Antimicrobial Resistance: How Research is Tackling the Challenge

13 February 2019, Churchill Room, House of Commons

Speakers

Professor Jonathan Van-Tam
Deputy Chief Medical Officer

Dr Jonathan Pearce
Associate Director, Biological Medicine, Medical Research Council, Chair, AMR Funder's Forum

Dr Susan Hopkins
Healthcare Epidemiologist Consultant in Infectious Diseases and Microbiology at Public Health England, Honorary Clinical Senior Lecturer at Imperial College London

Professor Mark Woolhouse
Professor of Infectious Disease Epidemiology at the University of Edinburgh

Professor William Gaze
Professor at The European Centre for Environment and Human Health, part of the University of Exeter Medical School

Professor Clare Chandler
Associate Professor in Medical Anthropology at LSHTM, co-Director of the LSHTM Antimicrobial Resistance Centre

Professor Fiona Watt
Executive Chair of the Medical Research Council

Chaired by Stephen Metcalfe MP, chair of the Parliamentary and Scientific Committee and member of the Science and Technology Committee (Commons)

Key points

- A co-ordinated cross-government approach to research and implementation is required across all sectors to contain and control antimicrobial resistance (AMR)
- Better collection and use of data at scale linked to health and economic impacts will support progress across disciplines
- Policy makers and academics must work together to define the key questions and develop evidence-based interventions that could work in practice
- The UK must continue to build capacity and support interdisciplinarity, ensuring that we have the skills and the workforce needed to support translation.
- The UK is leading the way in developing new business models to incentivise the development of new antibiotics
- The UK must continue to influence global research strategies and policy on AMR, leading by example

Summary

The chair began by saying that the 2013-2018 AMR strategy and its refresh signalled the government rising to the significant challenge of AMR. The UK can continue to lead in this global challenge, reducing antibiotic usage, developing best practice, leading research, building capacity, creating national and international networks, educating and informing the public and influencing the international research and policy agenda.

Professor Jonathan Van-Tam outlined the vision of the refreshed strategy, where, by 2040, AMR is contained and controlled. While much has been achieved, significant challenges remain; the environment is still poorly understood in the context of AMR, practical clinical and applied health research is needed to evaluate public health measures to drive down infections; we must work with industry partners, with a pilot for a new model to take antibiotics out of the normal reimbursement system imminent. A co-ordinated approach across all sectors is needed. Research is critical to all of this.

Dr Jonathan Pearce outlined how in 2013 the MRC established the UK AMR Funder's Forum to co-ordinate the UK's research response to AMR. This bought together government departments with all seven research councils, as well as the research community both nationally and internationally.

The important areas outlined in the new strategy – reducing infection in humans, animals, food and environmental systems, reducing the use of antibiotics and developing new interventions - will rely on robust surveillance linked to health and economic impacts, so we can understand the emergence of resistance, the impact of new interventions, and any unintended consequences.

Gaps do remain in AMR research. Drug pipelines are slow and there is a pressing need to understand and prioritise where, when and how AMR interventions work. UKRI, working with our government partners, is well placed to address the formidable and growing challenge by increasing co-ordination and co-operation with policy makers, international partners and industry, and targeting our investment on key research priorities.

Dr Susan Hopkins endorsed the aim of moving from eliminating AMR to control and contain. She outlined the "big strides forward" in the last five years in AMR-related human health: whole genome sequencing, which has allowed researchers to "track and trace" infection; big data, which is providing insights from every single patient in England; and behavioural insights, which have shown a need to shift the focus away from behaviour among individuals to the diverse practices, cultures and dynamics among health teams across the world.

The public health requirements for making further progress against AMR are better data linkage, combining data from hospital and the communities with genomics, human host factors and molecular biology; understanding disease; developing control measures and interventions. This work all needs to be underpinned by behaviour change and health psychology.

Government can support this work by ensuring continued investment in AMR over the next 5 to 10 years, and longer, in the UK. Global investment is also needed; we must lead by example, so we can bring G7 and G20 countries along with us.

Professor Mark Woolhouse emphasised that the long-term solution to AMR is not just more antibiotics. Global human consumption of antibiotics is growing, with livestock consumption growing faster. The UK government's emphasis on actions and research integrated across the human and livestock sectors is essential to making progress on AMR.

The emphasis on surveillance in the new strategy is welcome; you can't monitor progress against AMR without it. The challenge is joining up surveillance across these very different

sectors; if data is linked successfully it will show how AMR is moving between livestock, food, the environment and humans. Currently cross sectoral transmission studies using genomes have been unsuccessful because they are not large enough in scale. Research access to routine surveillance data will be crucial for understanding AMR spread.

Government can support research by supporting bold, mission-oriented funding initiatives at a large scale, with an integrated approach to both research and implementation. This would see co-ordinated activities across multiple sectors, multiple disciplines and parallel linked projects.

Professor William Gaze welcomed the increased emphasis on the environment in the refreshed strategy and the UKRI response. Environment in the context of AMR means built, farmed, natural, and within our own gut, the microbiome. We all live within it, hospitals, primary care and farms are nested within it, and it is the medium through which transmission occurs. It's not just about AMR circulation in the environment; there is a two-way flow of resistance to and from the environment. Progress has been made with initiatives around ecology, evolution and transmission.

It is key to move on from describing AMR in the environment to quantifying how that environmental AMR poses a risk of exposure, infection and transmission.

Government can support this work by providing further investment to understand drivers of AMR from an environmental perspective. While it is right that the current emphasis is on practices in low- and middle-income countries where the strength of the signal is high, the processes in high-income countries are still important and provide a more controlled system to which we have better access.

Professor Clare Chandler welcomed the recognition that AMR is a behavioural and wider social problem; this is reflected in the amount of social science research in the cross-council initiative and the new strategy. The key areas are social research on antibiotic use, interventions and reducing on our reliance on antibiotics.

Antibiotics have become embedded in our productive society and are part of our political economy. Individual interventions have limited impact because individual choice is limited by an environment that dictates our lifestyles, diets and habits. These structures need addressing; our reliance on antibiotics is generated by a quick-fix system that replaces hygiene, infrastructure, and equality with antibiotics. A good example is in research that suggests that we've come to equate medicines with care. People may not need an antibiotic; they need legitimacy to rest, to take time off and recover from an infection, but an active and large gig economy does not support this.

Government can support this work by continuing to support multidisciplinary research, and collaborating with researchers on research, working together on what could be potential feasible solutions. Bringing research from across different disciplines together with policy is vital.

Discussion

Diagnostics: There was discussion on how to support GPs in making decisions about antibiotic prescribing. Better diagnostics could support GPs in deciding to prescribe. There are no diagnostic tests imminent that will support this process; having the bacteria does not indicate whether you've got an infection and need an antibiotic. There is a need to understand what it is about a person that dictates the consequences of not getting an antibiotic. Work with big data is underway to support this by stratifying patients to see who suffers poor outcomes. It was noted that there are new technologies for diagnostics, but there is a public engagement and funding problem leading to poor uptake. There is also a behavioural aspect, so we need a better understanding of the interaction between the GP

and the patient. It was also highlighted that an incentivisation mechanism to support the use of diagnostics would also stimulate R&D in this area.

Partnership: The importance of key fundamental questions that still need to be answered was stressed. Stewardship is needed to ensure the quality of the questions and the potential translation underpinning research. Academics should work with appropriate stakeholders in securing research evidence to underpin "best practice" across government. It is difficult for an organisation like DEFRA to give advice on environmental issues without supporting evidence.

Infection prevention: AMR is global by nature and antibiotics are in some places a substitute for poor hygiene and a lack of access to clean water and closed sewage systems. In these places individuals frequently acquire drug-resistant bacteria, and there is a perception of a wave of resistance coming towards certain countries. Vaccines have also played a huge role in preventing infection. There is a lack of new vaccines for bacterial infections in development, and it's vital to support the vaccine research and development pipeline.

Antibiotics and alternative therapies: The pipeline for new drugs is at risk of drying up completely. There is a disconnect between research done in small companies and academic laboratories, and hospitals getting new treatments. There is little support for getting a disruptive device into a hospital, whereas if there is a partnership with a pharmaceutical company, there's an existing body of sales to support translation. It is difficult for SMEs to attract investment. There was a suggestion for a global initiative from the world's ten richest countries to pay for new drugs. The new model for reimbursing antibiotics is promising. While there is a need to support non-antibiotic drug development, the development of new drugs, new vaccines, and new diagnostics are large-scale long-term solutions that are not going to solve the problem in the short term.

Translation of research findings: While producing highly-cited research papers remains important, translation is becoming a core activity and an increase in knowledge exchange is taking place. UKRI is instrumental in this.

Research capacity: The UK does a great job in training PhD students but loses lots of talented people because the postdoctoral period is unstable. There needs to be continued support for interdisciplinary networks to strengthen research and development capacity. As the pharmaceutical industry disinvests we are at risk of losing the skills, workforce and expertise in bringing products through the antibiotic pipeline.

Concluding Statement: MRC executive chair Fiona Watt closed by welcoming the refreshed plan. AMR is a fantastic example of the type of co-ordination, partnership and integration that UKRI can achieve, she concluded. Under UKRI we are well-positioned to tackle AMR by focusing on the key issues that have been raised in this discussion: better data linkage, multiple interventions and mission-oriented research, and the building of cohorts of researchers interested in AMR.

Biographies

Professor Jonathan Van-Tam

Jonathan Van-Tam MBE, BMedSci, BM BS, DM, FFPH, FRCPath, Hon FFPM, CBiol, CSci, FRSPH, FSB graduated in Medicine from the University of Nottingham in 1987, trained in Public Health Medicine from 1991, and became a Senior Lecturer at the University of Nottingham in 1997, before serving with the pharmaceutical and vaccines industries from 2000.

He moved to the UK Health Protection Agency in 2004, where he was Head of the Pandemic Influenza Office, before returning to Nottingham in late 2007 as Professor of Health Protection.

His special interest in influenza spans 25 years and focuses on: epidemiology; transmission; vaccinology; and pandemic preparedness. He is co-Editor and chapter author of the textbook: Pandemic Influenza, which is now in its second edition. He has been a consultant to the World Health Organization on influenza since 2004. He sat on the UK Scientific Advisory Group for Emergencies (SAGE) during the 2009-10 pandemic crisis. His unit is an official WHO Collaborating Centre for pandemic influenza and research; and a UK Faculty of Public Health 'national treasure' training location for influenza research. He was previously Chair of UK NERVTAG (New and Emerging Respiratory Virus Threat Advisory Group). Jonathan was appointed Deputy Chief Medical Officer for England in October 2017.

Dr Jonathan Pearce

Jonathan Pearce joined the MRC in 2008. Prior to this Jonathan undertook academic research at Cambridge, Oxford and Toronto, followed by roles in life sciences venture capital and strategic consulting.

Jonathan is now Associate Director for Biological Medicine, and in his time at the MRC has had responsibility for Infections and Immunity, including chairing the £85 million UKRI AMR initiative and the UK AMR Funders Forum, leading the Council's £60 million precision medicine initiative, and establishing the Council's translational research funding scheme, the DPFS.

Dr Susan Hopkins

Susan Hopkins was appointed in April 2018 as the Deputy Director, National Infection Service of Public Health England leading on healthcare-associated infections and antimicrobial resistance (AMR). She is also the Clinical Director of Infection Services at the Royal Free London NHS Foundation Trust.

She trained in infectious diseases, microbiology and epidemiology in Ireland, US, France and the UK. She was appointed in 2006 as a

consultant in infectious diseases and microbiology, leading the hospital epidemiology programme at the Royal Free.

She chairs the oversight group for the English Surveillance Programme on Antimicrobial Use and Resistance (ESPAUR), which has been instrumental in developing novel surveillance methods, feedback to professionals and the public and interventions to reduce prescribing.

She also is a member of the Royal College of Physicians Infectious Diseases advisory group, advising the College on infections, a member of the MHRA anti-infectives advisory group providing expert input to antimicrobial authorisations, and a member of the NICE committee developing guidance for managing common infections. She regularly inputs and advises on European surveillance and guidelines, working closely with the European Centre for Disease Control and being nominated by other European countries to sit on their network committees relating to antibiotic use and resistance.

She holds honorary academic appointments at UCL and Imperial. She works with both the Imperial and Oxford NIHR Health Protection Research Units on Healthcare Associated Infections (HCAI) & AMR. Her active research interests are in the areas of antimicrobial prescribing, resistance and healthcare associated infections, though she regularly collaborates on other infections related to her clinical practice caring for patient's infections with chronic infections, immunocompromise, high consequence infections and tuberculosis.

Professor Mark Woolhouse

Mark Woolhouse is Professor of Infectious Disease Epidemiology at the University of Edinburgh. He studied biology and ecology at the Universities of Oxford and York and Queen's in Canada, then held Research Fellowships at the University of Zimbabwe, Imperial College London and Oxford, before moving to Edinburgh in 1997.

His research interests concern the population dynamics of pathogens, especially those associated with AMR and emerging infectious diseases, applying ecological and evolutionary approaches to combat threats to both human and animal health.

He is an expert on the epidemiology and transmission of AMR between livestock and humans, advocating a One Health approach to reducing the burden of resistance. He has written a number of high-profile articles on global policy on AMR, is a frequent invited speaker to audiences of academics, clinicians and the general public and makes regular contributions in the press and media.

He leads on AMR for Edinburgh Infectious Diseases – a grouping of over 800 scientists. He advises both national and international agencies (including DEFRA, FSA, WHO, US Institute of Medicine) and was awarded an OBE in 2002. He is a Fellow of the Royal Society of Edinburgh and of the Academy of Medical Sciences.

Professor William Gaze

William Gaze is Professor of Infectious Disease Epidemiology at the University of Edinburgh. He works on complex interactions within microbial populations in human, animal and environmental microbiomes in the context of antimicrobial resistance (AMR). Current and recent research income of ~£2 million includes NERC, MRC and BBSRC funding on evolution, dissemination and transmission of AMR in natural and farmed environments.

He has been invited to speak on AMR on five continents in the last two years and has advised UK and overseas governments, UNEP / WHO, European Environment Agency, Environment Agency and Defra.

He was recently awarded a NERC Knowledge Exchange Fellowship on "The Environmental Dimension of Antimicrobial Resistance: informing policy, regulation and practice".

Professor Clare Chandler

Clare Chandler is Professor in Medical Anthropology and the co-Director of the LSHTM Antimicrobial Resistance Centre, which works to inspire innovation through interdisciplinary engagements.

Her research interests lie in the application of anthropological methods and theory to policies and practices relating to medicine use, diagnostic testing, management of febrile illnesses and health care improvement interventions. Her current research focus is AMR.

Clare leads the Anthropology of Antimicrobial Resistance research group, a dynamic group of anthropologists addressing this issue through a number of research projects in Africa and Asia.

She is Principal Investigator for the ESRC funded Antimicrobials in Society (AMIS) Programme, which aims to bring fresh perspectives to social studies of AMR. The Programme includes empirical studies in Thailand and Uganda as well as the AMIS Hub web platform, which profiles high quality social research on AMR through a library of essential readings, people and projects listings, thematic summaries and commentaries.

Clare leads the social science research for the DfID-funded FIEBRE study, looking at antibiotic use and concepts of fever amongst a range of actors in Zimbabwe, Malawi and Myanmar.

Clare is working with the WHO to design methods to evaluate awareness of AMR amongst healthcare professionals in low- and middle-income country (LMIC) settings. The work includes qualitative and quantitative research in 13 LMICs to develop a tool to assess AMR awareness across human and animal practitioners.

She is also involved in studying AMR from a One Health perspective, with funded projects looking at antibiotic use in companion animals in the UK, as well as the measurement of antibiotic use in agricultural and human systems in low and middle-income countries together with partners at the International Livestock Research Institute.

Professor Fiona Watt

Fiona Watt obtained her DPhil from the University of Oxford, and carried out postdoctoral research at MIT, Cambridge, USA. She established her first lab at the Kennedy Institute of Rheumatology in London, and then moved to London Research Institute.

From 2006 to 2012 she was Deputy Director of the Cancer Research UK Cambridge Research Institute and Deputy Director of the Wellcome Trust Centre for Stem Cell Research, University of Cambridge.

As well as being the MRC's Executive Chair, Fiona is Director of the Centre for Stem Cells & Regenerative Medicine at King's College London, where she leads a team of 80 academic researchers. Internationally recognised in her field, she has expertise in the stem cells of healthy and diseased skin.