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Invited Commentary

CA-MRSA triangulation: Virulent strains, susceptible hosts, and contaminated environments

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Thanks to the innate genomic plasticity of microbial pathogens, the introduction of new risk factors, the availability of susceptible hosts, and discovery of novel pathogens, new or reemerging infectious diseases are recognized every few years. The last 3 decades have witnessed several such examples, from relatively uncommon granulocytic ehrlichiosis to Lyme disease to pandemic acquired immunodeficiency disease to the reemergence of tuberculosis worldwide. Some infectious diseases grow into epidemic or pandemic proportions, while others are largely restricted to a geographical region or become cyclical.

Methyicillin-resistant *Staphylococcus aureus* (MRSA) has been a known problem in hospitals and long-term care facilities for quite some time and has escalated during the last decade. MRSA now represents nearly 60% of all the *S. aureus* infections in an intensive care unit.[1] Patients with MRSA infections have longer hospital stays, increasing the financial burden on patients, hospitals, and health care insurance carriers. Over the last 10 years, highly adaptive and often virulent clones of MRSA have moved into communities, causing primarily mild to severe skin and soft tissue infections. These community-associated MRSA (CA-MRSA) are genetically different from hospital-associated MRSA (HA-MRSA) and cause disease in people in the community who have a different set of risk factors than those seen in cases of HA-MRSA infections. Infections due to CA-MRSA have affected large numbers of susceptible individuals, and increasing reports in the scientific literature suggest that it has reached epidemic proportions in many parts of the world. Affected populations are no longer restricted to certain ethnic groups, as was initially reported, but rather have extended to diverse populations, including homeless persons, professional athletes, jail inmates, military recruits, and individuals in the general population. The commonly recognized risk factors associated with CA-MRSA infections are living in a crowded and/or contaminated environment and probably practicing poor personal hygiene. Recently, tattooing and obesity have also been considered risk factors.[2-4] Virulence of CA-MRSA strains[5] is due to its ability to produce a plethora of toxins, especially pore-forming Panton-Valentine leukocidin (PVL), a cytotoxin encoded by *lukSF-PV*, which moves around conveniently in *S. aureus* through phage transduction. The PVL toxin is virtually ubiquitous in CA-MRSA strains. A succinct review on the clinical manifestations and management of CA-MRSA can be found in the January 2006 issue of the *Wisconsin Medical Journal*.[6] An accompanying editorial recommends the sentinel surveillance of CA-MRSA cases in Wisconsin.[7]

In this issue of the *Wisconsin Medical Journal*, Dr Proctor presents an array of interesting cases of CA-MRSA in individuals who were believed to be in otherwise good health. Implicit in his observations are the multifaceted traits of CA-MRSA that differ from commensal *S. aureus*. First, CA-MRSA strains seem to survive on a variety of fomites. Indeed, *S. aureus* is known to withstand prolonged desiccation and can survive on environmental surfaces of stethoscopes, door knobs, sinks, etc. for extended periods of time. Second, it is able to cause infection from presumably smaller doses of unsuspected inocula present on fomites. Third, some strains of CA-MRSA appear to be capable of penetrating the intact skin surface and causing disease in the deeper layers of tissue. The latter should be a matter of concern since any kind of skin injury or dermatitis will increase the

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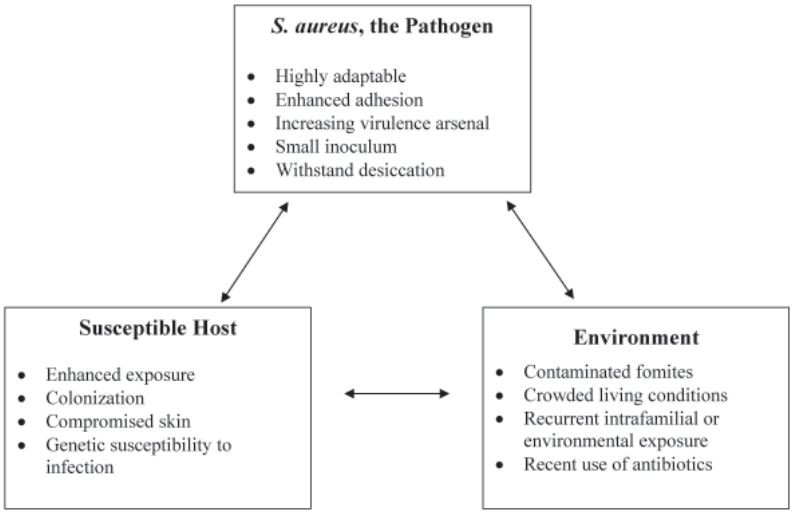

Figure 1. Possible combination of factors at the interface of pathogen, host, and environment that promote infections due to CA-MRSA.

risk of serious infection. These factors present a triangulation consisting of virulent strains, contaminated environments, and susceptible hosts (Figure 1). Unfortunately, it is not uncommon to find these factors present in many situations. What is also worrisome is that 1 of the cases in Dr Proctor's practice suggested the scope of intrafamilial transmission of CA-MRSA from seemingly normal family activities, such as sharing furniture, toilet seats, etc. Recent limited reports suggest that household pets and farm animals may also carry MRSA and have been implicated in transmission to their owners.[8]

The case reports presented by Dr Proctor are not unique to Wisconsin but highlight the problem in general. Indeed, MRSA was identified as the most common identifiable cause of skin and soft tissue infections among patients coming to the emergency departments in 11 US cities.[9] Ninety-nine percent of the MRSA strains belonged to the newer CA-MRSA clone USA300 (a nomenclature used by the Centers for Disease Control and Prevention) and 98% percent of them harbored PVL toxin genes. A rather concerning observation from that study was that a significant number of the 31% of methicillin-sensitive *S. aureus* also harbored PVL toxin genes and belonged to the USA300 clonal group. In other words, these virulent community-associated methicillin-sensitive *S. aureus* clones are 'waiting' to acquire genetic traits of methicillin resistance to become CA-MRSA. Diseases such as necrotizing fasciitis,[10] purpura fulminans,[11] and Waterhouse-Friderichsen syndrome,[12] once not commonly associated with *S. aureus*, have been reported to be due to CA-MRSA in the last few years. These reports suggest that *S. aureus* continues to be a versatile, highly evolving, and adaptable pathogen. It is likely that the enhanced pathogenicity of CA-MRSA is not due to PVL, but to a combination of several other virulence factors.[5]

S. aureus is ubiquitous in the human environment. Based on the analysis of 2001-2002 National Health and Nutrition Examination Survey data, Graham et al recently reported that the prevalence of colonization with *S. aureus* and MRSA are 31.6% and 0.84% respectively. [13]

With its ability to acquire antibiotic resistance and virulence genes by horizontal gene transfer from other staphylococci, *S. aureus* continues to evolve and adapt to possibly cause additional new diseases. Fortunately, most CA-MRSA strains are still susceptible to multiple classes of antibiotics and hence treatable with appropriate antibiotic administration with or without minor surgical intervention.[6]

Current understanding suggests that enhanced personal and community hygiene (e.g., in a household or correctional facility) could reduce its rate of spread and prevalence in the community-settings. Examples of community hygiene include covering skin wounds to avoid spread of the pathogen, avoiding sharing personal items, such as towel, razors, etc., or placing them on contaminated surfaces, such as unclean exercise equipment at health clubs, gymnasiums, and locker rooms.

Hopefully, in due time, we will learn more about the role of host susceptible genes that may predispose individuals to CA-MRSA infections. Meanwhile, keen awareness and good hygiene practices may keep it in manageable proportions.

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