

Australian scientists lobby for antimicrobial oversight body

Australian microbiologists say that all antibiotic use, human and veterinary, should be coordinated by a new supranational body to deal with growing resistance. Tony Kirby reports.

The days of high infectious disease prevalence in wealthy countries are now in the distant past, partly due to the success of antibiotics. But overuse and misuse of these drugs in both medical and veterinary settings has raised antibiotic resistance to alarmingly high levels. Australian microbiologists have decided that the window for action is shortening, and say that a new supranational body is needed to provide the necessary surveillance, education, and action to deal with this threat. Without concerted action, the experts say that resistance will continue to escalate and the end of the antibiotic era as we know it could be in sight.

Leading the calls are the members of the Australasian Society for Infectious Diseases and the Australian Society for Antimicrobials. At a 2-day crisis conference in Sydney in February, 2011, these and other experts from both veterinary and pharmaceutical spheres gathered to raise awareness of the issue. Members are now lobbying the Australian Federal Government to quickly establish this new body.

Effective surveillance of antimicrobial resistance and use has been identified as a key aspect of any national response. The Federal Government funds the Australian Groups on Antimicrobial Resistance (AGAR) to provide resistance surveillance of a small range of bacteria. But chair Graeme Nimmo says that this is not enough for comprehensive surveillance. "The costs of implementing a fit-for-purpose resistance surveillance system would be negligible compared to the economic losses incurred by having to treat antibiotic-resistant infections in large numbers in the population", he says. "AGAR's budget, currently AUD\$300 000 per year, would probably need to be doubled, plus an initial injection of \$1 million to get the system running." Nimmo adds that

the technology already exists to link up pathology laboratories nationwide, and the small investment required would ultimately prevent resistant infections and related loss of productivity.

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Nimmo and colleagues believe there needs to be a hard-hitting public health and media campaign to target overuse and misuse of antibiotics. Similar efforts in France and Belgium have seen antibiotic use and resistance fall in those countries, while in Sweden and the Netherlands use and resistance has always been low. All of these nations have health outcomes similar to those seen in Australia. A staggering 23 million community antibiotic prescriptions are issued each year across Australia (20 per 1000 population per day—twice the rate seen in the Netherlands). "We can see at least half of the Australian prescriptions are unnecessary...by comparing ourselves to the Netherlands", says John Turnidge, a paediatrician and antibiotic resistance expert at Adelaide's Women's and Children's Hospital. "It is safe to assume that rates and types of infections in the community are similar in the developed world, so there is no reason to suppose that Australians need to be treated more often." Overprescription of antibiotics costs Australians some \$200 million each year, while a system to control use would, says Turnidge, cost just \$2 million yearly.

Australia's Acting Chief Medical Officer, Chris Baggoley, says that the Federal Government takes antibiotic resistance very seriously, and has disseminated an Antimicrobial Stewardship guide, and is developing a comprehensive implementation

process. "In addition the National Prescribing Service is planning a 2-year programme of engagement about the use of antibiotics with community prescribers and with a mass audience, to commence in February, 2012", he adds.

Nimmo says that the attitudes of both patients and doctors must change. "Patients think that antibiotics will always be of benefit and mistakenly put pressure on practitioners for a prescription when it's unlikely bacterial infection is present. Meanwhile doctors, by overprescribing to minimise infection risk, are taking risk management to a level that is really not justified. Whether this changes will come down to the willingness of people to accept some uncertainty when the likelihood of bacterial infection is very low."

Turnidge is concerned about the increasing prevalence of resistant infections requiring more intensive interventions. Such patients need to repeatedly visit their general practitioner (or hospital), have their antibiotics changed, and, in the case of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), must undergo unpleasant drainage of boils either at the general practice or with a specialist. "Multiresistant

See [Perspectives](#) page 1827



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Escherichia coli is another infection on the rise", says Turnidge. "While it's unlikely that there will come a time when none of the common infections can be treated easily in the community, it's much more likely that we will see the costs of treatment spiral to an unsustainable level, because we will have to prescribe new and expensive agents due to increasing resistance."

CA-MRSA is causing problems in younger Australians because several strains contain the Panton-Valentine leukocidin (PVL) gene that causes more severe disease. Older people are less likely to get PVL-positive CA-MRSA because of immunity developed in the past. As a result, the average age of patients contracting PVL-positive CA-MRSA is 33 years, while for PVL-negative strains it is 53 years. Microbiologist Keryn Christiansen, a professor at the Path West Laboratory Service at Perth Royal Infirmary, says that since many firstline antibiotics no longer work against CA-MRSA, secondline treatments such as clindamycin should be the ones that general practitioners prescribe on the patient's first visit, rather than later visits—a big change in practice, but one that Christiansen believes must be brought in quickly.

Australia has also now reported eight cases of bacteria containing New Delhi metallo-beta-lactamase (NDM-1) enzyme that confers resistance on gram-negative bacteria (such as *E coli*) to almost all known antibiotics. Worryingly, in South Korea, there have been cases of completely resistant microbes. "Death would be very likely in such cases, since the higher the level of resistance, the higher the levels of mortality", says Nimmo. One function of the proposed new antibiotics oversight body would be to drive innovation for new antibiotics to crack this new wave of superbugs. Currently, drug companies do not see that big profits can be made since antibiotics have a shelf-life and restricted application. "One solution could be wildcard patents, where companies get an extended patent

for a profitable drug if they come up with a new antibiotic for public health benefit", says Nimmo.

"We sometimes forget that antibiotics regularly save many people from almost certain death", says Christiansen, who points out most of modern medicine is dependent on antibiotics, such as prophylaxis in joint replacement, complex abdominal surgery, transplantation, and cancer care. The experts agree that resistance taking hold in hospitals across Australia would have a big effect on the risk-benefit analysis of all these currently routine procedures.

The veterinary world must also play its part in any move to control antibiotic resistance. In animals, antibiotics are used for growth promotion and prophylaxis as well as acute infection. Yet while human antibiotic use in Australia is very high, Australia can draw on some past successes to illustrate the importance of effective antibiotic control in animals. In the 1990s, many developed and developing countries began using fluoroquinolone antibiotics in their livestock, but Australian experts predicted this could cause an epidemic of resistance. The then Federal Government subsequently did not authorise use of these drugs in food-production animals. As a result, resistance to fluoroquinolones such as ciprofloxacin in pathogens infecting Australian people is very low compared with other nations.

"Many livestock managers believe all their flocks or herds will die if they do not use continuous in-feed or in-water antibiotics, or there will be a major loss in production", says Peter Collignon, Canberra Hospital and Australian National University. But he points out that Denmark and other European countries have shown withdrawing routine in-feed antibiotics caused no difference to mortality in pigs or chickens, nor any loss in production or weight gain. Vets worldwide, especially those with a public health focus, are attempting to put this issue under the spotlight.

"There is always defensiveness in the livestock community, since some of its members believe that overprescription to humans causes all microbial resistance issues and that livestock farming is being unfairly blamed", says Collignon. "While it's true some resistant microbes have nothing to do with agriculture (eg, pneumococcus), many have an agricultural origin, such as salmonella and campylobacter. For *E coli* a lot of resistance comes through the food chain with food animals as the initial source. Agricultural antibiotic use is also becoming a factor in some cases of human MRSA."

As well as surveillance and education, the new antibiotic management body would also ensure that resistance is factored into whether drugs stay on the Federal Government's drug benefits scheme (making some more expensive thus preserving them for essential use only). They also believe there should be a new call from the National Health and Medical Research Council (NHMRC) for research grant proposals into human and animal antibiotic epidemiology and interventions.

"Given there are already a number of actors in this area, the Australian Government does not support the establishment of another agency but rather supports high-level co-ordination of approaches to these issues", says Baggoley. He says that this is already happening between the key players, including the Department of Health and Ageing and the Department of Agriculture, Forestry and Fisheries. These departments work with agencies such as the NHMRC, and the National Prescribing Service to develop a comprehensive strategy to respond to antimicrobial resistance.

But Nimmo and his colleagues believe that this action is not enough. "The scourge of antimicrobial resistance has increased inexorably over the years. The window for overcoming this problem is still open, but we must act decisively now."

Tony Kirby