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Keeping drug-resistant superbugs off the table

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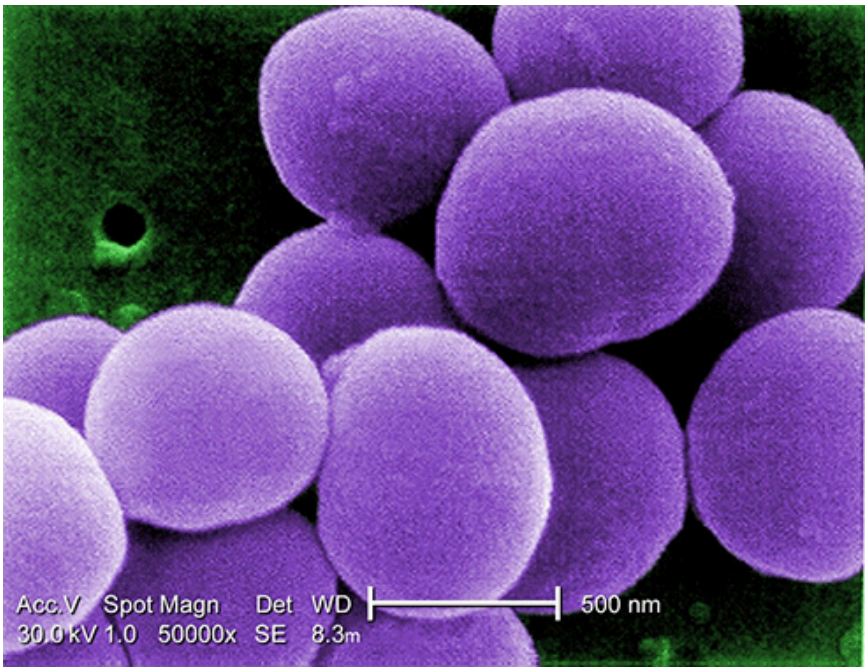
It's little wonder that Professor Lindsay Grayson has become a fierce advocate for legislative change to stop antibiotic-resistant superbugs from making their way into our food supply.



Credit: Centers for Disease Control & Prevention Public Health Image Library

Compared with just a few years ago, the director of infectious diseases and microbiology at Melbourne's Austin Health is already seeing stark differences in patients' responses to treatments.

'Before we do prostate biopsies, we screen patients who've recently been travelling to high-risk countries, such as China, India and Southeast Asia, for superbugs,' Prof Graysontold a senate inquiry last year.

'Increasingly we're finding that they're positive, so we need to give them an infusion of antibiotics to prevent infections because the tablets we would have given them three years ago will no longer work.

'In some regions, resistance rates for urinary tract infections also rose from 5 per cent to 20 per cent in a five-year period.'

Professor Grayson has described antibiotic-resistant superbugs as a 'tsunami on the horizon.'

It's not just hospital environments incubating these deadly pathogens. In northern China last year, tests at two sewage treatment plants turned up masses of proliferating 'superbugs' carrying a multi-drug resistant gene known to enable common bacteria – such as *E. coli*, *Salmonella spp.* and *Klebsiella pneumonia* – to survive even the strongest antibiotics. After the superbugs escape the water purification process, they can spread the resistance gene to otherwise benign bacteria in downstream soils, rivers and drinking water supplies via DNA fragments called plasmids .

Elsewhere, in the Netherlands and other parts of Europe where antifungal sprays are commonly used on crops, fungal infections among leukemia patients and others with compromised immune systems no longer respond to antifungal drugs.

Currently in Australia, regulations vary and are haphazardly enforced. In fact, selling products contaminated with antimicrobial-resistant (AMR) pathogens is technically not illegal.

The *Australia New Zealand Food Standards Code* sets maximum limits for antibiotic residues in food, but individual state and territory agriculture departments control and monitor antibiotic use.

Food imports are randomly tested for residues at the border. Just how frequently a product is tested depends whether it is considered low or high risk – and can vary from 5 per cent to 100 per cent of the time, respectively, according to a spokesperson for the Department of Agriculture, Fisheries and Forestry.

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DAFF also tests a small number of samples through the Australian National Residue Survey. According to Food Standards Australia, the residue survey shows less than 1 per cent of these samples exceed the Australian Standard for antibiotic residues.

A negative test result for antibiotics, however, is no guarantee a product is not contaminated with superbugs, as Prof. Grayson points out.

For example, in Europe, some chickens are routinely fed ceftiofur, a third-generation cephalosporin closely related to an antibiotic used in humans. Producers simply stop administering the antibiotic two weeks prior to sale: the latter being the time when animals are tested.

‘There may not be any drug left, but [a chicken] can still have the consequences of its previous use [ie a cargo of antibiotic-resistant bacteria],’ Grayson explains.

‘They’re relying on the fact there’s no legislation that requires food be free of superbugs [rather than just the antiobiotic itself].’

Professor Grayson, and others including Greens Senator Richard Di Natale, who pushed for last year’s senate inquiry into the lack of action on superbugs, argue that comprehensive legislation is essential. They are calling for a ‘One Health’ approach with comprehensive monitoring to ensure drugs are being used as appropriately – and sparingly – as possible, in both humans and animals.

There are some indications that change is on the way, albeit slowly. In its 2013-14 budget, the previous federal government committed $11.9 million over three years to develop a Australian National Antimicrobrial Prevention and Containment strategy. Last month, Professor John Turnidge was appointed to lead a national surveillance program focused on human antimicrobial resistance.

‘Our sense is that Australian food production is much safer than overseas – the regulations are in place, they’re not policed as well as they should be, but in general people do the right thing,’ says Prof. Grayson.

‘[However] we need a program that allows for routine testing of Australian foods, so we don’t just think it’s safe, we can prove it’s safe.’

Dr Pat Mitchell, a Victorian farmer and Research and Innovation Manager at Australian Pork Limited, agrees.

'Everyone should be subject to the same laws,' she says. 'If we're playing the game, we'd just like to be on a level playing field. What's the point of bringing in cheap food that's going to constitute a food safety issue?'

Credit: Graham Beards/Wikimedia Commons/CC BY-SA 3.0

In 2007 the World Health Organization released a list of 'critically important antibiotics to human health' and recommended against their use in food production. Some countries are following those guidelines better than others. So, while Denmark has banned the use of antibiotics as growth promoters (because some antibiotics have been traditionally used to improve animal growth and meat production), recent data from the pig industry found minimal change in overall volume of drugs used.

This is because producers are now 'relabelling' their use, according to Professor Grayson. 'None of the major countries fully adhere to that list. There's huge market pressure on price.'

Still, the Netherlands and Scandinavian countries are pushing ahead with integrated monitoring and management of antibiotic use in both humans and animals. Professor Turnidge and his colleagues are looking at this as a model for Australia.

'It's going to be three to five years before that occurs, because we need to build legislation and we need all the states and territories to sign up,' he says. That consensus has proved challenging in the past. In 1999 an extensive report and recommendations known as JETACAR were developed – most of which were never implemented.

'That essentially faded away, and a year ago a senate inquiry looked at why, and now we're back where we were in 2000,' Professor Turnidge says.

Despite the setback, Professor Turnidge remains optimistic. 'A lot of other things took precedence, such as concern over pandemics, but this time there's an understanding that we can't allow it to fade away again.'

CSIRO has been investigating alternatives to antibiotics, including new vaccines as well as agents to improve the effectiveness of existing vaccines, says Dr John Lowenthal, a research leader at the CSIRO's Biosecurity Flagship.

For example, researchers have been studying the use of cytokines – proteins naturally produced by the body's immune system following infection – to protect against disease, reduce inflammation, and enhance effectiveness of vaccines. (Vaccines generally do not have the problem of resistance because they enhance the body's natural defences, whereas an antibiotic operates separately from the body's normal defences.)

One particular cytokine known as gamma interferon has already been trialled in chickens, leading to better health, weight gains of up to 10 per cent, and increased protection from disease. However, Dr Lowenthal says it could be another decade before commercial products are readily available, as the regulatory process for approval is lengthy.

Such delays do not dampen the enthusiasm of some to keep pushing for change. 'I feel optimistic in the sense that, from a grass roots level, there's enormous support,' says Professor Grayson. 'What's maybe a bit frustrating is the very slow way that bureaucracy changes.'

Crisis becomes opportunity to cut back on pig-farm antibiotics

You don't have to tell Australian Pork Limited's Dr Pat Mitchell about the challenges of containing outbreaks among farm animals. When respiratory bugs broke out among the pigs on her fourth generation family farm seven years ago, the farm followed best practice protocol, selling its entire stock and scrubbing and disinfecting every last crevice of space.

Contented pigs: improving ventilation, hygiene, stocking rates and diet can help reduce disease rates in pigs, along with vaccination and minimal use of antibiotics. /CC BY-NC2.0)

Six months later, however, the infections returned. Not long after that, pig prices plummeted and feed prices rose. Losing money, the family closed the piggery and sold off all the pigs. During an ensuing two-year break, concern over the rise of antibiotic-resistant superbugs in the community escalated, prompting the family to minimise the use of antibiotics after re-establishing the farm.

They use vaccines where they can and have focused on improving farm management practices. That means things like targeting stocking rates, ventilation and hygiene, as well as techniques such as adding organic acids to the pigs' drinking water and feed to ensure the pH of the pigs' digestive systems inhibits the growth of harmful bacteria.

It's an approach that more Australian farmers and industry bodies are voluntarily making. In fact, Australian Pork Limited and the Pork CRC have funded more than 40 projects looking at ways to better monitor bacteria, reduce antibiotic use, and develop new diagnostics to better identify disease organisms and their mode of attack, enabling more effectively targeted prevention and treatment.