6 November 2013

Society for General Microbiology Consultation Response

Science and Technology Committee (Commons) – Antimicrobial resistance

Introduction

The Society for General Microbiology (SGM) is a membership organisation for scientists who work in all areas of microbiology. It is the largest learned microbiological society in Europe with a worldwide membership based in universities, industry, hospitals, research institutes and schools. The SGM publishes key academic journals in microbiology and virology, organises international scientific conferences and provides an international forum for communication among microbiologists and supports their professional development. The Society promotes the understanding of microbiology to a diverse range of stakeholders, including policy-makers, students, teachers, journalists and the wider public, through a comprehensive framework of communication activities and resources. Further information about SGM is provided in Appendix 1.

The prevalence of antibiotic resistance should not surprise us. The problem is an inevitable consequence of human behaviour, evolutionary pressures and the ability of micro-organisms to rapidly change their genetic makeup. Despite this we believe that the scientific community – and broader society – is ingenious and determined enough to discover solutions that overcome the problems of antimicrobial resistance.

Our emphasis in this consultation response is on the need for greater capacity in the basic research required to fight infection. Quite rightly basic research is proposed in the government's *UK Five Year Antimicrobial Resistance Strategy,*[1] as part of the overall solution to antibiotic resistance but details about how the research will be delivered were scarce. Basic research is, in our view, the only means of finding long-term solutions to the threat of antimicrobial resistance.

1. How has antimicrobial resistance developed in the past decade?

It is certain that micro-organisms can develop resistance to antimicrobial drugs; beyond this general statement, a more complex picture emerges in which some infections, notably, methicillin-resistant *Staphylococcus aureus* (MRSA) and HIV show, respectively, declining and stable levels of resistance,

[1] Department of Health/Department for the Environment, Food and Rural Affairs, *UK Five Year Antimicrobial Resistance Strategy 2013 to 2018*; https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf

while others, notably tuberculosis, register increases.[2] For a third, and very large group of infections, we have little or no data on resistance patterns: surveillance in these infections is not carried out. Treatment failure may be occurring, but neither it, nor antimicrobial resistance, is being systematically reported.[3] The most serious disease threats are from chronic infections including multidrug resistant tuberculosis, Gram-negative infections and hospital-acquired infections.

2. What are the gaps in our knowledge about antimicrobial resistance?

2.1. Diagnosis of antimicrobial resistance and routine surveillance of resistance rates

- Outside of a small number of infections, e.g., tuberculosis, we lack systematic data on the rates of antimicrobial resistance, both in the UK and overseas. The lack of data is due to an absence of inexpensive, standardised tests, and/or the fact that certain infections are not on policy-makers' 'radar'. Systematic data could, if collected, inform the focus of research, assist us in identifying the most urgent problems, and allow us to horizon scan.
- We have insufficient understanding of the evolution and spread of resistance. We have insufficient data on the use of combination therapies, co-drugs, and adjuvants that could increase or extend the performance of existing therapies.
- We lack rapid diagnostic tests for resistance in some organisms, notably, sexually-transmitted infections such as gonorrhoea. Such diagnostic tests would allow physicians to prescribe the most effective, tailored, treatments, and will contribute significantly to antibiotic stewardship (i.e., the right antibiotic for the right infection). Developments in genomics will be vital in this area. There is also a need for operational research to introduce new tests into the health service.
- We should encourage basic scientific research in areas relevant to resistance, e.g., studies of the mechanisms of emergence of resistant bacteria, drug discovery including natural products research, studies of the ecology of infection and the microbiome, infection diagnostics, vaccines, and immune responses to infection.

2.2. Expanding the working life of existing antimicrobial treatments and developing new ones

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[2] **Alan P. Johnson, John Davies, Rebecca Guy, Julia Abernethy, Elizabeth Sheridan, Andrew Pearson and Georgia Duckworth (2012).** Mandatory surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia in England: the first 10 years. *Journal of Antimicrobial Chemotherapy,* doi: 10.1093/jac/dkr561 (Figure 1); http://jac.oxfordjournals.org/content/67/4/802.full. **UK Collaborative Group on HIV Drug Resistance (2012).** Time trends in drug resistant HIV-1 infections in the United Kingdom up to 2009: multicentre observational study. *British Medical Journal,* doi: 10.1136/bmj.e5253, http://www.bmj.com/content/345/bmj.e5253. Public Health England, July 2013, 'Number and proportion of tuberculosis cases with first line drug resistance, UK, 2000-2012'; http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317139697461.

[3] To the best of our knowledge, no comprehensive account of UK resistance rates has been published since 2007; www.hpa.org.uk/Publications/InfectiousDiseases/AntimicrobialAndHealthcareAssociatedInfections/0712Antimicrobialresistance/.

- Antimicrobial resistance is an inevitable process; therefore, we need to ensure the drug development pipeline is adequately stocked. Currently, there is an urgent need to focus drug development on treatments against infections due to Gram-negative bacteria, particularly those resistant to carbapenems; antibiotics suitable for paediatric use; drugs to fight methicillin- and vancomycin-resistant *Staphylococcus* strains; and fungal infections (*Candida* and aspergillosis).
- We need greater understanding at the fundamental level of tried and tested antibiotic drug targets. These include how the bacterial cell wall is assembled, and how bacterial proteins are synthesised, and other essential processes both in model organisms and pathogens.
- Many drugs, especially in Gram-negative bacteria are not able to reach their targets due to membrane barriers. We need a more comprehensive understanding of how chemicals move in and out of bacterial cells. Studies on how to design compounds, adjuvants, and co-drugs to facilitate movement into cells should be encouraged.
- We need to focus attention on the problems of treating chronic and persistent infections (e.g., non-healing wounds, implanted device-associated infection, and cystic fibrosis respiratory infections). Currently, the research emphasis is often on acute infections – yet persistent infections require long-term antimicrobial treatment, thus contributing to the development of resistance. It is worth noting a recent initiative in the USA that targets research on chronic and persistent infections.[4]
- We need to focus a part of our efforts on screening plants and soil micro-organisms for natural products that could be used as drugs. The soil in particular has been the most productive niche to date for antibiotic discovery, and we should encourage research on particular bacterial taxa with known tendencies to make antibiotics, notably, *Streptomyces*. We need to reinforce expertise in microbial physiology, microbial culture techniques, taxonomy and ecology as well as invest in rapid high throughput robotic screening techniques.

3. Is there sufficient research and investment into new antibiotics or other treatments and methods to ensure continued protection against infection? If not, how could this be rectified?

- Risk-sharing via an international partnership appears to be the most common current means of stimulating antibiotic drug discovery. The major public-private partnership is the EU's €223.7 million Innovative Medicines Initiative 'Combating Antibiotic Resistance: New Drugs for Bad Bugs (ND4BB)'.[5] We should ensure the UK is contributing to, and benefiting from, all relevant international schemes.
- In the UK, private-sector antibacterial drug development is now primarily located in small pharmaceutical and biotech companies. We see evidence for a dynamic and innovative sector with more than 20 active firms across the UK – as we noted in a previous

[4] http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-12-020.html
[5] http://blogs.nature.com/news/2012/05/europe-targets-superbugs-with-public-private-effort.html

consultation response to the Science and Technology Committee.[6] The EU's Innovative Medicines Initiative, while often seen as the solution, is little help to this vital sector. Funders should therefore investigate what strategies we have in place currently, or could put in place, to support antimicrobial drug discovery in relevant UK firms, and promote fruitful interaction with the wealth of knowledge and skills in academia. For example, it may be useful to consider if a concentration of firms and researchers in one or more centres would encourage innovation.

- There is a need to encourage partnerships between academia and industry, and to incentivise firms to develop new antimicrobial treatments. The Wellcome Trust, for example, has a Seeding Drug Discovery initiative; the MRC has MRC Technology. Various forms of industry incentivisation (both push, and pull) need to be investigated, and those proven most effective should be implemented, particularly those measures that de-risk and unlock private sector investment (e.g., early-stage funding for proof of concept, pre-clinical work and toxicity testing). Industry is not going to take the initiative on its own.
- Research spending on antibiotic resistance from public funds appears to have been low. In the years 1997-2010, research on antibiotic resistance is reported to have received only 3.9% of total UK public-sector spending on infectious disease research.[7] The exact nature, causes, and effects, of this reported underfunding on the early-stage pipeline in antimicrobial therapies warrant investigation.
- We encourage projects shared between the Research Councils, Technology Strategy Board, and the National Institute for Health Research. Interactions should be built around a clear goal, and involve basic research, social science, and engagement with clinical and industrial fields. Interaction between academic researchers and clinicians should be encouraged for proof-of-concept studies that will draw buy-in from the private sector. We should explore roles for learned societies in promoting cross-working.
- Seek to interest microbiologists at all levels of academia and industry in the problems of antibiotic resistance and antimicrobial drug discovery. There has been a dwindling of interest academically in this type of research, exacerbated or even led by declining interest from Big Pharma. We should seek to train and interest graduates in this area by emphasising the life-saving nature of antibiotics and how they underpin modern medicine.
- Identify factors contributing to successful antibiotic drug discovery in the past and present, and what we might learn for the design of new programmes. This will require research by social scientists.
- Many organisations are conducting vital work examining the crisis in antimicrobial drugs, and seeking policy solutions. These include the European Commission; the UK's health, and environment, food and rural affairs departments; government bodies and learned

[6] Society for General Microbiology Consultation Response: Research and Development funding for science and technology in the UK, 28 August 2013. Please contact SGM for a list of firms.

[7] **Michael G. Head, Joseph R. Fitchett, Mary K. Cooke, Fatima B. Wurie, Rifat Atun, Andrew C. Hayward, Alison Holmes, Alan P. Johnson, and Neil Woodford (2013).** Systematic analysis of funding awarded for antimicrobial resistance research to institutions in the UK, 1997-2010. *Journal of Antimicrobial Chemotherapy,* doi: 10.1093/jac/dkt349, http://jac.oxfordjournals.org/content/early/2013/09/13/jac.dkt349.full. A word cloud available online shows this funding shortfall graphically - http://www.researchinvestments.org/. These data run until 2010 only; later data are not yet available.

societies overseas, such as the German Academies of Science; learned societies in the UK (e.g., SGM), think-tanks; research funders, notably the Wellcome Trust; and researcher networks and forums, e.g., the Infectious Diseases Research Network (IDRN).[8] These initiatives are valuable and should be encouraged, and could be linked via a 'Round Table' or forum, as has been suggested in Germany.[9]

- Recommendations emerged from a one-day meeting at the Wellcome Trust in May, including a call for the formation of cross-sector consortia, and a renewed role for the public sector; these should be explored.[10]
- Chemists and modellers have a vital role devising new antibiotics based on fundamental microbiological research. The UK has great scientific strength across academia, the research institutes, and the private sector (particularly start-ups and small and medium-sized enterprises), but interdisciplinary working will be critical and is something SGM actively seeks to promote.

4. What measures (including behavioural change) have been most effective in controlling the spread of resistant pathogens, and could such measures be used to control other pathogens?

No comment.

5. What global coordination and action is required to fight antimicrobial resistance and is the UK contributing enough towards cross-border initiatives?

No comment.

6. What are the strengths and weaknesses of the Government's 2013-2018 strategy for tackling antimicrobial resistance? What changes might be made to further strengthen the Government's action plan?

- Quite rightly basic research is proposed in the government's *UK Five Year Antimicrobial Resistance Strategy,*[11] as part of the overall solution to antibiotic resistance but details about how the research will be delivered are scarce.

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[8] SGM can supply a full list of the initiatives we are aware about – please contact us. SGM currently collaborates with other learned societies on antimicrobial resistance; these include the Biochemical Society, British Society for Antimicrobial Chemotherapy, Royal Society of Chemistry, Society for Applied Microbiology and Society of Biology.

[9] **Academy of Sciences and Humanities in Hamburg/German National Academy of Sciences Leopoldina (2013**). *Antibiotics Research: Problems and Perspectives*, p. 10; http://www.leopoldina.org/uploads/tx_leopublication/2013_06_17_Antibiotics_Research.pdf.

[10] **Antibiotic Action (2013).** *Lessons to be learnt from Pharma about Discovery and Development of New Antibacterial Drugs,* p. 3; http://antibiotic-action.com/wp-content/uploads/2013/08/Learning-Lessons-report.pdf.

[11] Department of Health/Department for the Environment, Food and Rural Affairs, *UK Five Year Antimicrobial Resistance Strategy 2013 to 2018*; https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf

- The SGM, in collaboration with other learned societies, is therefore pressing for a coherent strategic plan for research fighting infectious disease, including tackling the challenge of antimicrobial resistance.[12]

Society for General Microbiology – Chair of the Policy Committee:

- Professor Maggie Smith, University of York

Society for General Microbiology – Policy Committee:

- Professor Nigel Brown, Emeritus Professor, University of Edinburgh
- Professor Martin Cranage, St George's, University of London
- Dr Pat Goodwin, Consultant, C3 Collaborating for Health
- Professor Colin Harwood, Newcastle University
- Mr Scott Nicholson, University of the West of Scotland
- Professor Gill Stephens, University of Nottingham
- Dr Jeremy Webb, University of Southampton

The Policy Committee additionally sought information from Dr Mike Dawson (Novacta Biosystems Ltd), Professor David Denning (University Hospital of South Manchester), Professor David Dunn (MRC Clinical Trials Unit), Dr Malcolm Rhodes (University of Manchester), Professor Jodi Lindsay (St George's University of London), and Professor David Livermore (Lead, Antibiotic Resistance, Public Health England) in preparing this response.

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[12] For a programmatic statement of SGM's current policy approach, please see: Society for General Microbiology Policy Note: Antimicrobial Resistance Policy, 7 June 2013; http://www.sgm.ac.uk/en/policy/consultation-responses.cfm.

Appendix 1: The Society for General Microbiology

Vision

A world in which the science of microbiology provides maximum benefit to society.

Mission

To promote high-quality microbiological science, both nationally and internationally, to a diverse range of stakeholders.

Rationale

The potential socio-economic benefits arising from microbiology are substantial. They include:

- A healthier future (for humans, animals and plants) and a better quality of life, within the context of a sustainable natural environment.
- The development of biotechnology products (such as food, drinks, biopesticides, biofuels and medicines), which generate wealth and employment, and so support growth and innovation.
- The advancement of scientific knowledge, as a benefit in its own right, and to allow us to plan for the future and contribute to international solutions for global challenges, such as climate change, the burden of disease and food security.

Strategic priorities

To achieve its Vision and Mission, the Society will work towards the strategic priorities below.

- Publishing: to contribute to the science of microbiology through high-quality publications.
- Scientific conferences: to hold international scientific conferences to disseminate research knowledge and provide a forum for communication between microbiologists and to grow and support communities among them.
- Raising awareness: to inspire and educate people about microbiology, and allow them to make informed decisions which recognize the importance of microbiology and its advances.
- Influencing policy: to ensure that appropriate scientific information and expert opinion are made available to policy- and decision-makers and that the improvement of resources and infrastructure for microbiology is supported.
- Professional development: to promote microbiology as a career from school level onwards and support career and professional development of microbiologists.

The Society is a Charity registered in England and Wales (No. 264017) and in Scotland (No. SC039250) and a Company Limited by Guarantee, registered in England and Wales (No. 1039582).

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