

# Community-acquired methicillin-resistant *Staphylococcus aureus* in Central Australia

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## Abstract

To date, there has been scant information about the burden of methicillin-resistant *Staphylococcus aureus* infections in Central Australia. Our aims were to determine the proportion of *Staphylococcus aureus* infections due to methicillin-resistant strains in Central Australia, to characterise resistance to non-beta lactam antibiotics and to correlate findings with available demographic information. We retrospectively reviewed *S. aureus* isolates identified by the Microbiology Laboratory of the Pathology Department, Alice Springs Hospital between September 2005 and February 2006. Multi-resistance was defined as resistance to three or more non-beta lactam antibiotics. We identified the recovery site and extended antibiotic resistance profile of each isolate. Demographic data included place of residence, discharge diagnosis and ethnicity. There were 524 *S. aureus* isolates: 417 (79.6%) methicillin-sensitive *S. aureus*, 104 (19.7%) non-multi-resistant MRSA (nmrMRSA) and 3 (0.7%) multi-resistant MRSA (mrMRSA). MRSA accounted for 7/22 (32%) invasive infections and 91/474 (19.2%) cases of staphylococcal skin infections. Aboriginal people comprised 89 per cent (93/104) of patients with nmrMRSA; 57 per cent lived in remote communities, 21 per cent in suburban Alice Springs, and 18 per cent in Alice Springs Town Camps. Six per cent (6/104) of nmrMRSA were hospital-acquired. Of the nmrMRSA isolates, 57 per cent (59/104) were resistant to erythromycin and 7 per cent (7/104) to fusidic acid. All MRSA isolates were susceptible to co-trimoxazole. In conclusion, Central Australia has high rates of community-acquired nmrMRSA and low rates of multi-resistant MRSA. Erythromycin resistance in *S. aureus* is also common. These findings should prompt the review of antimicrobial prescribing guidelines for the region, especially for treatment of skin and soft tissue infections. *Commun Dis Intell* 2006;30:462–466.

**Keywords:** *Staphylococcus aureus*, methicillin resistance, community-acquired infection, Central Australia, Aboriginal

## Introduction

Methicillin-resistant (beta-lactam resistant) *Staphylococcus aureus* (MRSA) is increasingly recognised in non-health care settings around Australia, and Aboriginal Australians are among those most at risk.<sup>1,2</sup> A recent longitudinal study documented an increase of hospitalised patients with community-acquired MRSA from 4.7 per cent in 2000 to 7.3 per cent in 2004; the rise was especially marked in Darwin where the proportional increase was from 5 per cent to 20 per cent.<sup>3</sup> Community-acquired MRSA made up 23 per cent of *S. aureus* isolates from pyoderma lesions and throat swabs in a recent study conducted in remote Aboriginal communities in the Top End of the Northern Territory.<sup>4</sup> In addition, a recent cross-

sectional survey in a remote Queensland Aboriginal community reported that 15 per cent of children were found to carry MRSA, although the numbers were small.<sup>5</sup> It has been projected by one authority that methicillin resistance may eventually become as ubiquitous in *S. aureus* as penicillin resistance did several decades ago.<sup>6</sup> This trend has important implications for empirical antibiotic prescribing and infection control measures in hospitals, urban settings and remote communities. Johnson and others, in a recent editorial in the *Medical Journal of Australia*, proposed management guidelines that include routine collection of local data, microbiological culture and antimicrobial susceptibility testing in settings where *S. aureus* are important pathogens.<sup>7</sup>

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There are no published data from Central Australia, although anecdotal reports indicate increasing rates of MRSA infection. Alice Springs Hospital serves a population of 51,000 people living in a region of approximately 1 million square kilometres, and encompassing southern and central Northern Territory, northern South Australia, and eastern Western Australia. This retrospective study is based on laboratory isolates collected over a six month period. It provides the first documentation of the MRSA burden in Central Australia, both community-acquired and health care-acquired. The findings have implications for hospital and community antimicrobial prescribing guidelines.

## Methods

We reviewed the laboratory data for *S. aureus* isolates identified by the Microbiology Laboratory of the Pathology Department, Alice Springs Hospital (ASH) between September 2005 and February 2006. Colonies of gram-positive cocci were identified as *S. aureus* if they were catalase positive and tested positive for production of coagulase using Staphaurex® (Oxoid). The specimen site (blood, sterile body fluid, respiratory specimen, wound swab or screening swab) was recorded. As methicillin-sensitive *S. aureus* (MSSA) is not reported from screening swabs, these were excluded. Antimicrobial susceptibility testing was performed using a disc diffusion method in accordance with Clinical and Laboratory Standards Institute (CLSI) Methods.<sup>8</sup> The isolates were reported as MSSA or MRSA based upon the diameter of the zone of inhibition around an oxacillin 1 microgram Disc (Oxoid).

We also determined susceptibility to ciprofloxacin, erythromycin, flucloxacillin, fusidic acid, gentamicin, tetracycline and trimethoprim-sulphamethoxazole (co-trimoxazole) for all MRSA isolates using recommended CLSI methods. Clindamycin susceptibility was inferred when the isolate was resistant to erythromycin. This was based on data from the Top End of the Northern Territory,<sup>4</sup> acknowledging that clindamycin resistance might be over-estimated when due to the *msrA* mechanism rather than the *erm*-mediated mechanism.<sup>9</sup>

*S. aureus* was defined as non-multi-resistant (nmrMRSA) if resistant to methicillin and less than three other classes of non-beta lactam antibiotic.<sup>10</sup> Infections were classified as community or health care-acquired by the ASH Infection Control Unit; health care-acquired infection was defined as infection acquired after greater than 48 hours of hospitalisation, or within four weeks after discharge and due to an organism acquired during hospitalisation. Community-acquired infections were those considered to be present on admission to hospital and not able to be linked to previous admission to hospital.

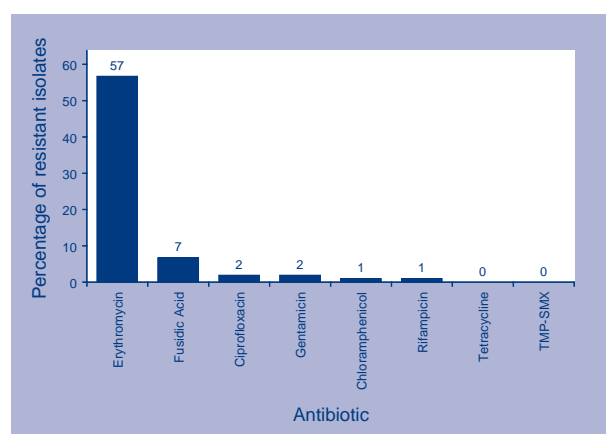
For each patient, we recorded the discharge diagnosis (coded as per the International Classification of Diseases), ethnicity (Aboriginal or non-Aboriginal), and place of residence, as noted in the medical records and/or electronic coding system. Proportions were compared using the Chi-squared test.

## Results

A search of laboratory and clinical records produced 524 *S. aureus* isolates: 417 (79.6%) MSSA, 104 (19.7%) nmrMRSA and 3 (0.7%) mrMRSA. An additional 56 MRSA isolates (49 nmrMRSA and 7 mrMRSA) were detected on 'screening swabs'; these were not included in the study. Six per cent of nmrMRSA infections (6 of 104) and one of three mrMRSA infections were coded by the ASH Infection Control Unit as being hospital-acquired. However, this is likely to be an under-estimate because the ASH Infection Control Unit did not include outpatients and dialysis patients in the hospital-acquired group.

Susceptibility testing demonstrated that all nmrMRSA and mrMRSA isolates were susceptible to tetracyclines and co-trimoxazole. The three mrMRSA isolates qualified as multi-resistant on the basis of resistance to gentamicin, erythromycin and fusidic acid in addition to beta-lactam antibiotics. Of the nmrMRSA isolates, 59 (57%) were resistant to erythromycin, and 7 (6.7%) were resistant to fusidic acid. Antibiogram data for nmrMRSA isolates are shown in Figure 1.

**Figure 1. Proportion (%) of antibiotic resistance in nmrMRSA isolates**

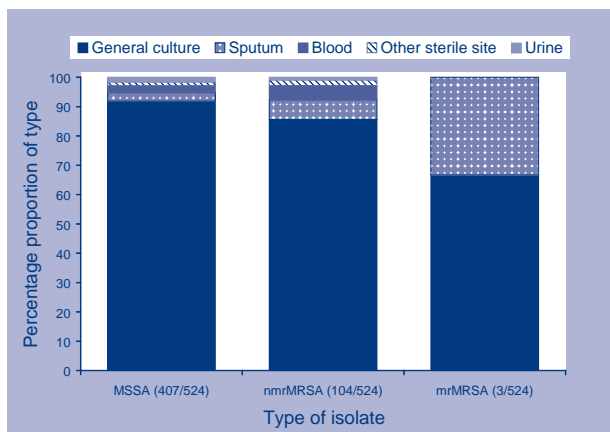


TMP-SMX = trimethoprim-sulphamethoxazole (co-trimoxazole)

Invasive staphylococcal infections (blood or other sterile site) accounted for 22 (5%) isolates; there were 15 cases of bacteraemia (10 MSSA, 5 nmrMRSA) and 9 infections at other sterile sites (5 MSSA, 2 nmrMRSA). Thus, 7 of 22 (31.8%) invasive *S. aureus* infections were due to nmrMRSA compared with 97 of 502 (19.4%) non-invasive infec-

tions (P=0.15). Skin swabs were the most common specimens received by the laboratory (Figure 2); 91 of 474 (19.2%) skin swabs yielded MRSA. The laboratory also had many specimens labelled 'general' category. When we reviewed their origin, 90 of 91 were found to be skin swabs. Thus, 'general' isolates have been counted with the skin isolates.

**Figure 2. Site of infection as a proportion of total number of infections of each *Staphylococcus aureus* type, Northern Territory**



Upon review of the clinical records of people with nmrMRSa, staphylococcal infection was included in the coded diagnoses on 58 of 104 (56%) occasions and appeared to be incidental to the primary diagnosis (not recorded as a significant finding) in the remainder. The most common staphylococcal infections were skin and soft tissue (Table) and 70 of 104 (67%) patients with nmrMRSa infection required hospital admission.

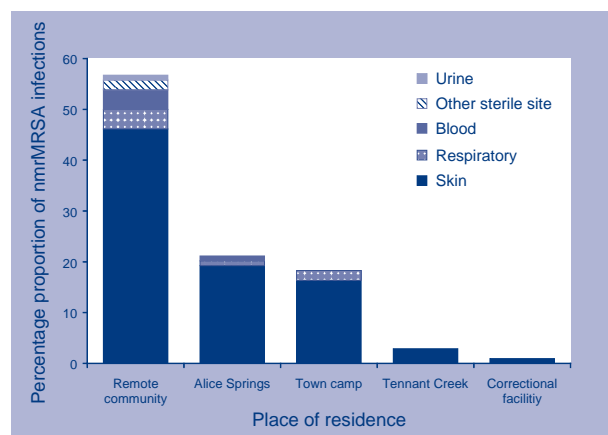
**Table. Discharge diagnoses for patients with nmrMRSa**

Diagnosis	n	%
Laceration or wound	20	19.2
Abscess	14	13.5
Surgical wound including compound fracture	8	7.7
Diabetic leg ulcer	3	2.9
Cellulitis	3	2.9
Burn	2	1.9
Pneumonia	2	1.9
Exacerbation of bronchiectasis	2	1.9
Other	4	3.8
Non-infective diagnosis only	46	44.2
Total	104	100

Eighty-nine per cent of patients from whom nmrMRSa was isolated were Aboriginal. The three mrMRSa isolates were from non-Aboriginal people. During the six month study period, Aboriginal people accounted for 80 per cent of admissions to ASH (unpublished data from ASH Separations data for the period including September 2005 to February 2006).

As shown in Figure 3, nmrMRSa was most commonly recovered from people who lived in remote communities - 59 of 104 (57%), followed by Alice Springs suburban residences - 22 (21%), Alice Springs town camps - 19 (18%), Tennant Creek - 3 (3%) and the Correctional Facility - 1 (1%). The three mrMRSa infections were in patients who resided in suburban Alice Springs.

**Figure 3. Place of abode of patients with nmrMRSa infection**



*Discussion*

Community-acquired non-multi-resistant MRSA infection in Central Australia has now become a major public health concern. Rates of MRSA infection greatly exceed those of the rest of Australia with the exception of the Top End of the Northern Territory,<sup>3</sup> Northern Queensland<sup>5</sup> and certain defined urban populations.<sup>1</sup> In Central Australia the burden of MRSA skin and soft tissue infection is largely borne by the Aboriginal population, especially people from remote communities. Moreover, the Aboriginal population is much more likely to develop life-threatening invasive disease as a result of skin and soft tissue infection than the non-Aboriginal population, and the outcome is worse.<sup>2</sup>

It is important to determine whether nmrMRSa was recently imported into Central Australia or arose *de novo* with local *S. aureus* strains acquiring the *mec* gene that encodes the low-affinity penicillin binding protein responsible for beta-lactam resistance (PBP2a). Knowing the source will, to some extent,

dictate the public health control measures required. Fortunately, *S. aureus* carry their 'pedigree' with them, written in the nucleotide sequences of seven basic housekeeping genes, and their lineage can be revealed using the molecular technique of multilocus sequence typing.<sup>11</sup> The *mec* genes and related genes (SCC*mec*) can also be typed to determine whether they are likely to be of community origin. It would be important to determine whether Central Australian strains have genes for the Panton-Valentine leukocidin, an important marker of skin infection and propensity to cause necrotising pneumonia.<sup>6</sup> It could be that in Central Australia we are experiencing an outbreak of MRSA, imported from Western Australia or the Top End. An alternative scenario is that we are witnessing an outbreak of an imported *mec* gene that is finding its way into long-established community strains of MSSA. A third scenario is that, in certain settings and perhaps promoted by local antimicrobial prescribing patterns, a *mec* gene crosses from a local non-*aureus* staphylococcus (such as *S. sciuri* on household pets – particularly dogs) into *S. aureus*. *S. sciuri* has previously been shown to be a plausible extra-species source of *mecA* for *S. aureus*.<sup>12</sup> Close contact between animals (especially dogs) and humans in Indigenous communities could potentially facilitate this process. In addition, nmrMRSA strains appear to have greater aptitude for establishing skin colonisation, displacing mrMRSA in hospital and other settings.<sup>6</sup> This could explain the relatively low rate of mrMRSA infection in ASH. Geographical or social isolation cannot realistically be invoked as the explanation because there is frequent traffic of patients and staff to intra- and inter-state hospitals.

High apparent rates of community acquisition indicate that attempts to contain MRSA need to be largely community-based. Examples of effective community interventions include 'Healthy Skin' programs, such as those employed in the Top End of the Northern Territory,<sup>13</sup> and installation of more swimming pools. Community pools have been associated with reduction in skin (and ear) infections.<sup>4</sup> Antimicrobial prescribing practices in remote communities could also be reviewed and modified if required.

Infection control precautions need reinforcement within hospital settings. We identified problems with classification of cases as health-care related or community-acquired MRSA. We also noted that isolation and contact precautions were instituted for only 8 of 24 inpatients with nmrMRSA infection during a recent two month surveillance period. Renewed enthusiasm of public health policy planners and health practitioners regarding regional infection control strategies would be welcomed.

The lack of efficacy of beta-lactams for up to one third of *S. aureus* infections in Central Australia contrasts with the preservation of beta-lactam susceptibility in other common local organisms: locally-acquired *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria gonorrhoea* are almost universally beta-lactam-susceptible. There is also a high burden of beta-haemolytic streptococcal infection, especially pyoderma, and the post-streptococcal sequelae of rheumatic fever and glomerulonephritis. These factors lead to widespread dependence upon beta-lactam antibiotics in community and hospital antibiotic protocols. The most commonly used guideline in the region is the Central Australian Rural Practitioners Association Standard Treatment Manual<sup>15</sup> and it advocates intramuscular benzathine penicillin G for treatment of skin sores. A key rationale for treating skin sores is to prevent harmful post-streptococcal sequelae rather than because of local pathology. However, staphylococcal and streptococcal skin lesions are frequently indistinguishable; the two pathogens are often found in the same lesion.<sup>3</sup> Our data, and those of McDonald *et al*, indicate that beta-lactam therapy may no longer be effective for around 20 per cent of skin sores in Northern Territory Aboriginal communities, and the pathogenic potential of nmrMRSA is clearly evident.

Difficulties in achieving timely specimen collection, transportation to a laboratory, and follow up of patients in isolated and mobile populations, render strategies based on culture results problematic. Overuse of agents active against MRSA will lead to rising resistance to such agents. Bearing in mind these considerations, the authors support ongoing use of a beta-lactam agent as empirical therapy for non-severe suspected staphylococcal infections, but in keeping with other Australian guidelines.<sup>7</sup> We also advocate collection and follow-up of swab specimens from skin and soft tissue infections, and use of an agent active against MRSA, for empirical treatment of severe suspected staphylococcal infections, or infection in a patient known to be colonised or infected with MRSA.

Erythromycin and clindamycin cannot be relied upon empirically as non-beta lactam alternatives, as 57 per cent of nmrMRSA isolates demonstrated erythromycin resistance. Macrolide resistance may be driven by the widespread use of this antibiotic class in Central Australia for highly prevalent respiratory tract infections, genital *Chlamydia* and trachoma (including occasional mass community treatments with azithromycin). The data presented here show that MRSA isolates in Central Australia are reliably susceptible to co-trimoxazole, a potential alternative for treating non-severe infections. However clinical efficacy demonstrated by trial data is lacking. Fusidic acid susceptibility must be confirmed before using this agent because resist-

ance was identified in seven per cent of our isolates. Topical use of fusidic acid is likely to promote resistance and is discouraged.<sup>16</sup> Randomised controlled trials comparing antibiotic treatment regimens for nmrMRSA, are eagerly awaited. A planned prospective clinical study with molecular typing of Central Australia isolates should further our understanding of *S. aureus* infection in this region.

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