

DEBATE SUMMARY

Responding to the rapid increase of Antimicrobial Resistance (AMR) in organisms

Held at The Royal Society on 4th June, 2014

The Foundation is grateful to the Wellcome Trust and the Technology Strategy Board for supporting this debate.

The hash tag for this debate is #fstamr .

Chair: **The Earl of Selborne GBE FRS**
Chairman, The Foundation for Science and Technology

Speakers: **Dame Sally Davies DBE FRS FMedSci**
Chief Medical Officer for England, and Chief Scientific Adviser,
Department of Health
Dr Jeremy Farrar OBE FMedSci
Director, The Wellcome Trust
Professor Patrick Vallance FRCP FMedSci
President, Pharmaceuticals R&D, GSK

DAME SALLY DAVIES said that the threat posed by AMR could not be overstated. Modern medical practice relied upon the widespread availability of effective antimicrobials but resistance to them was rapidly increasing and mortality was rising. AMR was probably now responsible for as many deaths in the UK as road traffic accidents. The ability of bacteria to develop resistance was currently the biggest issue but the threat from other micro-organisms was also growing.

But at the same time as the threats to human and animal health were growing, the ability to counter those threats by new drugs was diminishing. No new class of antibiotics had emerged for a quarter of a century. In part this might be due to the fact that microbiology had become a Cinderella science. In part it might be the consequence of drug companies finding that the incentives for innovations in other fields were much greater; after all a key element in any strategy for combating AMR is to restrict the use of antibiotics and ensure that they were prescribed only in countries and for diseases where they were really needed – not an encouraging message for those seeking a good return from costly drug development programmes.

A new business model was needed to make antibiotic research and development more

attractive. As examples of misuse of valuable antibiotics Dame Sally pointed out that in the USA 80 per cent of antibiotics consumed were used in animals; treatment with drugs was cheaper than prevention through improved hygiene. A particular problem in combating AMR was that it had to be tackled globally; borders were porous to microorganisms and the bad consequences of misuse of antibiotics in one country could rapidly be spread to others. The fight against AMR had to be fought in a variety of different ways: science, economics, healthcare practices (such as those which had helped to bring MRSA and *Clostridium difficile* infection under control) and international collaboration. Dame Sally concluded by urging all present to participate in the BBC public vote for the 2014 Longitudinal Prize¹ and press for the prize challenge to be “AMR – development of a rapid diagnostic”.

DR FARRAR said that his early career experience in a London hospital in the 1980s with HIV patients had left him with fear of being confronted with untreatable diseases. The growth of AMR was resulting now in the emergence of more untreatable diseases. If antibiotics became ineffective, existing

¹ www.bbc.co.uk/programmes/b006mgxf/vote

medical practice for surgery, childbirth and oncology would be unsustainable. In confronting this threat we needed to think globally and across all ages and species. In science micro-biology needed to work closely with pharmacology so that we understood better the way in which drugs and their targets interacted. We needed centres of excellence which brought these two disciplines together and in which academia and industry collaborated. We needed to understand better how obesity (a growing fact of life) affected drug dosage. We needed to combat counterfeit drugs or drugs with inadequate antibiotic content which resulted in a build-up of resistance.

He agreed with the previous speaker that a new business model was needed to provide incentives to industry appropriate to a situation requiring costly research and development to produce drugs which were then deliberately limited in their subsequent use. We also needed to devise strategies for combating disease other than that of identifying a microbe and then developing a drug to kill it. The future might lie in ways of enhancing the ability of people's immune systems to repel invaders or of assisting people's armoury of defences with the use of bacteriophages.

He believed that the current regulatory system for drugs needed a major overhaul. In particular greater harmonisation was needed internationally so that industry did not face so many different regimes for the approval of new drugs. He wondered whether the present World Health Organisation structure (where the need for compromises between over 100 different countries tended to produce inadequate results) was capable of coping with the modern challenges presented by the cross-border and cross-sector characteristics of AMR.

PROFESSOR VALLANCE agreed with much of the content of the previous two presentations. He underlined some of the difficulties facing drug companies in bringing new antibiotics to the market: that of finding a chemical giving a good lead, that of dealing with toxicity risks when the active substance had to exist in massive amounts to achieve the desired results, that of finding hospitals with the skills and teams necessary for proving clinically that the drug works, that of coping with the differing regulatory regimes in different countries.

On the last point, he pointed to the enviable position of the airline industry where a globally unified set of rules applied. He called for a broader discovery agenda with industry and academia working closely together to identify approaches for addressing bacterial infections which broke away from the traditional antibiotic model of "small molecule kills the microbe" and which boosted our own defences. He argued that the current patent life cycle was not compatible with the current need to restrict the use of new antibiotics in the interests of combating AMR. One way of reducing the disincentives to investment by industry in new drugs would be for there to be some form of commitment to buy before any commitment by industry to proceed to expensive clinical studies.

During the two discussion periods before and after dinner there was no dissent from the scale and nature of the challenges posed by AMR. One speaker compared them to those of climate change: international in nature, not regarded as an immediate crisis and therefore lacking adequate institutional arrangements conducive to solutions. As with climate change there was no simple single solution; AMR was a complex problem with multiple drives, for which a suite of solutions (tailored to the needs and situations in different countries) was required embracing economics, social science and regulatory change as well imaginative and multi-disciplinary research.

Many speakers emphasised that the international nature of the challenges complicated the task of finding solutions. Controlling the use of antibiotics was difficult in a country like India without a medical and pharmaceutical infrastructure found in a country like the UK. Moreover, as in the case of climate change, it was not an easy task to persuade less developed countries to be more sparing in the use of drugs which had been of such benefit in the past to developed countries because it had now become apparent that the consequences were a threat to everyone.

In response to the several contributions citing the experience with HIV where there had been a swift, energetic and concerted response this unexpected emergence of an untreatable disease, speakers pointed out that an important factor contributing to the production of effective medication, had been the existence of a huge and relevant science base on which the research and development

could draw. The fight against AMR had no such advantage.

It was suggested by a number of contributors that rapid and accurate diagnostic skills were an essential ingredient to any success in limiting the use (and dosage) of antibiotics to those situations for which there was no other remedy and ensuring that only the correct amount of the drug was administered. Was, it was asked, the traditional approach of pathogenic culture, apt for current needs?

The theme of improving incentives for drug companies to step up their research effort was picked up by many speakers. One contributor said that it was counterproductive for those urging greater care in the use of antibiotics to say that new drugs should be locked away; those, including taxpayers, who had contributed to the costs of development, were hardly likely to be impressed by such a message. The emphasis should be on the importance of ensuring that a drug of such immense value was used only in the most exceptional and deserving circumstances. Society was prepared to spend big money on insurance. Society should be prepared to spend good money on research to counter AMR as an insurance against a growth in the number and prevalence of untreatable diseases.

Considerable interest was expressed by many speakers in alternatives to antibiotics as weapons against bacteria, although warnings were given about the complexity of treatments to enhance the ability of a person's immune system to repel invaders. It was suggested that we needed a better understanding of how bacteria functioned so that some more subtle disabling process was used instead of the crude use of a massive killer dose; for example, study of the evolutionary mechanisms of bacteria might point to ways of intervening to interrupt the mutation cycle or for restoring a more harmonious balance between bacteria and their human or animal hosts.

It was noted by a number of contributors that the laxer regulatory environment for the use of antibiotics in animals, both as treatments and as productivity boosters, was indefensible. Much greater effort was needed to persuade vets and farmers and the food industry to be less profligate. It might be argued that as yet the evidence of causal links of harm to humans was not conclusive. But the test required for drugs administered to humans was that they should be demonstrably safe. That test should apply also to the use of antibiotics in animals.

Sir John Caines KCB

Open with Adobe Reader outside the browser and click on the URL to go to the sites.

TEDx Talk:

The drugs don't work: Sally Davies at TEDxAlbortopolis
www.youtube.com/watch?v=7evvWt8XN7o&feature=kp

Useful URLs:

AstraZeneca
www.astrazeneca.co.uk

Biotechnology and Biological Sciences Research Council
www.bbsrc.ac.uk

College of Emergency Medicine
www.collemergencymed.ac.uk

Department of Health, Antimicrobial Resistance Strategy
www.gov.uk/government/news/uk-antimicrobial-resistance-strategy-published--2

Economic and Social Research Council
www.esrc.ac.uk

Engineering and Physical Sciences Research Council
www.epsrc.ac.uk

The Foundation for Science and Technology
www.foundation.org.uk

Government Office for Science
www.bis.gov.uk/go-science

GlaxoSmithKline plc
www.gsk.com/explore-gsk/how-we-do-r-and-d/tackling-the-threat-of-antibiotic-resistance.html

House of Commons Science and Technology Select Committee Report on AMR
www.parliament.uk/business/committees/committees-a-z/commons-select/science-and-technology-committee/inquiries/parliament-2010/antimicrobial-resistance-amr/

Longitude Prize 2014
www.longitudeprize.org

Natural Environment Research Council
www.nerc.ac.uk

Pfizer
www.pfizer.co.uk

Research Councils UK
www.rcuk.ac.uk

Royal College of General Practitioners
www.rcgp.org.uk

Royal College of Obstetricians and Gynaecologists
www.rcog.org.uk

Royal College of Paediatrics and Child Health
www.rcpch.ac.uk

Royal College of Physicians of Edinburgh
www.rcpe.ac.uk

Royal College of Physicians of London
www.rcplondon.ac.uk

The Royal College of Anaesthetists
www.rcoa.ac.uk

The Royal College of Pathologists
www.rcpath.org

The Royal Society
www.royalsociety.org

The Royal Society of Medicine
www.rsm.ac.uk

Technology Strategy Board
www.innovateuk.org

The Technology Strategy Board is developing an innovation programme in the area of Anti-Microbial Resistance. If you would like to be involved, please contact Helen Kuhlman on Helen.Kuhlman@tsb.gov.uk.

Wellcome Trust
www.wellcome.ac.uk