

Staphylococcus aureus: a guide for the perplexed

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The differences between community-acquired and health care-associated MRSA explained

Staphylococcus aureus is one of the most important bacterial pathogens globally. About a quarter of us carry one or other strain at any one time, and, if we develop an infection, our own colonising strain is likely to be responsible.¹ All clinicians, from urban general practitioners to remote-area nurses, encounter *S. aureus* infections. In hospitals, *S. aureus* is responsible for most surgical-site infections, and their control poses a major challenge.

We have no effective vaccine against *S. aureus*, so for 50 years we have depended on the safe and affordable β -lactam antibiotics. However, in many large Australian hospitals, patients run the risk of becoming colonised with a hospital strain of *S. aureus*, many of which are β -lactam resistant — “golden staph” in the vernacular.² As β -lactam resistance is detected in the laboratory using methicillin or oxacillin, microbiologists call these strains “methicillin-resistant *Staphylococcus aureus*” (MRSA) (see Box 1 for acronyms). All MRSA harbour the *mecA* gene that encodes a modified cell wall protein to which no β -lactam antibiotic is able to bind.³ Strains of health care-associated MRSA (HA-MRSA) are usually not only resistant to β -lactam antibiotics, but also carry several other resistance genes or mutations. Typically, Australian HA-MRSA isolates are not only “methicillin-resistant” but also “multiresistant”, leaving only vancomycin and a very short list of alternatives as the last line of defence.

Fortunately, when clinicians have to prescribe antibiotics for *S. aureus* infections, the decision has been relatively straightforward — a β -lactam such as flucloxacillin or cephalexin if the infection is community-acquired (because MRSA has been rare in the community), or vancomycin if the patient has recently been in hospital. However, in the article by Nimmo and colleagues in this edition of the Journal (page 384),⁴ this neat epidemiological distinction is under attack. MRSA appears to be at large in the community, and the types of infections we associate with MRSA are changing. What is going on out there? Has MRSA escaped from the hospitals?

Evolution occurs far more rapidly in bacteria than in more complex organisms such as humans. Bacteria are constantly deleting and acquiring genes or mutations and trying out their new configurations in new situations. It does not particularly matter from where the genes come; any DNA will do provided it is useful. *S. aureus* has prospered because it is carried and spread by humans, but there is a silent competition going on between different strains of *S. aureus* to see which one can colonise and spread most successfully. How do we know this? Using increasingly sophisticated laboratory methods, it is possible to identify and track different strains (or clones) of *S. aureus*. The data reported from the Australian Group on Antimicrobial Resistance (AGAR) by Nimmo and colleagues reveal the spread in Australia of new strains of MRSA, which may actually be more virulent than HA-MRSA. These “community-acquired” MRSA (CA-MRSA) carry a distinct variant of *mecA* that is small enough to efficiently move between bacteria. Epidemiologically, a CA-MRSA infection is one

1 The ABC of MRSA

MRSA = methicillin-resistant *Staphylococcus aureus*

CA-MRSA = community-acquired MRSA

HA-MRSA = health care-associated MRSA

NORSA = non-multiresistant oxacillin-resistant *S. aureus* (also an MRSA)

PVL = Pantone–Valentine leukocidin, a virulence factor present in some *S. aureus* strains

that arises in a patient who has not had contact with the health care system (no admissions to hospital in the previous 12 months, no indwelling catheters, and not a resident of a long-term care facility). The AGAR study shows that CA-MRSA has not broken out of the hospitals, but has instead emerged independently when community strains of *S. aureus* have acquired *mecA* from other bacteria.⁴

And *S. aureus* is not just in the market for antibiotic resistance genes; any DNA that can give a competitive edge is being progressively collected and amplified. One example is the gene for Pantone–Valentine leukocidin (PVL), which probably provides some selective advantage to *S. aureus*, but in humans contributes to necrotising pneumonia and aggressive soft tissue infection. PVL, first described in 1932,⁵ is now present in more than 90% of the Queensland and south-west Pacific epidemic clones of CA-MRSA reported by AGAR.⁴ Paradoxically, these “superbugs” are sensitive to more antibiotics than HA-MRSA. β -Lactams such as flucloxacillin and cephalexin are not active, but clindamycin and trimethoprim–sulfamethoxazole may be useful alternatives. This characteristic resistance profile has also led to yet another acronym: “NORSA”, for non-multiresistant oxacillin-resistant *S. aureus*.⁶

Confused? The picture is confusing, and it is not static. AGAR has documented the stepwise increase in the proportion of community isolates of *S. aureus* that are MRSA in Australia, from 4.7% in 2000 to 7.3% in 2004.⁴ However, these data are drawn from teaching hospitals and private pathology laboratories and do not reveal the true extent of CA-MRSA carriage in the general community. To really understand what is happening, we require a population-based study to document the prevalence and movement of these new strains in the healthy majority. Who is carrying them? Do antibiotic prescribing practices play a role? Can we “profile” the typical CA-MRSA carrier, so that we can better select which antibiotics to prescribe empirically? What if CA-MRSA gets into a hospital; will it spread and replace HA-MRSA and cause even more serious hospital-acquired infections? What will we call it then?

The emergence of MRSA infections in patients without apparent risk factors poses a difficult problem for clinicians who see patients with infections likely to be caused by *S. aureus*, especially if the infections are severe. For patients with mild to moderate infections, obtaining appropriate cultures for susceptibility testing is important. For those with severe infections possibly caused by

See also pages 404 and 420

2 Suggested interim guidelines for suspected *Staphylococcus aureus* infections in community patients

- Obtain cultures for bacterial identification and drug susceptibility testing whenever possible.
- Discuss with the microbiology laboratory the patterns of resistance in the local area.
- Incision and drainage should be considered in all cases, and may be the only treatment required.
- For mild infections that require antibiotics but not admission to hospital:
 - Prescribe a β -lactam antibiotic initially (eg, flucloxacillin or cephalexin) unless allergy or documented previous CA-MRSA in the patient or the patient's family.
 - Review the patient.
 - Check the culture result.
 - If CA-MRSA is identified, follow the sensitivity pattern; clindamycin or trimethoprim-sulfamethoxazole are likely to be effective.
- For severe suspected community-acquired *S. aureus* infection:
 - Obtain cultures, commence intravenous flucloxacillin empirically.
 - Consider combining flucloxacillin with intravenous vancomycin if the patient is critically ill.
 - Continue flucloxacillin and cease vancomycin if methicillin-resistant *S. aureus* is excluded, as flucloxacillin is more effective than vancomycin for methicillin-susceptible *S. aureus* infections. ◆

S. aureus, intravenous flucloxacillin remains the drug of choice, as it is more effective therapy for methicillin-susceptible *S. aureus* bacteraemia.⁷ However, if the patient is critically ill or has risk factors for CA-MRSA infection, the addition of intravenous vancomycin is warranted (see Box 2).

Fifty years ago, all *S. aureus* strains were susceptible to penicillin, but 30 years later 80% of community strains worldwide had become penicillin-resistant, forcing us to respond with penicillinase-stable β -lactams, such as flucloxacillin and cephalexin. Nimmo and colleagues have shown that strains of CA-MRSA originally identified in Queensland, Western Australia and overseas do not respect state and

national boundaries, and we are likely to see increasing rates of CA-MRSA in coming years. Some of this change results from the overuse of antibiotics, and some is the inevitable result of rapid bacterial evolution to which we will have to adapt. Meanwhile, be alert, not alarmed, but some modification of the standard approach to *S. aureus* infections is indicated (Box 2).

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