Staphylococcus aureus bacteraemia: The Australia New Zealand Cooperative on Outcomes in Staphylococcal Sepsis (ANZCOSS)

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***Staphylococcus aureus* is such a common organism, both as a coloniser and cause of infection in humans, that it is easy to take it for granted. Microbiologists, infectious diseases specialists and infection control practitioners deal with the organism on a regular basis, from screening for methicillin-resistant strains (MRSA) in asymptomatic carriers to treating patients with life-threatening sepsis syndrome in intensive care units.**

Although it is a well known cause of morbidity and mortality, apart from the infection control problems posed by MRSA, it is easy to ignore the size of the problem and the rate of poor outcomes from serious *S. aureus* infections. Studies internationally have shown that crude mortality rates of 15-30% are not uncommon for invasive infection but, until recently, data on outcomes in Australia or New Zealand have been limited to a single institution.

In 2005-6 the Australian Group on Antimicrobial Resistance (AGAR) attempted for the first time to obtain a national snapshot of early mortality in *S. aureus* bacteraemia (SAB), by following up patients with positive blood cultures in 17 laboratories for 7 days after the time of blood culture collection or at discharge if sooner. Mortality data in that interval were available for 51% of 1511 cases, and was 11.2% [1]. Although this study provided some insights into the problem, there were serious concerns about its general applicability.

Thus, a group of laboratories/hospital across Australia and New Zealand were prompted to join forces in 2007 as The Australia New Zealand Cooperative on Outcomes in Staphylococcal Sepsis (ANZCOSS). The objective was to determine outcomes (early and later mortality) using prospective collection of a small but clearly-defined and objective data set (Figure 1). Support for the project was provided by the Australian Society for Antimicrobials, and a website was established for data entry. The entry criterion was a positive blood culture for *S. aureus* and the entry date was taken as the date of collection of the first positive culture if more than one set had been taken. By December 2007, 26 laboratories/hospitals had joined ANZCOSS, and outcomes were available for the first ~1000 cases. Of the 1052 completed cases, 1002 had mortality data at 30 days after the initial positive blood culture. The median age of cases was 63 years; 39% were older than 70 years and 11% were 18 years or less. The key features of the patients and their infections are listed in Table 1. Important findings included the 7% of cases caused by non-multi-resistant community type MRSA (CA-MRSA) strains. Of these, 36% had their onset in hospital, most consistent with those patients being colonised at the time of admission.

Crude mortality was chosen as the endpoint rather than attributable mortality, as the latter requires considerable judgement and can be subjective. Studies examining attributable mortality suggest that it is around 80% of the crude mortality [2]. Predictors of 30-day mortality by univariate analysis were age >70 years, European ethnicity, infection with MRSA, and more particularly with multi-resistant MRSA, infection onset in hospital, infection not originating from a medical device, principal clinical manifestation of L-sided endocarditis, pneumonia, or sepsis syndrome, and treatment with vancomycin. Vancomycin treatment, when used for the treatment of methicillin-susceptible *S. aureus* (MSSA) infection, resulted in a higher mortality (31%) that when treated with flucloxacillin (12%).

The important findings of the first analysis of these data are that:

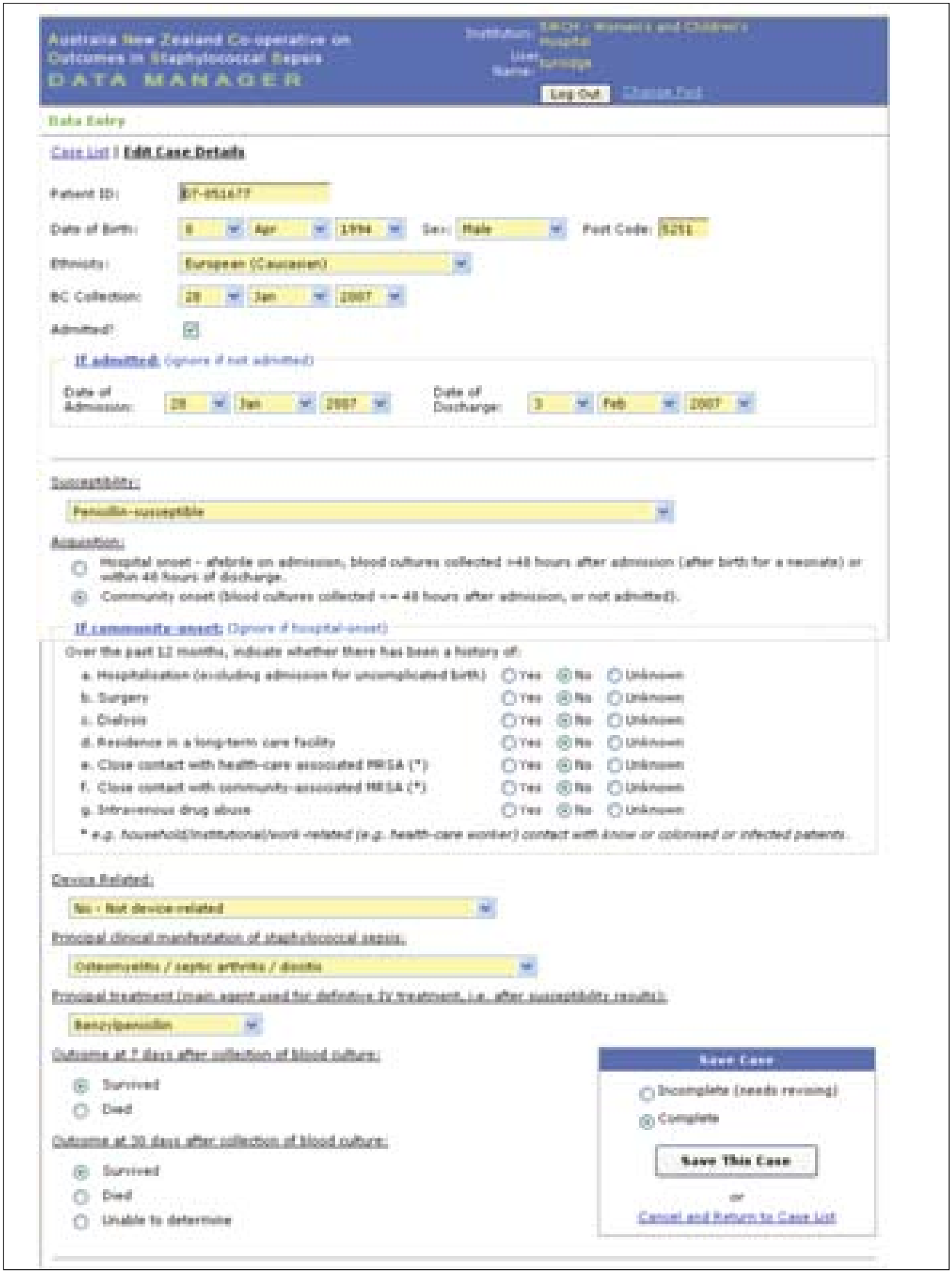

Figure 1. ANZCOSS objective data set.

- There is significant mortality from staphylococcal sepsis in Australia and New Zealand.
- MRSA remains an important contributor to this problem.
- CA-MRSA makes up a significant proportion of MRSA sepsis.
- There are poorer outcomes when vancomycin is used to treat MSSA infection compared to β-lactam treatment.

Using positive blood cultures as an entry criterion does not capture all serious invasive *S. aureus* infection. Nevertheless, it does account for the great majority of them, and is entirely objective. The database that has been established under ANZCOSS has not been designed to capture all risk factors for poor outcomes. Other factors, especially co-morbidities, are known to have a strong influence on outcomes [3]. Future versions of ANZCOSS may include capture of this kind of data.

Table 1. ANZCOSS key features of the patients and their infections.

Factor	Feature	Rate/value (%)
Demographics		
Sex	Male	61%
Ethnicity	European (Caucasian)	86%
	ATSI	2%
	Maori	1%
	Other	11%
Type of *S. aureus*		
Susceptibility	Penicillin-susceptible	11%
	MSSA	68%
	Multi-resistant hospital type MRSA	12%
	UK-15-like hospital type MRSA	2%
	Non-multi-resistant CA-MRSA	7%
Infection features		39%
Onset	Community	61%
	Hospital	39%
Device-related	Yes	36%
Infection types	Device infection without 2° focus	18%
	Skin and skin structure	16%
	Osteomyelitis/septic arthritis	12%
	No focus	12%
	Sepsis syndrome	10%
	Endocarditis	7%
	Pneumonia	8%
	Other	17%
Outcomes		
7-day crude mortality (n=1052)		11.6%
30-day crude mortality (n=1002)		20.9%
30-day mortality for MSSA infection (n=784)		18.6%
30-day mortality of MRSA infection (n=218)		28.0%
30-day mortality for ß-lactam treatment (n=635)		13.4%
30-day mortality for vancomycin treatment (n=258)		26.7%

Despite the above limitations, we believe that the data collected so far give our countries a reliable picture of the breadth and importance of SAB. Based on estimates made previously in Australia of about 6900 cases per annum [4], we estimate that we have accounted for about one third of all cases in that country. With a 30-day crude mortality of around 20% (accounting around 1400 deaths), SAB is a much more important and troublesome disease for the Australian community than meningococcal sepsis for instance, which, before the roll out of meningococcal C vaccine, accounted for about 300-400 cases per annum and 10% mortality (30-40 deaths).

Furthermore, the proportion of MRSA in SAB is of increasing concern. While hand hygiene programmes appear to be having some effect in reducing rates of multi-resistant healthcare-associated infections, the spread of community MRSA continues apace.

Further, our data, and those from other countries, confirm that vancomycin treatment yields poorer outcomes than β-lactams. As vancomycin is the 'gold standard' for MRSA bacteraemia treatment, and no other agent has demonstrated superiority consistently, MRSA bacteraemia will continue to have worse outcomes than MSSA bacteraemia, cost lives and consume more resources [5]. The combined needs for SAB surveillance with outcomes as a performance indicator and for the development of programmes to control MRSA in the community as well as hospitals has never been greater.

References

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Professor Turnidge is Director of the Laboratory Medicine Division at Women's and Children's Hospital in Adelaide. He is an Infectious Disease Physician and Microbiologist who has had a long career in Adelaide and Melbourne working with antibiotic resistance and appropriate antibiotic use. He is involved with many societies and committees, both nationally and internationally, dealing with issues of antibiotic resistance and their management. He was inaugural president of the Western Pacific Society of Chemotherapy, and co-founded the Australian Society for Antimicrobials. He was president of the 20th International Congress of Chemotherapy in Sydney in 1997. He has served on the scientific programme committees of the Interscience Conference on Antimicrobial Agents and Chemotherapy, and the European Congress for Clinical Microbiology and Infectious Diseases. He is currently a voting member of the Antimicrobial Susceptibility Testing subcommittee of the Clinical and Laboratory Standards Institute.

At a local level, Professor Turnidge has been involved with a range of committees related to the management of antimicrobial resistance, including JETACAR (the Joint Expert Technical Advisory Committee on Antimicrobial Resistance) and the Expert Advisory Group on Antimicrobial Resistance of the NHMRC.