MJA
The Medical Journal of Australia

Appendix 1

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.

Appendix to: Harris P, Paterson D, Rogers B. Facing the challenge of multidrug-resistant gram-negative bacilli in Australia. *Med J Aust* 2015; 202: 243-246. doi: 10.5694/mja14.01257.

Appendix 1: Definitions, epidemiology and resistance profiles of MDR Gram-negative bacilli in Australia

	Multi-drug resistance (MDR)	Extensive drug resistance (XDR)	Pan-drug resistance (PDR)
Definition[5]	Non-susceptible to ≥ 3 antimicrobial classes*	Non-susceptible to all but 2 or fewer antimicrobial classes*	Non-susceptible to all available antimicrobials
Frequency in Australia	Increasingly seen in community and healthcare associated infections	Rarely seen in the community, although increasing. Sporadic cases and outbreaks in healthcare settings	Very rare – occasional reports only
Nomenclature and terminology	Often extended-spectrum beta-lactamase (ESBL) producers. AmpC beta-lactamase intrinsic to some species (e.g. *Enterobacter*, *Citrobacter* and *Serratia* spp.) and may be expressed at high levels. AmpC increasingly spread on plasmids to new species. Genes from the $bla_{CTX\text{-}M}$ family are the most common mediator of ESBL harbouring Enterobacteriaceae in Australia and worldwide.	'Carbapenem Resistant Enterobacteriaceae' is used as an umbrella term based on the phenotype (regardless of the mechanism of resistance). Metallo-beta-lactamase (MBL)-producers have been the most common CRE in Australia. Isolates harbouring the bla_{IMP}, gene have been involved in local outbreaks. Importations from overseas include a wider variety of genes including the 'New Delhi Metallo-beta-lactamase' (bla_{NDM}) which originated from the Indian sub-continent. The *Klebsiella pneumoniae* carbapenemase 'KPC' (bla_{KPC}) is a prevalent cause of CRE in many parts of the world including North America and Europe. The gene $bla_{OXA\text{-}48}$ is an emerging cause of CRE especially in patients from North Africa, Turkey and The Middle East.	A subset of XDR bacteria – would usually be described using the same technical terms as XDR bacteria, with additional resistance mechanisms
Typical beta-lactam resistance	ESBL-producers: most penicillins and cephalosporins - key feature is ceftriaxone resistance. May remain susceptible to piperacillin-tazobactam	All penicillins, cephalopsorins and carbapenems. The key feature is carbapenem resistance	All beta-lactam antibiotics

Other resistance	Frequently resistant to some aminoglycosides (e.g. gentamicin), fluoroquinolones (e.g. ciprofloxacin), trimethoprim-sulfamethoxazole, tetracyclines and macrolides. Amikacin activity may be preserved.	Almost always resistant to aminoglycosides, fluoroquinolones, trimethoprim- sulfamethoxazole, tetracycines and macrolides	Resistant to all other antibiotics including 'salvage' agents such as colistin, fosfomycin and tigecycline.
Common Gram-negative isolates in Australia	*E. coli* and *K. pneumoniae* harbouring an ESBL. AmpC producers (e.g. *Enterobacter* spp.) may become MDR by overexpression of AmpC plus other acquired resistance mechanisms (e.g. porin mutations)	*E. coli*, *Klebsiella* spp, *Enterobacter* spp., *Proteus* spp. and others. Carbapenem resistant *Acinetobacter* spp. or *P. aeruginosa* occur in specific patient groups and settings.	Occasionally seen in Enterobacteriaceae, *Acinetobacter baumanii* and *P. aeruginosa* isolates
Common clinical presentations and epidemiology	Healthcare associated infections. Patients with long-term urinary catheters. Nursing home patients. Travellers recently returned from high-incidence countries.	Patients with any healthcare contact in countries of high-incidence (e.g. India, China, Greece) or critical care environments in many countries in North America and Europe. Patients from critical care settings in Australian hospitals that are known to be endemic. Occasionally seen in travellers to endemic countries without healthcare contact	Rare as a primary isolate. Most often seen with the evolution of resistance during treatment of XDR bacteria. Patients usually have significant other illness and have had very extensive antibiotic exposure

*Non-susceptible includes bacteria that are 'intermediate' and 'resistant' in vitro. Antimicrobial categories are available from Magiorakos et al.[5]