ANTIBIOTIC RESISTANCE: ARE WE ON THE BRINK OF A GLOBAL HEALTH DISASTER?
Nearly 90 years after the discovery of penicillin, governments and health organisations across the globe are facing up to a deeply alarming reality: the increasing resistance of infectious bacteria to antibiotics. **Katie Lewis** asks what is being done about this – and what the future holds for the treatment of infectious disease.

**IMAGINE A WORLD** where it is impossible to safely administer innovative cancer treatments or surgical transplants. A world where intensive-care medical procedures – such as stent implantation and surgical operations – are simply too risky to perform because of the access they give bacteria to the bloodstream. A world where the act of childbirth could easily be fatal or where a common strep throat could lead to death.

This is a world without antibiotics – the drugs that treat or prevent bacterial infection, the drugs that we have grown to rely on so heavily. This is a world that existed not that long ago.

Take the unfortunate case of Albert Alexander as an example. In December 1940, he was accidentally scratched by a rose thorn – from which he picked up an infection that ravaged his whole body, causing abscesses to erupt on his head and the necessary removal of one eye. This Oxfordshire-based police constable became the fourth ever patient to be treated with penicillin, but although his condition improved as a result of the drug, limited supplies meant that the meagre resources ran out by the fifth day of treatment. On 15 March 1941, he died.

**DEADLY DRUG RESISTANCE**

Fast-forward 75 years to today, and death as a result of a minor scratch seems almost unimaginable. But behind the glossy exterior of 21st Century healthcare lies a disturbing truth: just a few generations after they were first discovered, antibiotics have begun to lose their efficacy.

To scientists and health practitioners, this does not come as a shock. The decline in effectiveness of antibiotics has been a creeping, insidious trend for decades – in fact, it is something that Sir Alexander Fleming, the pioneer of penicillin treatment, warned might happen. Upon accepting the Nobel Prize in Medicine in 1945, he said: “There is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant”.

It seems that Fleming’s prophecy has come true. With the increasingly widespread – and often inappropriate – use of drugs over the years, more and more strains of bacteria have developed resistance. In November 2015, scientists in southeastern China raised international alarm when they noticed a rogue gene present in many bacterial samples they had collected from hospitals in the region. Named MCR-1, this gene secretes an enzyme that makes bacteria resistant to colistin – a powerful antibiotic used as the last line of defence against a range of infections. Most researchers agree that the gene emerged as a result of the overuse of colistin in farm animals – and it is deeply concerning because drug resistance genes can be passed from one bacterial cell to another and between different types of bacteria.

It is therefore unsurprising that antibiotic resistance has been termed the “single greatest challenge in infectious diseases today” by the World Health Organization (WHO)’s Assistant Director-General for Health Security Dr Keiji Fukuda. Across the world, it is estimated that 700,000 people die each year as a result of drug-resistant bacteria – and a report from the Review on Antimicrobial Resistance predicts that this number will rise to 10 million by 2050 if current trends continue unabated.
Against this frightening backdrop, what is being done to tackle the problem of antibiotic resistance — and is it possible to prevent an antibiotic apocalypse in the future?

SHOULD GOVERNMENTS BE DOING MORE ABOUT ANTIBIOTIC RESISTANCE?

According to many experts, governments are not doing enough to combat antibiotic resistance. A WHO report on global antimicrobial resistance published in April 2015 revealed that only a quarter of the 133 countries that responded to a WHO survey have national plans in place to preserve antimicrobial medicines like antibiotics. Moreover, major gaps were identified across all six WHO regions when it comes to preventing the misuse of antibiotics and reducing the spread of antimicrobial resistance. The report also highlighted that public awareness of the issue is low in all regions and that there is a notable lack of programmes to prevent and control hospital-acquired infections.

Professor Colin Garner, Chief Executive of Antibiotic Research UK tells International Innovation that governments need to undertake a raft of actions to combat the threat of antibiotic resistance. “These include simple infection and prevention control, reducing the use of antibiotics in agriculture, educating the public and professionals to safeguard our existing antibiotics, not allowing antibiotics to be purchased over the counter, delinking the relationship between new antibiotic sales and revenues — and generally raising the profile of antibiotic resistance and antibiotic drug development,” he says.

On a positive note, there is growing recognition of antibiotic resistance — and this has led to its increased prominence in high-level policy debates. Antibiotic resistance was one of the main topics in last June’s G7 Summit, where more countries committed to introduce and advance effective control strategies. In the US, for instance, the Federal budget passed in late 2015 increased spending in this area by $375 million and the National Institutes of Health (NIH) has received $100 million for antibiotic resistance research.

Meanwhile, back in January at an event at the World Economic Forum in Davos, Switzerland, a Declaration was released that had been signed by companies representing nearly the entire global drug industry. It put forward a plan to tackle drug-resistant infections, calling for the better and more appropriate use of existing antibiotics and for increased investment in R&D for new antibiotics.

THE CASE FOR DRUG DEVELOPMENT

Developing new antibiotics capable of combating emerging forms of resistant bacteria is crucial. In fact, a major reason for the current crisis is that not enough new drugs have been developed in recent decades. Put off by high costs and the rapid loss of efficacy, most major pharmaceutical companies stopped making new antibiotics years ago. Between 2004 and 2014, only nine new antibiotics were approved by the Food and Drug Administration (FDA) — presenting a stark contrast to treatments for chronic diseases, where more than 400 medicines were in development in 2014.

Because the most easily discoverable antibiotics have already been found, scientists today are left with the difficult, expensive and time-consuming task of finding new and potent chemicals for drug development. Garner from Antibiotic Research UK points out that basic research into resistant bacteria needs to be much better funded by governments around the world.

“Tackling antibiotic resistance, however, is not just about money but new ideas,” he adds. “Until antibiotic research is an attractive career path for young scientists, we will not find these new innovative approaches.”

WHAT DOES ANTIBIOTIC RESISTANCE MEAN FOR FUTURE TREATMENTS?

The question is: are we on a one-way track towards a world where there are no longer any effective treatments? According to Professor Laura Piddock, Director of Antibiotic Action, such a scenario is “extremely unlikely”. In an interview with International Innovation, she points out that there are still “many effective drugs for many infections” and that new drugs are in the pipeline, with 39 potential new antibiotics currently in development for the US market.

Because bacteria evolve very quickly — that is, they develop mutations that make them resistant to drugs and/or pass drug resistant genes between bacterial cells and strains — the development of resistance is a natural phenomenon that will never be completely eradicated by human efforts. However, collective global action can certainly go some way towards mitigating its effects.

“There is no ‘one way’ to combat antibiotic resistance,” says Piddock. “The issue requires a multidisciplinary approach. We need new drugs. We also need to preserve the effectiveness of the drugs that we do have — and we need to stop the spread of antibiotic-resistant bacteria by using them very carefully.”

Interestingly, other less orthodox treatments aimed at killing bacterial infections are beginning to gain traction. Phage therapy — the use of viruses to kill bacteria pathogens — has been used for decades in Russia, and current research is exploring avenues for introducing medicinal phage products in the West. Meanwhile, fecal transplants for addressing Clostridium difficile colitis — a sometimes fatal condition caused by a disturbance in the normal bacterial flora lining the colon — have been publicly accepted in some European countries including the UK.

Ultimately, winning the war against antibiotic resistance and ensuring the continuation of effective treatments against infectious diseases is an uphill challenge. Yet it seems that it is a challenge that can be overcome through the ingenuity of scientists, sustained resource allocation and stronger public awareness of the issue. If we want to avoid any repetitions of the Albert Alexander case, we all have a responsibility to take action.