

# Pandemic preparedness: no time to wait on drug resistance

To tackle the 'second pandemic', we need global co-operation as we learn the lessons of the Covid-19 pandemic: this was the crux of the message at the British Council and UK Science and Innovation Network's event, Pandemic Preparedness: no time to wait on AMR', which took place on 16 March.

Antimicrobial resistance (AMR) is a natural phenomenon. Bacteria, viruses, fungi and parasites evolve over time until they no longer respond to the drugs we've devised to keep them at bay. This makes infections harder, or impossible, to treat. Unchecked, drug resistance will herald a post-antibiotic era, and the end of medicine as we know it.

In the face of this threat, pressure is growing for meaningful action – and one of those putting that pressure on is the keynote speaker at the event, Professor Dame Sally Davies, the UK's Special Envoy on antimicrobial resistance, or AMR.

Dame Sally was Chief Medical Officer for England and Chief Medical Adviser to the UK government from March 2011 to September 2019. She now advocates globally on tackling AMR. Her style is as straightforward as the title of her book on the subject, <a href="The Drugs Don't Work">The Drugs Don't Work</a>. It comes across whether she is describing the reasons for the overuse of medicines – 'Antibiotics have become a sticking plaster for weak health systems, or a preventive measure for unhygienic living conditions. After all, they're cheaper than hygiene.' – or reminding us of the role we all play in the build-up of drug-resistant microbes, spreading through our oceans on microplastics, and through our agricultural practices: 'Just remember that animals, and I include us, pee or poo more than 70 per cent of an antibiotic out into the environment.'

# Why a 'second pandemic'?

At first, it may seem that Covid-19 and antimicrobial resistance share little common ground. However, the statistics of drug resistance are startling. Every year at least 700,000 people lose their lives to drug-resistant infections. 'This includes 23,000 in the US, 33,000 in Europe and over 60,000 new-born babies who die of neonatal infections – that's sepsis – in India even though each of these deaths could be prevented,' Dame Sally reminded the audience at the event. 'This figure is going to rise to 10 million by 2050 if we don't take action.'

Dame Sally stressed that we have an opportunity now to galvanise the world against the emerging threats of these two forms of pandemic.

'AMR remains mine and world's biggest challenge,' she said, 'and this is really important at the moment because here we are in the midst of not just one pandemic, but two. Covid is that acute pandemic of the media headlines. But AMR is that chronic, silent pandemic... the slow one that continues to grow in the background and around the world.'

### The 'first' pandemic fuelling the 'second'?

However, the reality of frontline medicine shows why there are no easy solutions. Dame Sally cited a recent study, focused primarily on China, the US, Italy and South Korea, and covering the first major wave of Covid-19 to June 2020. 'This indicated that around 75 per cent of Covid-19 patients receive antibiotics, despite the fact that only 3.5 per cent – and 14.3 per cent of patients when they're hospitalised – have bacterial co-infection and need antibiotics. This is where policymaking faces the stark realities of the pressures that clinicians are under in hospitals over the world.'

Increased surveillance of this phenomenon of Covid-19 exacerbating drug resistance is already underway in many countries. Another speaker at the event, Professor Boyana Beovic, specialises in intensive care and is assistant medical director of the University Medical Centre in Ljubljana, Slovenia. For the past two years has been president of the Intersectoral Coordination Mechanism for Prudent Use of Antimicrobials at Slovenia's Ministry of Health.

Professor Beovic discussed a survey she is conducting to tease out data on the use of antibiotics during the pandemic. The hope had been that use might have fallen, given expectations of lower numbers of patients in surgical wards, that hospital wards in general might be less crowded, and that personal protective equipment and infection control measures would be in place.

Answers have come in from 23 countries and 82 hospitals. 'The results were quite heterogeneous and discouraging. Actually, in most of the countries 70 to 80 per cent, and in some of some countries like North America *all*, of the patients admitted for Covid received antibiotics on admission,' she said. What's more, she added, the antibiotics in use were broad spectrum drugs. 'As time went on, at least in our country, we observed quite a lot of resistant bacteria.'

Preliminary results from other countries are showing similar results, an increase in the use of broad-spectrum antibiotics and an increase in resistance. Professor Beovic also highlighted the inevitable and unavoidable reliance on unskilled staff in clinical settings. This had not

helped, she said, as infection control measures were followed less strictly. In her view, at least for a while, the pandemic has not dented the drug resistance problem. If anything it may have fuelled it.

# Crucial to cooperate

Monitoring data across many countries is just the start of trying to understand – and tackle – the increase in AMR.

Dame Sally is determined to focus minds in the year ahead as the world tentatively looks beyond Covid-19 to a number of international meetings. These include the G7 Summit in Cornwall in June, and the UN's COP26 meeting on climate change in Glasgow in November, both under UK presidency and both opportunities to garner worldwide support for new ways to tackle the issue of antimicrobial resistance.

One approach might be to ensure it is discussed in the powerful finance sections of these meetings, not just in the health tracks. The aim is to persuade nations to view tackling drug resistance and pandemic preparedness as an investment, not a consumable.

Dame Sally is clear that it is urgent we use the lessons of the past year, because climate change and environmental degradation are now intersecting with human health in a three-way crisis made real by Covid-19.

Some lessons are simple, but powerful, such as rigorous infection control to break the chains that allow microbes to thrive. Others include the need for clear communication and the critical role of global cooperation, both political and scientific. Then there is the need to strengthen public health systems and surveillance, whether through traditional epidemiology or by tracking genetic evolution.

#### Tackle both issues together - together

However, there are some bright prospects ahead, as some of the event's speakers made clear.

Dr Agata Starosta is researching the detailed inner workings of a spore-forming bacteria, called *Bacillus subtilis*. In 2018, she was awarded a fellowship for young researchers from the Ministry of Science and Higher Education in Poland. She described a process called 'quorum sensing', a form of bacterial messaging.

'Quorum sensing is a way for bacteria to communicate, so if they come from the same species they have similar chemicals and they can sense that. If it's a foreign bacterium then they know, they can kind of smell that. So some of those preying bacteria use this mechanism to kill other bacteria or control their growth in their surroundings.'

She made clear this is early, basic science, but promising for the future.

Dame Sally is a strong supporter of the promise of innovation. 'Covid-19 is the first pandemic we're facing in our digital age. Using technology and data to overcome it and

strengthen our health systems in doing so is an opportunity we must not pass up, not least because it helps us to work collaboratively across borders and languages.'

Dr Tomas Szemes is a molecular biologist, head of the Genomics and Bioinformatics Laboratories at the Comenius University Science Park in Bratislava in Slovakia, and R&D director of a biotech start-up called Geneton. His research focuses on the human genome and the genomes of microbes. In particular, he sees promise in the use of so-called 'phage therapy', using phages, the 'enemies of bacteria', as he called them.

Phages are easily produced, have few side effects, and are specific to a particular strain of the bacteria. Their downsides are they are not easy to model and they don't actually kill the bacteria, but rather reside within them.

Nevertheless, Dr Szemes sees potential for the foundation of personalised treatments. This would see scientists rapidly diagnose the genomics of a patient's infection, then devise a focused individual therapy for that patient, perhaps using a cocktail of targeted phages.

Finally, Professor Serap Suzuk Yildiz, clinical microbiologist in the Ministry of Health Microbiology Reference Laboratory at the Department of National AMR Surveillance in Turkey, told the meeting about a national action plan focussed on detailed surveillance, for which Turkey is acting as a pilot. The project aims to be an early warning system. It is tracking drug resistance in its own population, and that of Syrian refugees, and expects to report in the summer of 2021.

#### **Consumer pressure**

One important shift is the result of increased consumer awareness of the issue. A number of fast food chains in the US now display notices indicating that they do not use antibiotics. Investors too are choosing not to support food producers unless they move away from antibiotic use in their supply chains.

In the meantime, Dame Sally continues to raise awareness of barriers to pandemic preparedness as these are highlighted by her work on drug resistance. Put simply, these include the overuse and misuse of antimicrobials, and structural and societal inequities. Dame Sally is clear about her goal. 'Antimicrobial treatments are the bedrock of modern medicine. We don't want to lose that. They should be classed along with water and sanitation as infrastructure for health.'

Education and data, as always, are key, as is the fight against misinformation, Dame Sally said. She cited an online debate in Romania which featured an audience survey of 45,000 people. Some 15 per cent of respondents still believed antibiotics treat viruses.

Nevertheless, she remains optimistic. 'Our evidence has to have the power to change the narrative and secure health outcomes not only for Covid-19, but for AMR as well. And we've got to learn to communicate more effectively to everyone.'

By Susan Watts - Moderator, Covid-19 Dialogues, 2021