AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

AURA Antimicrobial Use and Resistance in Australia

AGAR

2018 Sepsis Outcome Report

Factsheet for antimicrobial stewardship programs

As part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System, the Australian Group on Antimicrobial Resistance (AGAR) conducts targeted surveillance of certain pathogens causing bloodstream infections in Australia. Together with the Australian Passive Antimicrobial Resistance Surveillance (APAS) system and the National Alert System for Critical Antimicrobial Resistances (CARAlert), this data and reporting provides a comprehensive picture of antimicrobial resistance (AMR) in Australia.

AGAR monitors AMR, epidemiologic and genetic patterns in bloodstream infections in Australia relating to three main organisms: *Staphylococcus aureus*, enterococcal species and gram-negative organisms. The 2018 AGAR Sepsis[1] Outcome Report provides analyses of data on AMR associated with episodes of bacteraemia, reported by 36 public and private laboratories across Australia in 2018.

Up-to-date information on local AMR is important to ensure antimicrobial stewardship initiatives respond to changing resistance patterns. This factsheet summarises key findings from the report and outlines some of the major implications for clinical care.

Gram-negative bloodstream infection

Extended spectrum beta-lactamases (ESBLs) continue to increase in Australia

The proportion of ESBLs[2] increased in 2018. Almost one in seven (14.5%) *E. coli* bacteraemias now harbour ESBLs. Higher rates occur in hospital-onset disease. ESBLs contribute substantially to ceftriaxone resistance in *E. coli*. Ceftriaxone is not recommended as first-line empiric therapy in Therapeutic Guidelines: Antibiotic for many syndromes where gram-negative infections are suspected.

Ceftriaxone and ciprofloxacin resistance in *Escherichia coli* is common

Ceftriaxone resistance in community and hospital-onset *E. coli* bloodstream infections was 12.2% and 19.8%, respectively. Ciprofloxacin resistance in the same settings was 14.4% and 19.8%, respectively. Fluoroquinolones are no longer reliable for empiric oral step-down therapy in gram-negative infections. Improving compliance with guidelines for the treatment of syndromes where gram-negative sepsis is of concern, as recommended in Therapeutic Guidelines: Antibiotic, will improve appropriate empiric prescribing.

Gram-negative bacteraemias where ceftriaxone and/or piperacillin–tazobactam may not be recommended for treatment are more common in hospital-onset infections

In 2018, *E. coli* caused almost two thirds (60.4%) of community-onset bloodstream infections but only 36.3% of hospital-onset infections. Organisms such as *Enterobacter* species or organisms harbouring plasmid-mediated ESBLs are more common in hospital-onset bacteraemias. Empiric therapies recommended for hospital-onset infections should account for these differences in organism spectrum and susceptibility patterns.

Resistance to antimicrobials varies by organism, state and territory and place of onset

Gram-negative susceptibility varies by organism (Table 1), and by state and territory. *E. coli* with ESBLs[2] varied from 9.8% in Tasmania to 17.8% in Victoria. Fluoroquinolone resistance in *Klebsiella pneumoniae* was 24.6% in Victoria compared to 5.6% in Queensland. Review of local antibiograms, as recommended by National Safety and Quality Health Service Standards Action 3.16, is important to support locally appropriate antimicrobial prescribing.

[1] Sepsis is a clinical syndrome of dysregulated host response to infection. Sepsis can occur without bloodstream infection (bacteraemia). Bloodstream infection is not always accompanied by sepsis.
[2] Refers to ESBL phenotype – see 2018 AGAR Sepsis Outcomes Report for details of methodology

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Table 1: Resistance[§] (EUCAST) for common gram-negative organism-antimicrobial combinations

Organism	Number	Gentamicin	Ceftriaxone	Piperacillin–tazobactam	Ciprofloxacin
E. coli	4,570	8.4%	13.4%	6.0%	15.2%
K. pneumoniae	1,095	4.4%	9.4%	7.9%	11.3%
P. aeruginosa	730	–*	-†	11.1%	7.7%

* Not applicable; as of January 2020 EUCAST has removed breakpoints for gentamicin based on poor activity as a single agent against *Pseudomonas*.
† *P. aeruginosa* is intrinsically resistant to ceftriaxone
§ Since January 2020, EUCAST has redefined "I" as "susceptible—increased exposure", meaning it is not included with "R" in the non-susceptible category, as had been done previously.

Enterococcal bloodstream infection

Different clinical manifestations cause *Enterococcus faecalis* and *E. faecium* bloodstream infections

E. faecalis caused the majority of community-onset bacteraemia (69.0%) whilst *E. faecium* dominated hospital-onset episodes (58.6%). Urinary tract (25.1%) and 'unknown focus' (14.3%) are the most common manifestations in *E. faecalis* bacteraemia. In contrast, febrile neutropenia (21.1%) and biliary tract infections (17.9%) are the most common for *E. faecium*. These differences may impact empiric therapy choices for enterococcal disease; ampicillin is not reliable empirically for *E. faecium*.

The relative contribution of *vanA* and *vanB* genes to vancomycin resistance in *E. faecium* (VRE) varies by state and territory

vanA strains were the most common cause of VRE bacteraemia in New South Wales, Queensland, Western Australia and the Australian Capital Territory; the *vanB* genotype dominated elsewhere. This may have implications for therapeutic choices at a local level because *vanA* strains, as opposed to *vanB*, are teicoplanin-resistant.

Staphylococcus aureus bloodstream infection

Methicillin resistance remains common, varying in magnitude by state and territory

In 2018, methicillin-resistant *S. aureus* (MRSA) bloodstream infections occurred commonly (17.4%). Rates varied from 8.2% in Tasmania to 40.3% in the Northern Territory. The majority of MRSA disease was caused by community-associated MRSA (CA-MRSA) (76.8%).

Resistance to clindamycin is common

Although not recommended empirically for MRSA sepsis, clindamycin and trimethoprim-sulfamethoxazole are commonly used as oral step down choices.

Clindamycin resistance[3] was 13.7% in all *S. aureus* bloodstream infections; 31.2% in methicillin-resistant and 10.0% in methicillin-susceptible infections. In contrast, resistance to trimethoprim-sulfamethoxazole, as an alternative oral step-down agent was 3.3% in all *S. aureus* bacteraemias, rising to approximately one in ten in MRSA infections (9.9%).

Healthcare-associated MRSA (HA-MRSA) is dominated by one clone, ST22-IV

ST22-IV, a HA-MRSA clone, is the most common HA-MRSA clone in Australia (77.1%). This clone emerged from aged care settings in other countries. Reviewing surveillance cultures from aged care residents may assist in optimal empiric choices for these patients.

International comparisons

Australia now outranks the European Union and European Economic Area (EU/EEA) average in *E. coli* third-generation cephalosporin resistance (13.6% versus 13.4%), in methicillin resistance in *S. aureus* (17.4% versus 14.1%), and is second only to Cyprus for the rate of *E. faecium* vancomycin resistance (45% versus 59.1%) in countries under surveillance. Resistance to vancomycin in *E. faecium* in the EU/EEA is 17.1%.

Optimising antimicrobial use and infection control practices is essential to improve the safe delivery of healthcare in Australia. Changing patterns of resistance mean that preserving the efficacy of reserve antimicrobials by ensuring they are used only when absolutely indicated is more important now than ever.

Considerations for clinical care

The changing epidemiology of multidrug resistant bacteria may have significant implications for local practice depending on the context of the organisation and the cohort of patients. Of particular note is the steady increase in rates of fluoroquinolone-resistance in *E.coli* that has emerged in the community which is concerning given the limited number of oral antimicrobial therapy available.

[3] Clindamycin resistance includes inducible and constitutive resistance (inducible or constitutive) see 2018 AGAR Sepsis Outcomes Report for details of methodology

For more information please visit:
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