Wildlife Health Australia

Antimicrobial resistance and Australian wildlife

Fact sheet

Introduction

Antimicrobial resistance (AMR) is recognized as an issue of emerging global importance. Antimicrobial resistance impairs effective medical and veterinary treatment of bacterial and other microbial infections. It may increase treatment costs and negatively impact animal health, welfare and animal husbandry practices. There is substantial documentation of the existence of AMR in both humans and domestic animals.

In recent years, there has been increasing interest in the presence of AMR in both wildlife and the environment. Free-ranging wildlife populations may act as sentinels for AMR in the wider environment and resistant microorganisms may be cycling through wildlife and back into the ecosystem. Although studies on AMR in wildlife are growing in number, only a small number of studies on AMR in Australian wildlife have been published. There is growing evidence that AMR in wildlife is associated with proximity to humans or domestic animals and that AMR may have an impact on the health of wildlife individuals and populations. A better understanding of the Australian situation is required. Antibiotics must not be used in Australian wildlife unless prescribed by a registered veterinarian and “Critically important antimicrobials (CIA) for human medicine” should not be used in wildlife.

Mechanisms of antimicrobial resistance

There are naturally-occurring antimicrobial producing bacteria in the environment and bacteria have evolutionary abilities to develop resistance to antibiotics. Development and use of antimicrobials by humans has driven the emergence more and different types of AMR. Antimicrobial resistance is commonly seen in many bacterial species, but development of multiple drug resistances are of particular concern (Power 2019).

There are a range of mechanisms by which bacteria may become more resistant to the impacts of antimicrobial agents. These include:

- decreased cell membrane permeability to the drug
- active extrusion of the drug from the bacterial cell
- modification of the cellular target (protein) of the drug
- inactivation of the drug.

Antimicrobial resistance can be acquired through a number of mechanisms, including natural genetic mutation or horizontal transmission of plasmid-located resistance genes (Vittecoq et al. 2016). It is believed that AMR is primarily linked to exposure to antimicrobials (or antimicrobial residues), which select for resistance genes. Thus, clinical misuse of antimicrobial drugs may be the major driving force in AMR (Sayah et al. 2005). A major focus of managing AMR has been to reduce the inappropriate use of antibiotics in both humans and animals. However, it is known that AMR can be promoted through other mechanisms such as the occurrence of naturally produced antibiotic molecules in soil, which may develop a defence from natural competition between different types of soil microbes (Vittecoq et al. 2016).

Transfer of resistant bacteria (or resistance genes) between hosts may occur through direct contact of the host with bacteria or from indirect consumption of contaminated food and water. There is a strong link between AMR in humans and its occurrence in domestic animals (Angulo et al. 2004). Increased convergence of humans and domestic animal with wildlife and environmental habitats (e.g. water sources) are recognised to provide additional opportunities for resistant bacteria to enter the environment.

Antimicrobial resistance and wildlife

Antimicrobial resistance has been reported in wildlife, both in Australia and overseas. However, the role of wildlife and the environment in the spread of AMR, and the relative importance of the various mechanisms by which wildlife may acquire AMR, is not fully understood.

In general, wild animals are less likely to be directly exposed to antimicrobials than domestic animals or humans. AMR genes in the environment may result from a mix of naturally occurring resistance, those present in animal and human waste, and the selective effects of pollutants. AMR detection wildlife (both globally and in Australia) is an increasing correlated with proximity to humans, which indicates **humans are driving the transfer of AMR organisms to wildlife** (Power 2019).

Transfer of AMR between humans and/or domestic animals and wildlife could occur through environmental contamination with antibiotic resistant bacteria, with water being the most significant vector for transmission (Power 2019). Significant pathways include environmental contamination (particularly water sources) with human or livestock waste (Allen et al. 2011; Guenther et al. 2011; Wellington et al. 2013; Radhouani et al. 2014; Greig et al. 2015). Treatment of livestock and aquaculture systems with veterinary antimicrobials may result in AMR contamination of the environment (Barton and Ndi 2012). This may include application of manure from intensive livestock production. Microbes, antimicrobial agents and AMR genes may then be cycled and re-cycled through soil, ground water, marine water, wild animals, crops, shellfish and livestock (Wellington et al. 2013).

Injured, diseased and orphaned wild animals may be taken into human care for treatment, which may include administration of antimicrobial medication, or they may be inadvertently exposed to antimicrobial residues through excreta of other treated animals and humans. Some treated wildlife cases are returned to the wild (once they have returned to health and functionality), but may carry resistant microbes acquired whilst in care, thereby providing a potential avenue for AMR to enter wildlife populations and the environment in general.

Threatened species management may involve captive breeding of wildlife species for release into the wild, as part of sanctioned recovery programs. These individuals may have been exposed to antimicrobials, residues, resistant bacteria or resistance genes during their time in a captive environment. In a similar way to rehabilitated wildlife, release of these individuals into the wild may increase opportunities for AMR to enter the environment/ free-ranging wildlife compartment (Power et al. 2013).

Free-ranging wildlife populations have the potential to act as reservoirs for AMR and emerging resistant pathogens. This role could become more significant as wildlife, livestock and people are brought into closer contact through changes in land use and climate change (Radhouani et al. 2014).

A scoping review of published research evaluated the role of wildlife in transmission of AMR to the food chain, and found that 309 of 866 relevant primary research articles reported AMR in wildlife, with AMR transmission reported in 110 (Greig et al. 2015). Reported risk factors for transmission of AMR/bacteria from wildlife to food animals, environmental sources or humans included presence of wild birds, shared range and contamination of water by wildlife. Proximity to human populations is also known to influence AMR in wildlife (Radhouani et al. 2014).

AMR is also documented as common, or increasing in prevalence, in marine wildlife in other parts of the world (Stoddard et al. 2008; Rose et al. 2009).

Presence of antimicrobial resistance in Australian wildlife

A limited number of studies have examined AMR in Australian wildlife (see Power 2019 for more details).

Mammals

A low, but widespread, prevalence of AMR was found in strains of *Enterobacteriaceae* isolates from 77 species (14 families) of wild Australian mammals, collected from all jurisdictions of Australia (Sherley et al. 2000).

Free-ranging and captive yellow-footed (*Petrogale xanthopus*) and black-flanked rock-wallabies (*P. lateralis*) and Tammar wallabies (*Macropus eugenii*), surveyed in South Australia, were found to be hosts for a number of *Staphylococcus* spp. demonstrating AMR. Resistance to β-lactam antimicrobials was found in approximately one-third of isolates. Multi-drug resistant staphylococci were found in free-ranging wallabies in a remote area (the APY lands of north-west SA) without significant contact with humans or prior exposure to antibiotics (Chen et al. 2014; Chen et al. 2015; Chen et al. 2016).

Integrons associated with clinical AMR were found in almost half the faecal samples from brush-tailed rock-wallabies (*P. penicillata*) in a captive breeding program, later released into the wild as part of a sanctioned species recovery program (Power et al. 2013).

A higher prevalence of *E. coli* and more frequent evidence of resistance genes commonly identified in human clinical cases was found in captive Australian sea lions (*Neophoca cinerea*), compared to free-living individuals from SA and WA. This suggests that factors involved in captive management of wildlife may contribute to establishment of AMR in these species (Delport et al. 2015).

There are unpublished reports of AMR in a free-ranging Australian sea lion (*E. coli*) and New Zealand fur seal (*Arctocephalos fosteri*; *E. faecium*) (Power 2019). There are also limited reports of resistant bacteria in Australian mammals held in captivity overseas (Takle et al. 2010).

The chapter “Antimicrobial resistance” in “Current therapy in medicine of Australian Mammals” (Power 2019) provides a useful overview of the mechanisms of AMR as well as more detail on knowledge in Australian mammalian wildlife.

Birds

An increased prevalence of *E. coli* with virulence-associated genes, and multi-drug resistant strains of *E. coli*, was found in wild birds in Australian veterinary and rehabilitation facilities compared to wild suburban birds (Blyton et al. 2015). Evidence of AMR, including biota apparently derived from humans AMR, was found in gut flora of silver gulls (*Chroicocephalus novaehollandiae*). Silver gulls are a focus of AMR study as they are a highly gregarious species with high levels of contact with humans and other bird species. As silver gulls often feed at waste depots, it is likely that they provide a direct pathway for transmission of bacteria (and their resistance genes) from the human compartment to wildlife (Dolejska et al. 2016; Mukerji et al. 2019). Further evidence of AMR involving *E. faecium* and *E. dispar* was found in colonies of silver gulls in NSW (Oravcova et al. 2017). A wide-ranging study in silver gulls around coastal areas of Australia with high human habitation (n=562) found a widespread and high levels of occurrence of resistance to cephalosporin and fluoroquinolone in *E. coli* and evidence of resistance to carbapenem and colistin (all critically important antimicrobials). There was accompanying evidence that the resistance clones are moving from humans into gulls. It is likely that silver gulls, due to their behaviour and ecology, have the ability to accumulate and disseminate resistant bacteria over very large distances. Silver gulls share roosting sites with other bird species, including those which migrate globally and they inhabit waterbodies alongside ducks and wading birds, which may travel further inland to farming areas, potentially increasing exposure of farmed animals to AMR (Mukerji et al. 2019).

There are unpublished reports of AMR in little penguins (*Eudytula minor; E. coli)* (Power 2019).

Reptiles

Evidence of AMR involving a range of enteric bacteria (including a high level of multiple drug resistance) was found in green turtles (*Chelonia mydas*) from a variety of sites on the Great Barrier Reef in Qld. Samples from turtles involved in rehabilitation were significantly more likely to show multiple drug resistance than samples from turtles at other study sites (Ahasan et al. 2017).

Surveillance and research

Wildlife disease surveillance in Australia is coordinated by Wildlife Health Australia. The National Wildlife Health Information System (eWHIS) captures information from a variety of sources including Australian government agencies, zoo and wildlife parks, wildlife carers, universities and members of the public. Coordinators in each of Australia's States and Territories report monthly on significant wildlife cases identified in their jurisdictions. NOTE: access to information contained within the National Wildlife Health Information System dataset is by application. Please contact admin@wildlifehealthaustralia.com.au.

WHA coordinated wildlife surveillance programs and the national eWHIS database have the capacity to capture data on the occurrence of AMR in free-ranging wildlife. Cases of multi-resistant bacterial infections and AMR in free-ranging wildlife in Australia have been reported to WHA through the national wildlife disease surveillance program. Cases include multi-resistant *Klebsiella* sp. in an eastern grey kangaroo (*Macropus giganteus giganteus*), koala (*Phascolarctos cinereus*), galah (*Eolophus roseicapilla*) and tawny frogmouth (*Podargus strigoides*), resistant *Staphylococcus* sp. (coagulase negative) in a koala, and resistant *Enterobacter* sp. in a bar-shouldered dove (*Geopelia humeralis*), New Zealand fur seal (*Arctocephalus forsteri*) and a koala.

Wildlife populations have the potential to act as sentinels for environmental contamination and may be useful targets for AMR surveillance programs. Research is required to better understand how resistant bacteria move between wildlife, the environment, food and humans and the relative importance of these groups in the maintenance and dispersal of AMR. Surveillance and research could include:

- investigation of the extent of AMR within the Australian free-ranging wildlife population and the environment
- usage of antimicrobials for the treatment of wildlife cases presenting to zoo hospitals, wildlife rehabilitation centres and private veterinary clinics.

Additionally, work is required to understand the potential impact of AMR on the health of wildlife species.

For more information on AMR and the development of the National Antimicrobial Resistance Strategy for Australia, see the websites of the Australian Government Department of Agriculture and Water Resources (www.agriculture.gov.au/animal/health/amr) and Department of Health (www.health.gov.au/internet/main/publishing.nsf/Content/ohp-amr.htm).

Antimicrobial stewardship in Australian wildlife

There are currently no nationally-agreed guidelines for the use of antimicrobials in Australian wildlife with the aim to minimise the spread of AMR. In many cases, knowledge of pharmacokinetics of antimicrobials in wildlife species remains limited. Many antimicrobials are used in an "off-label" capacity in wildlife and doses, frequency and duration of delivery and route of administration may be extrapolated from other wildlife or domestic species. Although there is limited evidence-based data on how best to minimise AMR in Australian wildlife, recommendations on use may be based on current knowledge and best practice in use of antimicrobials across both human and animal sectors.

The following issues should be considered when addressing use of antimicrobials in Australian wildlife:

- Antibiotics should not be used in Australian wildlife unless prescribed by a registered veterinarian.
- "Critically important antimicrobials for human medicine" should not be used in wildlife (WHO 2018).
- Biosecurity and infection prevention and control should be emphasised when working with wildlife, to prevent or minimise the risk of infection. This may include measures such as hygiene, asepsis, isolation, work flow practices, appropriate housing and husbandry and reduction of physiological stress for the patient (see the National Wildlife Biosecurity Guidelines www.wildlifehealthaustralia.com.au/Portals/0/Documents/ProgramProjects/National_Wildlife_Biosecurity_Guidelines.PDF).
- The need to treat wildlife with antibiotics (including the choice of a suitable antimicrobial) should be confirmed through early, thorough and appropriate clinical and diagnostic investigation by the veterinarian (including microbiology and culture and sensitivity).
- The appropriate drug, dose, frequency, duration and method of delivery should be determined by the prescribing veterinarian, based on the information gathered above.
- Patients receiving antibiotic therapy should be regularly reviewed by the veterinarian.
- Extension or changes to treatment regimes should only occur after appropriate case review by the veterinarian.
- The use of other modalities for management of wounds (and in similar situations) in wildlife should be considered, for example best practice wound management, including the use of topical antiseptics surgical debridement and advanced wound care products. Where possible, topical antibiotics should be used over systemic antibiotics.
- Antibiotics should not be used for any other non-antimicrobial purpose, unless backed by scientific evidence (and prescribed by a registered veterinarian for this purpose).

Conclusion

Antimicrobial resistance is an emerging issue for human, domestic animal, wildlife and ecosystem health. The presence and significance of AMR in wildlife (both native and feral) and the environment of Australia should continue to be a focus of research and data collection. Medical treatment of Australian wildlife, including administration of antimicrobials, should be carefully supervised by wildlife veterinarians and the potential for selection of resistant bacteria should be considered when treating and managing all species of wildlife. A precautionary approach is recommended when managing wildlife in a hospital or rehabilitation setting. The wider impact of AMR in wildlife is likely to increase in importance as alterations in land use, climate change, animal movements and human activities bring wildlife, livestock and people into closer contact.

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To provide feedback on this fact sheet

We are interested in hearing from anyone with information on this condition in Australia, including laboratory reports, historical datasets or survey results that could be added to the National Wildlife Health Information System. If you can help, please contact us at admin@wildlifehealthaustralia.com.au.

Wildlife Health Australia would be very grateful for any feedback on this fact sheet. Please provide detailed comments or suggestions to admin@wildlifehealthaustralia.com.au. We would also like to hear from you if you have a particular area of expertise and would like to produce a fact sheet (or sheets) for the network (or update current sheets). A small amount of funding is available to facilitate this.

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