Unraveling the Dynamics of Community-Associated Methicillin-Resistant Staphylococcus aureus

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(See the Major Article by Popovich et al on pages 1067–74.)

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Since the first description of the community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) strain USA300 [1] in the 1990s, this pathogen has emerged worldwide [2]. Within a decade, USA300 has become the most prevalent cause of community-acquired S. aureus infections in many settings in the United States [3]. Originally causing infections mainly in individuals without recent healthcare exposure, USA300 is increasingly causing hospital-acquired infections. There is, therefore, an urgent need for infection control measures. Although person-to-person transmission in the community must be the driving force of this epidemic [4], transmission dynamics and risk factors for colonization are still not well understood [5]. The study of Popovich et al in this issue of Clinical Infectious Diseases [6] is a next step in elucidating the dynamics of USA300. In their study they demonstrate that, compared to individuals not infected with human immunodeficiency virus (HIV), patients with HIV are more likely to be colonized with USA300 at hospital admission and that they are carrying USA300 at multiple body sites, such as the nares, throat, axillae, inguinal regions, and perirectal area, and in wounds, if present. Importantly, 38.5% of the USA300 carriers would have remained undetected if only nasal cultures had been obtained.

This study emphasizes 2 important aspects in the transmission dynamics of USA300. First, there are patient groups with a higher risk of colonization, but whether this results from more activities with increased transmission risk, higher bacterial load of carriers, and/or a longer duration of carriage is still unknown. Second, there is huge variation in colonization patterns between carriers, but it remains unknown if and how colonization at different sites is related, and whether the duration differs between sites.

These aspects are important for our understanding of the transmission dynamics and for the design of effective infection prevention strategies. For many pathogens (eg, for hospital-associated MRSA), mathematical models have been used to provide both theoretical and quantitative estimates for intervention strategies [7–9]. If the most important transmission routes are known, such models are cheap and fast alternatives to large-scale intervention studies for comparing the relative effects of different interventions. The few available models for USA300 [10–13] are restricted to subpopulations, either incarcerated persons or hospitalized patients, and assume that all individuals in the population are equally susceptible to acquire USA300. More complex models, integrating spread in the community and within healthcare and other relevant settings, are not available, reflecting our lack of knowledge of the transmission dynamics. There are at least 5 important unknowns in the USA300 transmission dynamics: (1) the duration of carriage with USA300 at different body sites; (2) the interaction between USA300 and other S. aureus genotypes (both MRSA and methicillin-susceptible S. aureus); (3) the modes of spread of USA300, that is, the relative importance of sexual contacts, use of shared equipment, or transmission through temporarily contaminated hands of healthcare workers; (4) heterogeneity
between different groups of individuals; and (5) interaction between these different groups.

The duration of infectiousness is unknown. Two studies in young healthy persons revealed that 4% of new military recruits carried CA-MRSA, including USA300, and 33%–35% were still colonized after 8–10 weeks [14, 15]. Others have reported infections that developed immediately after acquisition (ie, bypassing the colonization state) [16, 17]. However, a mean duration of colonization of several weeks would require high transmission rates to prevent USA300 from going extinct. If that is not the case, the USA300 epidemic could still be explained if the average duration of colonization is much longer and has been underestimated in studies because of misclassification (ie, too-low test sensitivity or screening restricted to the nares), or if there is substantial heterogeneity in transmission capacity of USA300 in subgroups (ie, there are certain core groups that drive the epidemic). Transmission also occurs frequently within sporting teams, among men having sex with men [18], in daycare centers, and in jails [13, 19], which implies that mathematical models for USA300 should incorporate nonhomogeneous mixing patterns.

Only 80% of the human population seems susceptible to colonization with S. aureus, and only half of them are persistently carrying S. aureus in the nares [20]. Whether this also applies to USA300 is currently unknown. Another aspect that is not well understood is immunity against USA300, or any other S. aureus genotype. Antibodies against S. aureus and immunological memory seem insufficient to prevent reinfection. Yet, S. aureus carriers had lower mortality from subsequent bacteremia caused by other S. aureus genotypes than noncarriers, suggesting immune modulation of the inflammatory response in carriers [21]. Yet, to the best of our knowledge, no evidence exists that immunity affects carriage with S. aureus.

There may also be interaction between USA300 and other S. aureus strains, for example, due to colonization resistance. If colonization with USA300 would be mutually exclusive with other S. aureus genotypes, the total population at risk would be markedly lower, and deliberate colonization with S. aureus could be an effective preventive measure for spread of USA300. However, data suggest otherwise. Patients with USA300 skin and soft-tissue infection are frequently colonized in other sites than the nares [6, 22, 23], and military recruits with and without S. aureus colonization had similar acquisition rates of CA-MRSA [15]. Finally, parameters may change over time, such as antibiotic selective pressure or susceptibility of populations for S. aureus colonization (eg, due to pneumococcal vaccination).

Some countries have maintained extremely low nosocomial infection rates of MRSA by nationwide use of stringent infection-control measures. Whether such measures will be effective in countries with frequent transmission of USA300 in the community is unknown. In theory, rapid identification of carriers followed by contact precautions for carriers might be effective [7]. Extramural spread of USA300, however, may rapidly exhaust isolation capacity and nosocomial spread of USA300 will further compromise effective control strategies [24–26]. In fact, a scenario in which USA300 outcompetes other MRSA genotypes in hospital settings is far from excluded [12], especially when USA300 would acquire additional resistance traits. This could reprise the mid–20th century penicillin-resistant staphylococcal pandemic [27]. However, as the natural history of USA300 colonization and disease (eg, duration of carriage, immunity and interference with other genotypes, and the relevant network structures within the population) have not been adequately characterized, proper forecasts of the USA300 epidemiology are difficult and we strongly advocate more well-designed studies to determine these critical unknowns.

References


Notes

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