Antibiotic resistance: applying the lessons of the past

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Professor Dame Sally Davies, the Chief Medical Officer for England, created a media storm with her evidence to the House of Commons Science and Technology Committee in January. She said, ‘It is clear that we might not ever see global warming; the apocalyptic scenario is that when I need a new hip in 20 years I’ll die from a routine infection because we’ve run out of antibiotics’.

She would like antibiotic resistance to be added to the government’s National Risk Register of Civil Emergencies, joining flu pandemics, terrorist attacks and catastrophic floods like the 1953 North Sea storm surge that killed 307 in England, 19 in Scotland and more than 200 at sea (the last time a national emergency was declared for the UK). Volume 2 of Dame Sally’s annual report Infections and the Rise of Antimicrobial Resistance, published in March, provides the evidence.

If I were an orthopaedic surgeon I might jibe at the notion that routine infections follow hip replacements on a regular basis – they don’t, because the obsessional implementation of measures to prevent infection has been the norm ever since Professor Sir John Charnley pioneered the procedure 50 years ago.

But, as a microbiologist, it is hard for me to disagree with Dame Sally’s rhetoric. It is a good guess that in time some of the MPs she was addressing will need hip replacements, and she was right to scare them so, because antibiotic resistance making the treatment of infection more difficult, more complex, more expensive and sometimes impossible is one of the big problems facing healthcare policymakers everywhere.

Emergence of resistance
Antibiotics have been the victims of their own success. Sir Alexander Fleming said in his 1946 book on penicillin that ‘Press publicity in the last few years has given many people the idea that penicillin is a panacea, but throughout the book it is emphasised that penicillin is not a ‘cure-all’ . . . many patients will demand it from their doctor . . . perhaps this volume will help the doctor to resist the pressure’.

Inappropriate prescribing and poor adherence have contributed to the emergence of resistance. The counsel of perfection is to prescribe antibiotics only after a microbiological diagnosis with antibiotic sensitivities has been made. But waiting is often not an option. Pneumonia needs rapid attention.

About 80 per cent of antibiotic prescriptions in the UK are in the community. Most prescriptions are empirical, relying on the clinical acumen of the prescriber. It is hard to see fundamental changes in this regard happening quickly. Rapid microbiological testing has made many advances, but obtaining therapeutically useful information at the bedside in minutes is not in sight for most common pathogens.

Mechanism and spread of resistance
Antibiotic resistance is an evolutionary response to antibiotic attack. Minority members of a microbial population already with resistance mechanisms gain a selective advantage and become dominant, as penicillinase-producing Staphylococcus aureus strains did in the 1940s.

Sometimes the selection of a mutation leads to resistance developing very rapidly, as happens with rifampicin, which binds to the enzyme RNA polymerase, stopping the synthesis of messenger RNA. About 1 in every 100 000 bacteria have RNA polymerase molecules with a mutation that doesn’t affect the function of the enzyme but makes it resistant to rifampicin. They grow unhindered in its presence.

The development of antibiotic resistance during treatment is bad for a patient. But by far the most worrying aspect is its spread. Genetic studies indicate that MRSA has only evolved on a very few occasions. But they have spread nationally and internationally, mostly from patient to patient and from carriers.

And antibiotic resistance genes spread within bacterial populations as well. DNA is transferred by bacteria having sex, being infected with viruses, and by taking up naked DNA itself. Such events are happening in your intestines while you read this editorial.
**What is to be done?**

Lessons from the past are there. Apply them. Ever more rational antibiotic prescribing will reduce the selection pressure fostering the emergence of resistance. Preventing the spread of resistant strains requires obsessional and vigorous infection control (we didn’t take MRSA seriously enough in the UK decades ago and patients paid a heavy price). Robust surveillance is essential because microbes evolve in real time.

But one thing from the past now looks like a forlorn hope. Whenever resistance appeared, Big Pharma came up with a new drug. Now, all the obvious bacterial targets have fallen. And spending half a billion on developing a drug that might fail, and if successful cures after a few days, is a very challenging business proposition. Dame Sally is right to be worried. So should we be!

**Declaration of interests**

None to declare.

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