As referenced by Cluzet et al, a prior published study showed that antibiotics to treat a clinical infection were associated with a shorter duration of MRSA colonization [24]. I agree with the authors, though, that it is not clear why only clindamycin shortened duration in the present study and not trimethoprim-sulfamethoxazole, which was prescribed a near equal number of times for treatment. It is worth noting that clindamycin was more commonly prescribed to index cases aged <18 years; however, Cluzet et al found no interaction between age and clindamycin treatment in their model that predicted time to clearance of MRSA colonization.

As one final point, I would like to comment on the observation that receipt of mupirocin and/or chlorhexidine baths was not associated with a shorter duration of MRSA colonization in the study being discussed. Prior studies have shown eradication therapy to be effective in decreasing MRSA colonization and subsequent infection, but these studies paid close attention to adherence [21, 25, 26]. Cluzet et al appropriately mention a number of limitations that might have impacted their assessment of the association between the use of mupirocin and/or chlorhexidine/bleach baths and the time to clearance of MRSA colonization. They specifically mention that compliance with these 2 agents was not determined and that decolonization regimens may have been given more commonly to patients with a perceived higher risk of recurrence.

Overall, Cluzet et al have presented stimulating results from a well-designed study that took great efforts to longitudinally follow the MRSA colonization status of a cohort of patients and their household members following diagnosis of community-acquired MRSA SSTI. Both the shorter duration of time to clearance of MRSA colonization and the putative association between SSTI treatment with clindamycin and a shorter duration of MRSA colonization deserve further investigation.

Note

Potential conflict of interest. Author certifies no potential conflicts.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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