In Focus

Epidemiology of MRSA in Australia

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Methicillin-resistant *Staphylococcus aureus* (MRSA) has presented challenges to laboratories and clinicians since it first appeared in Australia in the mid-1960s. However, in spite of its long presence and familiarity, a clear understanding of its epidemiology has only been possible with the recent advent of sequence-based typing methods (see the article by O’Brien and Giffard, page 131).

Archaic MRSA

*Staphylococcus aureus* resistant to methicillin were reported soon after its introduction in 1960. The initial reports were from the United Kingdom 1 and it was not until 1968 that MRSA was reported in Australia by Rountree and Beard 2. These ‘archaic’ MRSA were limited to relatively few institutions, were not associated with widespread epidemics and appear to have been less virulent than later healthcare-associated MRSA 3. They were generally streptomycin-, tetracycline- and erythromycin-resistant but were susceptible to gentamicin. Using multi-locus sequence typing (MLST) and SCCmec typing, archaic MRSA have been characterised as ST250-MRSA-I 4.

Epidemic multi-resistant MRSA in our hospitals

Gentamicin-resistant MRSA were first reported in Melbourne in 1976 by Perceval et al. 5 and in Sydney soon thereafter 6. Subsequently, major epidemics of multi-resistant (including gentamicin-resistant) MRSA beginning in the late 1970s were reported in Melbourne and Sydney hospitals 6, 7. It was associated with considerable morbidity and mortality and spread easily between institutions. Once established in an institution, MRSA were difficult to control and consequently usually became endemic. Similar epidemics occurred in the other Australian capital cities in the 1980s. Vickery et al. found that these new MRSA formed a distinct group by phage typing compared to earlier strains 8. Similarly, Warren Grubb’s group was able to demonstrate that this new ‘eastern Australian’ MRSA (EA-MRSA) was genetically different from MRSA previously isolated in Australia and Europe 9. Early surveys by the Australian Group for Antimicrobial Resistance (AGAR) showed EA-MRSA was endemic in New South Wales/ACT, Victoria, Queensland and South Australia by the mid-1980s but not in Western Australia (WA) 10, 11. The control of EA-MRSA in WA is a remarkable feat given the history of MRSA in the remainder of the country. In 1985, Pearman et al. reported control of an outbreak of EA-MRSA at Royal Perth Hospital 12. They were able to contain the spread of the outbreak by an exhaustive programme of screening of patients and staff and by transfer of patients to a dedicated isolation facility (after isolation in the ward in which MRSA was detected had failed to control the outbreak). Establishment of stringent infection control procedures based on extensive screening of patients and staff and on notification of MRSA has allowed WA to maintain consistently low rates of healthcare-associated MRSA infection (see also the article by Coombs, van Gessel and Christiansen, page 140).

MLST/SCCmec typing of EA-MRSA and its progeny AUS-2 and AUS-3 have characterised these strains as ST239-MRSA-III. It appears that this clone was first reported in Australia 13 and subsequently spread to the United Kingdom and beyond. It is now found on all inhabited continents and goes by a variety of names including EMRSA-1, the Hungarian strain and the Brazilian strain 14. As EA-MRSA is unique among MRSA strains in Australia in being uniformly resistant to multiple classes of antimicrobials, it is possible to follow trends using multi-resistant MRSA as a surrogate as shown in Figure 1. It can be seen that Brisbane has had a generally downward trend in prevalence since 1989, while Melbourne, Adelaide and Darwin have seen reduced prevalence in recent years.

Community MRSA appears

Community-acquired MRSA (CA-MRSA) was first reported in WA.
In the early 1990s from indigenous people living in different communities in the Kimberley region (15, 16). Colloquially known as ‘WA-MRSA’, CA-MRSA in WA was subsequently identified throughout the State and now accounts for up to 10% of the State’s community S. aureus infections. CA-MRSA notification rates per 100,000 population continue to increase dramatically throughout WA, particularly in the remote country health regions. In 1983, the overall rate of MRSA notifications was 10/100,000 in the country health regions and 7/100,000 in the metropolitan health regions. By 2006, the State’s MRSA notification rate increased to 179/100,000, of which 144/100,000 were CA-MRSA. In the metropolitan health regions the CA-MRSA notification rate was 134/100,000, while in the Kimberley health region the CA-MRSA notification rate had increased 40-fold to 391/100,000 (17).

Molecular analysis of the early strains of CA-MRSA in WA showed these strains were different from MRSA isolated from hospitals in eastern Australia. Most of the CA-MRSA isolates had a similar pulsed-field gel electrophoresis (PFGE) pattern and have subsequently been characterised as ST8-MRSA-IV (18).

In the mid 1990s a number of laboratories in eastern States noticed the appearance of non-multi-resistant MRSA causing furunculosis in outpatients with an apparent association with Polynesian ethnicity (19). Further studies showed that this epidemic was due to a southwest Pacific (SWP) MRSA strain (ST30-MRSA-IV) identical to that characterised by the Western Samoan phage pattern (WSPP) in New Zealand (20). This strain carries the genes for Panton-Valentine leukocidin (PVL), an exotoxin that has been associated with furunculosis and necrotising staphylococcal pneumonia. PVL has also been found in numerous other CA-MRSA strains around the world (21).

Infection due to the SWP strain in Caucasians were unusual, but in 2000 a cluster of cases of CA-MRSA in Caucasians occurred in Ipswich, Queensland. An observational study revealed that these cases were due to a new strain, initially identified as the ‘R pulsotype’ by PFGE and subsequently known as the Queensland Clone (QLD) (ST93-MRSA-IV) (21, 22). Like the SWP strain, it carried the genes for PVL and has been associated not only with furunculosis but also fatal necrotising pneumonia (23, 24). It has since spread throughout Australia to become one of the dominant epidemic strains of CA-MRSA.

Unwelcome arrivals

EMRSA-15 (ST22-MRSA-IV) is an epidemic strain described in the UK and Germany that appears to be very well adapted to the healthcare environment. In Australia it was first reported in WA where it was thought to have been introduced by healthcare workers from the UK (25). It is characterised phenotypically by non-ß-lactam resistance to ciprofloxacin or to ciprofloxacin and...
erythromycin and by the lack of urease production. It is now found throughout Australia and is a major healthcare-associated strain in New South Wales.\textsuperscript{26, 27}.

In the United States USA300 MRSA (ST8-MRSA-IV), has not only become the predominant cause of community-acquired infection but has also rapidly emerged as a major cause of healthcare-acquired infection. Sporadic reports of this strain have been reported in Australia, Canada, Denmark, Germany, Japan, Switzerland and the United Kingdom. In addition to carrying the PVL genes, USA300 has also acquired an arginine catabolic mobile element (ACME) which does not normally occur in \textit{S. aureus} but has been detected in \textit{Staphylococcus epidermidis}.\textsuperscript{28} It has been hypothesised that the presence of ACME may contribute to the coagulase-negative staphylococci-like traits found in USA300 such as its ability to metabolically alter the local pH on the skin of the host. This change in pH may increase the ability of USA300 to persist on intact skin and consequently facilitate spread by skin contact. Furthermore, USA300 carries a unique PVL sequence variant resulting in an amino acid substitution on the interactive surface of the \textit{LukF-PV} component and, as a consequence, may enhance PVL function.\textsuperscript{29}

In WA, the number of USA300 MRSA isolated per year since 2003 has increased several-fold. Overall, 89 USA300 strains from 78 patients have been characterised, with 92% of these isolates causing skin and soft tissue infections predominately with abscess formation. Over 60% of patients were younger than 40 years. A total of 76 (85%) isolates were erythromycin-resistant, 35 (39%) ciprofloxacin-resistant, nine (10%) tetracycline-resistant and five (6%) mupirocin-resistant. Of the erythromycin-resistant strains, 88% were clindamycin susceptible (inducible resistance not detected). To prevent USA300 MRSA from becoming established in both the WA community and its hospitals, the WA Health Department has recently commenced a ‘search and destroy’ policy for all PVL-positive CA-MRSA strains isolated in WA. In addition, in some acute care hospitals, screening has been extended to all high risk and surgical unit admissions.

New York Japan (NY-Japan) (ST5-MRSA-II) MRSA is a major EMRSA clone that has been reported in several USA States, Canada, Brazil, Mexico, China and Korea. Although infrequently reported in Europe, this clone has been described in Hungary. An outbreak of NY-Japan was recently reported in the south west of WA which involved the area’s regional hospital, several community hospitals and long-term care facilities, as well as two teaching hospitals located in the Perth metropolitan area.\textsuperscript{30} This strain is typically resistant to ciprofloxacin and erythromycin and is urease positive. Sporadic isolates throughout Australia have been reported in recent AGAR surveys.

Several other imported MRSA clones have also been isolated in Australia including the healthcare-associated strains EMRSA-16 (ST36-MRSA-II), EMRSA-17 (ST247-MRSA-I), Irish-1 EMRSA (ST8-MRSA-II) and Irish-2 EMRSA (ST8-MRSA-VI); and several PVL-positive CA-MRSA strains including Taiwan CA-MRSA (ST59-MRSA\textsubscript{V}), European CA-MRSA (ST80-MRSA-IV) and USA400 (ST1-MRSA-IV).

**Current trends**

The MRSA epidemic in Australia can be viewed as a series of concurrent epidemics due to a variety of clones associated with distinct clinical and epidemiological characteristics. There is evidence that the major healthcare-associated epidemic clones, EA-MRSA and EMRSA-15, are waning at least in some regions. A recent study in Queensland showed a reduction in EA-MRSA phenotype from 19% of inpatient pus, tissue and fluid \textit{S. aureus} isolates to 9% between 2000 and 2006, with a similar decrease for blood culture isolates.\textsuperscript{31} AGAR data from the 2005 hospital survey showed that an increasing proportion of healthcare-associated MRSA infections was due to clones previously associated with community infection particularly in WA, South Australia and Queensland (Figure 2 – AGAR, unpublished data).\textsuperscript{32} However, MRSA remains the major cause of healthcare-associated infection in Australia and continued efforts in screening and isolation and heightened hand hygiene are warranted.

The situation in the community is also changing with the overall prevalence of MRSA increasing while the proportion of clones continues to change. The Queensland clone is now dominant in community MRSA infections in Australia (Figure 3 – AGAR, unpublished data). This is of concern as the Queensland clone is PVL positive and has been associated with severe and fatal infections in healthy young adults. These rapid changes in the community have put MRSA on the public health agenda, with WA once again leading the way with a major public health intervention.

**References**

Figure 2. Proportion of CA-MRSA clones among MRSA isolated in the 2005 AGAR survey of hospital-acquired *S. aureus* infection.

Figure 3. Proportion of CA-MRSA clones among MRSA isolated in the 2006 AGAR survey of outpatient *S. aureus* infection.

*PVL positive clones

National: 20.7% of MRSA

National: 56.1% of MRSA

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Geoffrey Coombs (Please see details on page 114).

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