Office of the Prime Minister's
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Kaitohutohu Mātanga
Pūtaiao Matua ki te Pirimia

Antimicrobial Resistance

An imminent threat to Aotearoa, New Zealand

From the Office of the Prime Minister's Chief Science Advisor, endorsed by the Science Advisory Network.

Summary

Before the discovery of antimicrobials in the early 1900s, millions of people died from infections. Antimicrobial resistance is an international problem recognised by the World Health Organisation and the World Bank. Aotearoa, New Zealand has high antimicrobial use in humans compared with other developed countries, increasing our risk profile. Poor communities, Māori and Pasifika, the very young, the very old, immune-compromised, and critically ill patients are most impacted by infections, for which there will no longer be effective treatments, leading in many cases to death. The risk can be mitigated by: reducing unnecessary antimicrobial usage; measures to prevent the spread of AMR organisms; increasing monitoring and surveillance; infection control response systems; and research into how AMR genes enter NZ and are transmitted.

The issue

- Antimicrobial agents (which include antibiotics) were one of the greatest discoveries of the 20th century, saving the lives of countless people and enabling surgeries and cancer treatments to be carried out safely.
- Some antimicrobials are being rendered ineffective globally and people will, increasingly, die from untreatable infections.
- Aotearoa, New Zealand has one of the highest human usages of antimicrobials of any developed country and we are at risk of running out of effective antimicrobials to treat many infections.
- Antimicrobial resistance (AMR) will affect all people. The people most affected by a lack of effective antimicrobials will be Māori and Pacifica, the poor, the young, the elderly, immune-compromised and critically ill, hospitalised patients.
- Animal welfare in NZ and food production in many parts of the world is also dependent on the availability of effective antimicrobials.
- The use of antimicrobials in farmed and companion animals can lead to AMR in humans; therefore, antimicrobial use and AMR in both humans and animals must be tackled together.
- Although we have some NZ data on animal use and responsiveness to intervention, we do not have enough information to help contain the increasing risk of AMR; furthermore, there is incomplete information for use in humans in NZ.

Background

Antimicrobials are drugs that are toxic to bacteria, viruses, fungi, and parasites and have been the most effective medicines in history, saving millions of lives. The most important antimicrobials are antibiotics. The development of resistance amongst bacteria is reducing the effectiveness of these drugs, ultimately meaning people will die from untreatable infections.

Resistance develops when, essentially, all of the pathogens that are susceptible to a particular agent succumb to treatment, and only tolerant and resistant ones remain, passing the resistance genes onto future generations of microbes. The genes that are responsible for resistance can be mobile and can move between bacteria. The problem is exacerbated by the overuse of antimicrobials, which provides an environment in which resistant organisms can thrive. The complexity around the drivers of resistance for bacteria, viruses, fungi, and parasites also presents a considerable challenge. Despite greater coverage of the looming issue, there remains a lack of emphasis on AMR and routes of transmission.

As described by the World Bank[1] antibiotic overuse is analogous to the 'tragedy of the commons', wherein, without effective regulation and governance, a resource is squandered by individuals for their own short-term gain. As effective antimicrobial treatment is part of the global 'commons', containment of AMR represents a global public good.

A global problem

There are some concerning international trends that could also affect NZ's health and economy:

- AMR is a rapidly evolving emergency in global public health that requires action across all government sectors and society;[2]
- Without effective antibiotics, the success of surgery, bone marrow transplants and cancer chemotherapy, and treatment of other serious illnesses will be compromised;[2]
- The cost of health care for patients with resistant infections is many times greater than care for patients with non-resistant infections;[2]
- In 2017, 558,000 people developed multi-drug resistant TB globally and drug resistance is starting to complicate the fight against HIV and malaria, as well.[3]

A recent study in China, where antibiotic overuse among humans and non-therapeutic use in animals is widespread, reported that bacteria resistant to an antibiotic that is the last-line-of-defence (colistin) were present in the gut of 15% of people on average and as high as 33% in one province.[4] Furthermore, the production of animal protein in much of South-East Asia has become dependent on the non-therapeutic use of antimicrobials in swine and poultry. The World Bank[1] estimates that global GDP will decline by 1.1 to 3.8% annually post-2030 because of AMR or between US$1 and 4 trillion annually. Moreover, low income countries would experience greater drops in economic growth than wealthy countries.

The current status in Aotearoa, New Zealand

Currently rates of AMR are relatively low, but increasing, and are disproportionately high in Māori and Pasifika communities. In 2015, community-based patients in NZ had one of the highest use of antimicrobials in the world. For example, per capita use in NZ is up to three times more per person than Norway or Denmark.[5] NZ is in the early stages of an epidemic of a transmissible AMR threat known as CPE (carbapenemase-producing Enterobacteriaceae) that requires a coordinated infection control response at the national level across the entire NZ health sector.[6] Primary-care-based antibiotic consumption increased by 49% from 2006 to 2014 and children's exposure to antibiotics approaches 100% by five years of age.[7,8,9,10] Furthermore, the World Bank highlights that the increased costs associated with AMR will unduly penalise the poor and vulnerable.[1] Indeed, Māori and Pacifica are at greatest risk, with hospital admissions for infection two to four times more common than in NZers of European or Asian descent.[8] Access for vulnerable groups must not be compromised in responses to AMR.

From a Primary Industry perspective, although acknowledged as important by veterinarians, the scale of the risk of AMR is not well understood amongst farmers or veterinarians. Although the NZ Vet Association has a vision to reduce antibiotic use, many veterinarian practices do not have prescribing policies. Although we have assessments of antibiotic use in the human community,[11] data on patterns of antimicrobial use and responsiveness to intervention, we do not have the surveillance data to help monitor and contain AMR.

What is needed urgently in NZ

- Building on existing baseline data,[12,13,14] a detailed assessment of current use of antibiotics, appropriateness of use, and the extent of AMR in humans and animals.
- Laboratory based surveillance in both humans and animals to identify emerging and persisting patterns of AMR.
- Comprehensive use of recording systems for:
    - prescribing and dispensing statistics;
    - data on environmental isolates.
- Research [biological, vaccines, rapid diagnostics,[15] drug development, transmission studies, infection prevention and control, environmental (e.g. on the impact of non-antibiotics that cause AMR), drug development, social, econometric] on the best ways to contain the crisis.
- A widespread and continuing education programme to healthcare professionals, trainees, the public, and in schools on the dangers of inappropriate prescribing.
- Response systems and pathways to investigate and respond to significant changes over time in AMR in both humans and animals.
- A nationally coordinated infection prevention and response plan to address epidemic transmissible AMR threats such as CPE in healthcare facilities. This must include surveillance and response systems and pathways for responding to outbreaks and increases in incidence.

There is a NZ Antimicrobial Resistance Action Plan Governance Group in place. It is, largely, holding a watching brief and is not resourced to achieve AMR containment. Antimicrobial resistant strains are monitored by ESR's Antimicrobial Reference Laboratory[11] and rely on diagnostic laboratories to identify and send isolates.

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References cited

1. World Bank. 2017. Drug resistant infections: a threat to our economic future. March 2017. World Bank Group. http://www.worldbank.org/en/topic/health/publication/drug-resistant-infections-a-threat-to-our-economic-future.
2. World Health Organisation. 2018. Antimicrobial resistance. http://www.who.int/en/news-room/fact-sheets/detail/antimicrobial-resistance.
3. Global tuberculosis report 2018. Geneva: World Health Organization; 2018. License: CC BY-NC-SA 3.0 IGO.
4. Shen, Y et al. 2018. Anthropogenic and environmental factors associated with high incidence of mcr-1 carriage in humans across China. Nature Microbiology. https://doi.org/10.1038/s41564-018-0205-8.
5. New Zealanders consuming lots of antibiotics without benefit. RadioNZ interview with Dr Mark Thomas, Aug 17th 2018. https://www.radionz.co.nz/news/national/364341/new-zealanders-consuming-lots-of-antibiotics-without-benefit-study; Klein, E.Y., et al., 2018: Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci 115 (15) E3463-E3470. doi: 10.1073/pnas.1717295115. Epub 2018 Mar 26.
6. Australasian Society for Infectious Diseases (ASID) position statement: Minimum specifications for New Zealand's response plan for Carbapenemase Producing Enterobacteriaceae. https://www.asid.net.au/documents/item/1492
7. Thomas MG, et al. 2014. Rising antimicrobial resistance: a strong reason to reduce excessive antimicrobial consumption in New Zealand. NZ Medical Journal 127: 72-84;
8. Baker MG, et al. Increasing incidence of serious infectious diseases and inequalities in New Zealand: a national epidemiological study. The Lancet 2012:379(9821):1112-1119.
9. Williamson DA, et al. 2016. Trends, demographics and disparities in outpatient antibiotic consumption in New Zealand: a national study. Journal of Antimicrobial Chemotherapy 71: 3593-8.
10. Hobbs MR et al. 2017. Antibiotic consumption by New Zealand children: exposure is near universal by the age of 5 years. Journal of Antimicrobial Chemotherapy 72: 1832-40.
11. https://surv.esr.cri.nz/antimicrobial/antimicrobial_resistance.php
12. https://surv.esr.cri.nz/surveillance/antibiotic_consumption.php
13. https://www.esr.cri.nz/home/about-esr/our-science-in-action/combating-antimicrobial-resistance/
14. https://www.foodsafety.govt.nz/elibrary/industry/antimicrobial-resistance-in-bacteria.pdf
15. A recent Nature editorial suggesting solutions: https://www.nature.com/articles/d41586-018-07031-7

Further reading

An accessible guide to the science behind AMR: https://royalsociety.org.nz/what-we-do/our-expert-advice/all-expert-advice-papers/antimicrobial-resistance/

An accessible text on AMR by Assoc Prof Siouxsie Wiles: https://www.bwb.co.nz/books/antibiotic-resistance

UK review of AMR: https://amr-review.org/

More on use in animals: Hillerton JE, Irvine CR, Bryan MA, Scott D, Merchant SC. Use of antimicrobials for animals in New Zealand, and in comparison with other countries. New Zealand Veterinary Journal 65, 71–77, 2017.