Community-acquired methicillin-resistant *Staphylococcus aureus*: Getting over it

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There are three sure things in life: death, taxes and antimicrobial resistance appearing on the heels of the introduction and widespread use of an antimicrobial agent. *Staphylococcus aureus* has always been a poster child for the emergence of antimicrobial resistance (1). Penicillin-resistant strains of *S aureus* surfaced immediately following the introduction of penicillin in the late 1940s; within a few years, most hospital strains were penicillin resistant. There was also the rapid emergence of methicillin-resistant *S aureus* (MRSA) following the introduction of methicillin in the 1960s. While the replacement of nosocomial methicillin-susceptible *S aureus* by MRSA has proceeded at different rates in different regions, the overall global progression has been relentless. MRSA became common in Canadian health care facilities later than in the United States; however, since the early 1990s, nosocomial MRSA in Canada has steadily and irrevocably increased (2).

The current chapter in this story is the progressive dissemination of community-acquired MRSA (CAMRSA), mirroring the experience with penicillin-resistant *S aureus* 50 years ago (1). In fact, CAMRSA has been common in some Canadian communities for almost 20 years (3). Northern Aboriginal communities in the prairies have been primarily affected, although there have been rare reports of outbreaks and community spread elsewhere (4). Now, Canadian CAMRSA has appeared in populations at risk identified elsewhere in North America and Europe. These populations include incarcerated people, as described in this issue of the *Journal* (pages 343-348), as well as parenteral drug users, homeless people and other marginalized groups. Even in communities with long-standing experiences with CAMRSA, more severe *S aureus* infections may now be recognized. The specific strains identified in Canada are the same as those reported outside our borders and are usually characterized by the presence of Panton-Valentine leukocidin (5). The *pvl* gene is associated with more serious infections, particularly skin and soft tissue infections and pneumonia.

A relatively unique feature of CAMRSA in Canada is that a high proportion of strains are mupirocin resistant (5). Mupirocin resistance is principally a characteristic of the strains isolated from northern Aboriginal communities in the prairies, where CAMRSA has been present since the 1980s (3).

Subsequent widespread use of mupirocin in these communities has, predictably, been followed by the emergence of mupirocin resistance (5). Fortunately, Canadian CAMRSA strains, as elsewhere, generally remain susceptible to several oral antimicrobials, such as trimethoprim/sulfamethoxazole, doxycycline and clindamycin.

The medical and public health response to a previously unappreciated virulent organism with potential unique attributes is to consider it to be a 'new' organism – 'emerging' in the current parlance. Generally, this response entails characterizing the epidemiology, morbidity and mortality, managing cases, and controlling transmission. This idea of 'uniqueness' of MRSA has been the paradigm within which the response to nosocomial MRSA has developed. However, genetic rearrangement in microorganisms is ceaseless, and countless genetic variants of an organism are the norm. Acquisition of resistance genes, *pvl* genes or other virulence genes is simply a manifestation of this diversity. CAMRSA is not exceptional.

The paradigm of CAMRSA as 'extraordinary' also suggests humans and the microbiological environment are distinct entities – us and them. But we do not stand apart from microorganisms. Human beings and microorganisms are part of the same environment and, often, are interdependent. *S aureus* is part of the normal flora of the anterior nares of humans. No amount of isolation, restriction or handwashing alters the reality that approximately 20% of adults are permanent nasal carriers of *S aureus*, and that another 60% are intermittent nasal carriers. And the more ill people are, the more likely they are to be colonized. Separation, barriers and intense handwashing have some role in health care settings to delay or prevent transmission of microorganisms, including *S aureus*. The goal is to prevent acquisition by patients at increased risk of serious infection because of interventions or immune impairment secondary to disease and treatment. But outside of the health care setting, effectively eliminating the transmission of commensal bacteria between humans cannot, and arguably should not, be prevented.

The apocalyptic vision of untreatable strains of common community pathogens is repeatedly raised and may ultimately prove true, but we are not there yet. In addition to the antimicrobials already mentioned, linezolid, rifampin, fusidic acid, quinupristin-dalfopristin, tigecycline and vancomycin,

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together or in combination, provide treatment options for MRSA. The need to support and prioritize discovery and development of new antimicrobial agents is also repeatedly highlighted. The systematic clinical evaluation of antimicrobials already available would, however, be of more immediate value, including clarifying when not to use antimicrobials. The political and scientific agenda in Canada (as in other developed countries), however, favours the discovery agenda rather than expanding the knowledge base for optimal use of available antimicrobials. A better understanding of how best to use, or not use, existing agents would resolve many therapeutic questions for CAMRSA.

Where should we go with CAMRSA? The sky is not falling; this is the anticipated evolution of a ubiquitous human colonizer and pathogen. It is simply another skirmish at the antimicrobial-microorganism interface. Morbidity and mortality in the general population attributable to the introduction and spread of a more virulent strain of *S aureus* that is also methicillin resistant do need to be characterized. Practical, effective strategies to limit morbidity should be identified, implemented and evaluated. The same can be said for any *S aureus* strain, irrespective of susceptibility. With respect to CAMRSA, practitioners must have access to timely information describing the regional spectrum of resistance to facilitate appropriate antimicrobial therapy. Pursuing all strains of this ubiquitous human commensal through widespread or nonselective screening for colonization or decolonization of carriers should be discouraged. These approaches are unlikely to limit transmission or morbidity, and antimicrobial-based interventions for patients who are not infected will have the opposite effect: increased resistance. Canada has already harvested the

fruits of widespread mupirocin use, with substantial resistance to the only current agent recommended for decolonization.

The approach to the management of *S aureus* infection in the community is one of basic hygiene – washing, cleaning and laundering – together with appropriate care of wounds and management of active infections. Optimal approaches to the management of infections – both antimicrobial and nonantimicrobial – need to be promoted and refined. Vaccine strategies are always relevant, but such an approach remains speculative for *S aureus*. There are also many research opportunities: the predictors of organism virulence and transmission, the efficacy of therapy, and the outcomes in the community for persons colonized by specific *S aureus* strains are just a few of the outstanding issues. But framing all of our approaches must be an acknowledgement and continuing appreciation that human beings and their commensal organisms are inseparable.

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