

Microbiology TODAY

43:4 November 2016

The Mobile Microbe

Global surveillance of infectious disease | A spotlight on Bluetongue virus | Chytridiomycosis | Mapping the urban genome | Globalisation of antibiotic resistance | The Great Pox

Microbial Diseases of Travel

Australia's biosecurity | Foodborne diseases | Bird flu | Dengue | Tuberculosis | Drug-resistant *Neisseria gonorrhoeae* | Zika virus infection

CHLORAMPHENICOL CAPSULES

Widely distributed throughout the body, including CSF¹

Oral levels comparable to i.v. levels²

Rarely implicated with *C.difficile*^{3,4}

Effective against serious infections including:

- *H. influenzae*^{1,5}
- Typhoid^{1,5}
- MRSA²
- VRSA⁶
- *Neisseria*^{1,5}
- *Legionella*^{1,5}
- *Rickettsia*^{1,5}
- *C.difficile*⁷⁻¹⁰
- *E. coli*¹



Abbreviated Prescribing Information Chloramphenicol Capsules BP 250mg

Presentation: Hard Gelatin Capsules.

Indications: Typhoid fever and life-threatening infections, particularly those caused by *Haemophilus Influenzae*, where other antibiotics will not suffice.

Posology: For oral administration.

Adults and elderly: 50 mg/kg body weight daily in 4 divided doses. For severe infections (meningitis, septicaemia), this dose may be doubled initially, but must be reduced as soon as clinically possible. Children: Not recommended.

Contra-indications: Known hypersensitivity or toxic reaction to chloramphenicol or to any of the excipients. Should not be used for the prophylaxis or treatment of minor infections; during active immunisation; in porphyria patients; in patients taking drugs liable to depress bone marrow function; during pregnancy, labour or by breast-feeding mothers.

Special warnings and precautions for use: Use only if other treatments are ineffective. Use should be carefully monitored. Reduce dose and monitor plasma levels in hepatic or renal impairment; in the elderly; and in patients concurrently treated with interacting drugs.

Interactions: Chloramphenicol prolongs the elimination, increasing the blood levels of drugs including warfarin, phenytoin, sulphonylureas, tolbutamide. Doses of anticonvulsants and anticoagulants may need to be adjusted if given concurrently. Complex effects (increased/decreased plasma levels) requiring monitoring of chloramphenicol plasma levels have been reported with co-administration of penicillins and rifampicin. Paracetamol prolongs chloramphenicol half-life and concurrent administration should be avoided. Chloramphenicol may increase the plasma levels of calcineurin inhibitors e.g. ciclosporin and tacrolimus. Barbiturates such as phenobarbitone increase the metabolism of chloramphenicol, resulting in reduced plasma chloramphenicol concentrations. In addition, there may be a decrease in the metabolism of phenobarbitone with concomitant chloramphenicol use. There is a small risk that chloramphenicol may reduce the contraceptive effect of oestrogens. Chloramphenicol reduces the response to hydroxocobalamin. Chloramphenicol is contra-indicated in patients taking drugs liable to suppress bone marrow function e.g. carbamazepine, sulphonamides, phenylbutazone, penicillamine, cytotoxic agents, some antipsychotics including clozapine and particularly depot antipsychotics, procainamide, nucleoside reverse transcriptase inhibitors, propylthiouracil.

Pregnancy and Lactation: The use of chloramphenicol is contra-indicated as the drug crosses the placenta and is excreted in breast milk.

Effects on ability to drive and use machines: No significant effect on driving ability.

Undesirable Effects: Reversible dose related bone marrow depression, irreversible aplastic anaemia, increased bleeding time, hypersensitivity reactions including allergic skin reactions, optic neuritis leading to blindness, ototoxicity, acidotic cardiovascular collapse, nausea, vomiting, glossitis, stomatitis, diarrhoea, enterocolitis, Gray Baby Syndrome particularly in the newborn, which consists of abdominal

distension, pallid cyanosis, vomiting, progressing to vasomotor collapse, irregular respiration and death within a few hours of the onset of symptoms.

Overdose: Stop chloramphenicol immediately if signs of adverse events develop. Treatment is mainly supportive. If an allergy develops, oral antihistamines may be used. In severe overdosage e.g. Gray Baby Syndrome, reduce plasma levels of chloramphenicol rapidly. Resin haemoperfusion (XAD-4) has been reported to substantially increase chloramphenicol clearance.

Pack size and Price: 60 capsules £377.00

Legal Category: POM.

Market Authorisation Number: PL17736/0075.

Market Authorisation Holder: Chemidex Pharma Limited, 7 Egham Business Village, Crabtree Road, Egham, Surrey TW20 8RB, UK.

Date of preparation: January 2016.

See Chloramphenicol Capsules Summary of Product Characteristics for full prescribing information.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Essential Generics on 01784 477167.

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Editorial

As I write my final editorial on a cool, golden September morning, I have just returned to Norwich from a series of conferences and holidays that have given me opportunities to travel with my own set of microbes and to pick up others.



Despite robust efforts with regular bouts of hand washing and 'avoiding the ice', I have collected at least a couple of self-limiting colds along the way. On the cold front, I look forward to the next couple of weeks as the new cohort of students arrive on campus bringing the inevitable 'freshers' flu' (that I manage to catch on an annual basis) with them.

Travel is a constant backdrop to life on Earth and it is here to stay. The impact that travel and microbiology has on our modern lives cannot be underestimated and creates an exciting topic that underpins my final edition of *Microbiology Today*. September 2016 also marks a significant milestone in our global battle with a fundamental threat. The United Nations has just signed a declaration to combat the proliferation of antimicrobial resistance. Without a shadow of a doubt, the spread of antimicrobial resistance has been exacerbated by the travel and migration of microbes, flora and fauna across the globe. The articles that we have brought together for this exciting, joint edition emphasise this concern. The set of articles that we have been lucky enough to commission for this edition hark

back to the past, report on the present and project into the future. I would like to thank each author who has generously spent time writing the fantastic articles that populate this issue. Firstly, Alan P. Johnson and Joanne Freedman for 'Global surveillance and response to the threat posed by infectious diseases'; Meredith Stewart with 'A spotlight on Bluetongue virus'; 'Chytridiomycosis as a cause of global amphibian declines' by Thomas J. Burns, Mark S. Greener and Paul A. Hoskisson; 'Cracking the genetic code of our cities': researchers around the world aim to map the urban genome' written by Sofia Ahsanuddin, Ebrahim Afshinnkoo and Christopher E. Mason; and finally to David M. Livermore for his article 'Globalisation of antibiotic resistance'. Personally, I was delighted to have had one last opportunity to write for *Microbiology Today* with my article on syphilis, 'The Great Pox'. Finally, I would like to give a sincere thank you to Derek Gatherer for his wonderfully timely Comment on 'The voyages of Zika virus'.

My last three years as Editor of *Microbiology Today* have been an absolute privilege. I have enjoyed my tenure hugely, and each edition of this magazine has given me a sense of great pride and

pleasure. Each article that has crossed my desk has emphasised the marvel of microbiology and engaged with new audiences and new readers. As Editor I am incredibly proud of the opportunities that we have given to young researchers to develop their writing skills, and communicate their knowledge and passion about their own research and research interests.

Lastly, as I step down from this role I would like to give special thanks to Ruth Paget, our Managing Editor: you have been brilliant. Also, a big thank you to each and every member of the Editorial Board for your sparky ideas, the generous access to your individual research networks and your amazing problem-solving skills. I know I leave the incoming Editor in safe hands. Rowena Jenkins I would like to introduce you to our readers and to wish you well. I know that you will learn a lot and enjoy this new challenge hugely. Well, that's it from me except to say a warm goodbye and thank you for three great years.

Laura Bowater

Editor

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Geospatial map of *Enterobacteriaceae*.
Afshinnekoo *et al.*, 2015

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From the President

This month, a number of events, including the launch of the Early Career Microbiologists' Forum and the Sir Howard Dalton Young Microbiologist of the Year Competition at Charles Darwin House, have reminded us of the emerging talent within the microbiological field.



Congratulations to Lindsay Broadbent from Queen's University Belfast, who takes away this year's Young Microbiologist's coveted prize – and heartfelt congratulations to all of the finalists, shortlisted from an initial field of 600 poster presenters, to represent their Divisions at the competition. These presentations made our recent Annual General Meeting (AGM) highly engaging as we reflected on the previous year's activities and successes. Thanks also to Sir John Skehel and Evelyn Doyle and attending honorary members who spoke to guests about their personal experiences in developing a career in the microbiological world.

I've recently had the pleasure of seeing the Society's work and influence from a number of angles. I attended one of the Irish Division Focused Meetings, partnered with the Irish Society for Immunology, Exploring the Microbe–Immune System Interface, that took place in Cork, and also the joint Focused Meeting with the British Mycological Society in Exeter, The Dynamic Fungus, which both attracted excellent audiences. These meetings exemplify our commitment to collaborate with complementary societies to explore interdisciplinary research themes. Our Focused Meetings enable and empower members to propose and organise

meetings outside of our main Annual Conference as a research vignette (often in partnership with others). Focused Meetings can be proposed and put into place quickly, so that emerging topics and more specialised symposia can be explored and discussed. The two meetings that I attended had strong representation from early career microbiologists describing 'at the coalface research' as offered papers and as high-quality posters. These were also illuminated and expanded on by leading experts in their respective disciplines, giving a truly international perspective. Having an appropriate blend of invited and offered talks at our meetings anticipates the Society's increasing commitment to ensure that our community has the opportunity to attend the meetings and participate actively by presenting their work.

We are also analysing carefully the results of our membership questionnaire. The analysis is ongoing but it emerges that our members place a very high value on the raft of networking opportunities that the Society offers. We intended therefore to ensure that networking is further enhanced in the way we organise future events. The impact of the survey will be integrated into the challenges that Council will

undertake to enable us to become the type of member organisation that you want and deserve.

This November issue of *Microbiology Today* is in collaboration with another of our international partners – the Australian Society for Microbiology's publication, *Microbiology Australia*, and is a bit of a bumper issue. Again we have set out an issue that has many articles of general interest as well as specific reviews on a theme that will appeal to virologists, bacteriologists and eukaryotic microbiologists.

You will see that we have begun a major policy review of the topic of the microbiome. The Society's policy work has massively increased our impact on government and the general public. Through this work we also harness the extraordinary range of bespoke expertise within our membership. The final outputs from this microbiome policy study will be published in the coming year, but again this underlines the vision of the Society, defined by our officers, staff and members, to put the membership to work and to ensure that microbiology is a participants' sport and not just one for spectators.

Neil Gow

President

president@microbiologysociety.org

From the Chief Executive

Next month, our Deputy Chief Executive, Dariel Burdass, will leave the Microbiology Society after 17 years. This is a major event for the Society, and not just because Dariel is the longest-serving member of staff and knows more about the organisation than anyone else in the office. The list of her achievements during her time here is enormous and covers a very wide range of our activities.



She developed many of the Society's activities that are designed to reach out to non-scientific audiences. They are too numerous to mention, and there are many highlights. In 2012, the Society won a Silver-Gilt Medal at the Chelsea Flower Show for an exhibit called the New Green Revolution, for which Dariel was the driving force. It encouraged gardeners to take an adventure in soil, and appreciate the extent to which the healthy growth of plants depends on the communities of microbes below the surface. Our education website, Microbiology Online, which Dariel pioneered, now gets around a million hits per year, demonstrating just how much interest there is in microbiology. She also wrote the inspirational book, *The Good, The Bad and The Ugly – Microbes*, to support the teaching of microbiology in schools.

In recent years, Dariel has led the Antibiotics Unearthed project, which is crowdsourcing the hunt for novel drugs against infectious disease. The general public, students and educators can get involved by sampling the soil in their local area, with the samples then analysed for chemical compounds generated by soil bacteria, which may have antibiotic properties. It is an illustration of how Dariel's projects can capture the wider

imagination that earlier this year, we were invited to sample the soil in the garden of 10 Downing Street.

As Dariel's time at the Society progressed, she began to take on wider responsibilities and led the development of our new website, and the Society's distinctive brand, which continues to draw appreciative comments from many quarters. She has championed the Society's international role and has been very involved with the Federation of European Microbiology Societies (FEMS).

When Council took the decision to build a new area of activity – policy work – it was to Dariel they turned to make it happen. From nothing, she built the Society's capacity in policy remarkably quickly. It is a mark of just how impactful that work has become that in September, the Microbiology Society was one of the participants in a meeting at the United Nations in New York, at which governments from around the world agreed to coordinate their collective funding for antimicrobial resistance so they can deliver maximum benefits.

More recently, Dariel took on the job of revising the Society's strategic plan, no easy task given the choices we must continually make about where to invest across the huge array of different ways in which we could advance the science of microbiology.

Dariel will be familiar to any member who has been at any of the Society's Annual Conferences for the past 17 years, or at many other scientific meetings, AGMs, outreach events and other occasions. She is well known to dozens of Council and Committee members past and present, and has worked with thousands of members and innumerable external partners over the years. Throughout that time, she has spread her infectious enthusiasm for microbes, for the Microbiology Society and for everything we strive to achieve. The discipline of microbiology in the UK and Ireland, and around the world, is healthier because of what she has done and what she has achieved at the Society.

Dariel is not going far – she will be the new Chief Executive of the Physiological Society, a learned society that serves the physiological community in many of the same ways that we at the Microbiology Society serve our members. I know that many, many members of the Microbiology Society will want to join me in wishing Dariel every success in her new job.

Peter Cotgreave

Chief Executive

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News



Membership subscription rate increase

At the Society's Council meeting in July, it was agreed to increase subscription rates for most membership categories from September 2016.

This will be the first increase in three years. During this period we have continued to invest in supporting the membership with the introduction of: new training courses; the Early Career Microbiologists' Forum; the Champions initiative; more flexible joining options; increased networking opportunities; and an improved calendar of scientific meetings and events. Additionally, we have realigned our grants programme to make it easier for the 600 members we support this way to identify, apply for and report against a grant.

It remains a strategic aim of the Society to keep investing in its membership. Members are currently being consulted on how we can further improve and enhance the membership offering for the future, and the findings from this will help shape a renewed and revised membership offering in 2017.

Please see the table below for the new membership subscription rates.

	Card/cheque	Direct Debit
Full Member	£77	£67
Full Concessionary Member	£35	£30
Postgraduate Student Member	£35	£30
Undergraduate Student Member	£15	£10
International Associate Member (excluding UK and Ireland)	£22	n/a
International Associate Member (middle-income countries)	£22	n/a
International Associate Member (low-income countries)	Free	n/a
School Representative Member	£18	£15
School Corporate Member	£18	£15
Affiliate Member	£15	£10

Antibiotics Unearthed pop-up events

Two successful pop-up events were held this summer at Garwnant Forest, Methyr Tydfil, and Kielder Forest, Northumberland, as part of Antibiotics Unearthed. The team would like to thank the volunteers – without your help, the events would not have been the successes that they were. To find out more about what is currently happening in the Antibiotics Unearthed project, see page 192.

Young Microbiologist of the Year

Lindsay Broadbent, Queen's University Belfast, was presented with the Young Microbiologist of the Year award for 2016. She gave her talk, entitled 'The role of IFN λ 1 in RSV infection and its potential as a novel anti-RSV prophylactic', at the Annual General Meeting this September. Mariya Goncheva won second place, with Ethan Morgan and Andrew Frey taking joint third place in the competition.

More details about the Young Microbiologist of the Year finalists can be found on the Society's website: <http://microb.io/ymoy2016>.

Congratulations to our 2017 Prize Lecture winners

The Society is pleased to announce the Prize Lecture winners for 2017. These Prizes are awarded in recognition of significant contributions to the field of microbiology, and each winner will present a Prize Lecture at the Microbiology Society Annual Conference 2017, taking place from 3–6 April in Edinburgh. Please see the news story online for more information about each winner: <http://microb.io/prizelectures2017>.

Deaths

It is with regret that the Society announces the death of the following members:

Dr Jennifer Moyle, who joined the Society in 1956; **Professor Harold Perkins**, who joined the Society in 1962.

Contact mtoday@microbiologysociety.org if you wish to notify the Society of the death of a member whose details can be included in this section.

Author surveys

Earlier this year, the Microbiology Society surveyed over 800 authors to find out their experience of publishing with our journals. This was a first for the Society, and we would like to extend our thanks to all who took part.

The survey was conducted in May 2016 across five of the Society's journals: *Microbiology*, *Journal of General Virology*, *Journal of Medical Microbiology*, *JMM Case Reports* and *International Journal of Evolutionary and Systematic Microbiology*.

For more information, please see page 187.

Leaving a Legacy

Members are now able to remember the Microbiology Society in their Will, helping us to support the future of microbiology and the next generation of microbiologists. Your bequest will help us achieve our vision of *a world in which the science of microbiology provides maximum benefit to society*. For full details, please see the Society's website: www.microbiologysociety.org/legacy.

Society events

We have had a fantastic run of meetings this year, from the highly successful 2016 Annual Conference to our seven Focused Meetings, including two organised by our Irish Division. For more information on upcoming events for 2017, please see page 184.

Grants deadlines

Date	Grant
1 December 2016	Travel Grants to present at conferences/attend short courses between 1 January and 31 March 2017.
30 January 2017	Grants for support to attend the Annual Conference 2017.

Rolling application

Local Microbiology Event Sponsorship

All members can apply for funds to support microbiology-related events, e.g. sponsored talks.

Grants are changing!

This summer, the Society's Council approved changes to the grants programme after it was reviewed, to ensure that funds were being used in the best way possible to contribute to our members' professional development. The changes make our entire programme strategically relevant, address underspending and ensure that we are adding value to the member experience. Members can find out more via the enclosed insert accompanying the magazine and by visiting the grants pages of the website: www.microbiologysociety.org/grants.

We'd like to hear about your membership experience

Thank you to everyone who has taken part in the Membership Research Project, either by completing the questionnaire or participating in a workshop. Your input has been invaluable in helping us gain a deeper understanding of what's working well and what needs to change for the future. There is still time to have your say – if you have views about our membership offering, please email Paul Easton (Head of Membership Services) at p.easton@microbiologysociety.org.

The winner of the £50 Amazon voucher, drawn at random from those who completed the membership questionnaire, is Mohammed R. Mohaisen.

Correction

In the last issue of *Microbiology Today*, we incorrectly printed that penicillin was discovered in Edinburgh.

Sir Alexander Fleming discovered penicillin in St Mary's Hospital, London.

Contributions and feedback

The Society welcomes contributions and feedback from members. Please contact mtoday@microbiologysociety.org with your ideas.

Benjamin Thompson

Head of Communications

b.thompson@microbiologysociety.org

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5

REASONS

TO PUBLISH WITH US

WE ARE A LEADING PUBLISHER IN THE FIELD OF MICROBIOLOGY

The Microbiology Society has been publishing research for **69 years**, and now has a portfolio of **six peer-reviewed journals**, with over **3,500 articles submitted in 2015**.

1

2

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Unlike commercial publishers, we invest our publishing surplus to advance the understanding and impact of microbiology by connecting and empowering communities worldwide, through: **international conferences, professional development, policy, education and outreach**.

3

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4

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Global surveillance and response to the threat posed by infectious diseases

Alan P. Johnson & Joanne Freedman

The international spread of infectious disease has long been recognised. As early as the 14th century, even though the microbial aetiology of communicable diseases was not understood, international travellers were kept in quarantine to prevent the spread of diseases such as the plague. In modern times, the ready availability of international air travel and other forms of rapid transport has made containing the spread of disease even more of a challenge.

To this end, International Health Regulations (IHR) were developed by the World Health Organization (WHO) in 1969 to enable countries to work together to prevent and control public health threats while at the same time trying to avoid unnecessary interference with international travel and trade. The IHR have their origin in the International Sanitary Regulations,

originally devised in Paris in the mid-19th century in response to the need for international cooperation in public health following the cholera epidemics that hit Europe in 1830 and 1847.

The importance of surveillance

The development of interventions to control the spread of infectious diseases requires an understanding



of their underlying epidemiology. The cornerstone of epidemiology is surveillance, which comprises the collection, collation and analysis of data on the occurrence and burden of disease and the dissemination of information to those who need to know; this will include public health officials, policy-makers, healthcare professionals and the public. While many countries, at least in high-income economies, have national surveillance systems, global surveillance coupled with action to control disease spread is much more complex, requiring international cooperation and sharing of information. As an example of this, Public Health England has published its Global Health Strategy (2014–2019) as part of its commitment to improving health globally. At a wider geographical level, the European Centre for Disease Prevention and Control (ECDC) coordinates a number of pan-European surveillance networks for a range of diseases (Table 1), with responsibility for provision of national data resting with competent bodies in each country. For surveillance of antibiotic resistance, a further network known as CAESAR (Central Asian and Eastern

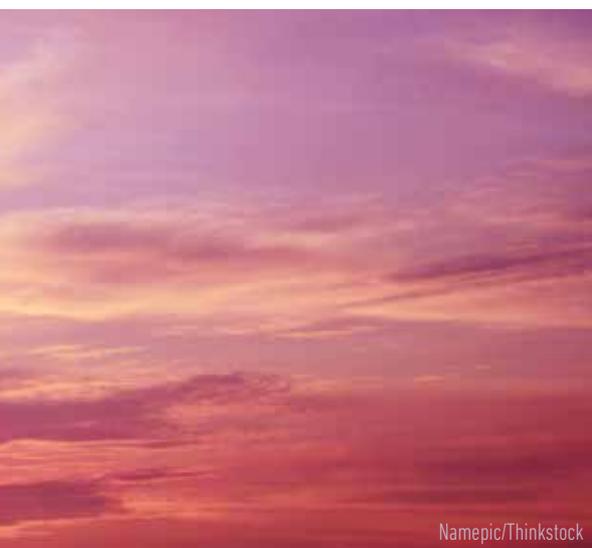
Table 1. Surveillance networks managed by the European Centre for Disease Control covering a range of infections

Disease area	Networks
Antimicrobial resistance and healthcare-associated infections	<ul style="list-style-type: none"> • European Antimicrobial Resistance Surveillance Network (EARS-Net) • Healthcare-associated infections Network (HAI-Net) • European Surveillance of Antimicrobial Consumption Network (ESAC-Net)
Emerging and vector-borne diseases	<ul style="list-style-type: none"> • Emerging Viral Diseases-Expert Laboratory Network (EVD-Net) • European network for sharing data on the geographic distribution of arthropod vectors, transmitting human and animal disease agents
Food- and waterborne diseases and zoonoses	<ul style="list-style-type: none"> • Food- and Waterborne Diseases and Zoonoses Network (FWD-Net) • The European Creutzfeldt–Jakob Disease Surveillance Network (EuroCJD) • European Legionnaires' Disease Surveillance Network (ELDSNet)
HIV, STI and blood-borne viruses	<ul style="list-style-type: none"> • European Network for HIV/AIDS Surveillance • European Network for STI Surveillance • European Network for Hepatitis B and C Surveillance
Influenza and other respiratory viruses	<ul style="list-style-type: none"> • European influenza surveillance network (EISN)
Tuberculosis	<ul style="list-style-type: none"> • European tuberculosis surveillance network
Vaccine-preventable diseases and invasive bacterial infections	<ul style="list-style-type: none"> • EUVAC-Net (measles, rubella, mumps) • European Network for Pertussis Surveillance • European Invasive Bacterial Infections Surveillance Network (EU-IBIS) • European Diphtheria Surveillance Network (EDSN)

European Surveillance of Antimicrobial Resistance), established by the WHO Regional Office for Europe, the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the Dutch National Institute for Public Health and the Environment (RIVM) includes all countries of the WHO European Region that are not part of the European Antimicrobial Resistance Surveillance Network (EARS-Net).

In 1995, a resolution was submitted to the World Health Assembly, urging all WHO Member States (MS) to strengthen surveillance and reporting of re-emerging and new infectious

diseases. In response, the WHO created a global surveillance system comprising a 'network of networks' which link together existing local, regional, national and international networks of laboratories and medical centres into a super surveillance network. Participants include the WHO Collaborating Centres and Regional Offices, national and international public health bodies and centres of excellence such as the ECDC, the US Centers for Disease Control and Prevention (CDC), reporting networks of UN agencies (e.g. UNICEF) and the Training in Epidemiology and Public Health Intervention Network (TEPHINET),



Namepic/Thinkstock

which provides field epidemiology training programmes in 88 countries. Other participants include non-governmental organisations such as the Red Cross, the Red Crescent, Médecins Sans Frontières and Medical Emergency Relief International (Merlin).

Following the epidemic of severe acute respiratory syndrome (SARS) in 2003, the IHR were revised in 2005 to further strengthen surveillance and response capability. The revised IHR (2005), which are legally binding, came into force in July 2007, and represent an agreement between 196 countries, including 194 WHO MS, to build capacity to detect, assess and report public health threats in a timely manner. There is also a requirement to ensure that international ports, airports and ground crossings have the capacity to deal with public health threats and limit the spread of disease into neighbouring countries. However, in practice such activities are very resource-intensive, and in 2015, only 43% of participating countries reported having achieved full compliance.

Sharing information via the Internet

In addition to the formal surveillance activities described above, a vast amount of data is now collected and shared using the Internet, with freely available electronic discussion sites being valuable sources of information. This is particularly important for the collection of information from low-income countries, which often lack robust surveillance systems due to lack of resources and poor national infrastructure. The scope of this approach may be worldwide [e.g. ProMed (Program for Monitoring Emerging Diseases)], regional (e.g. PACNET in the Pacific region) or

national (e.g. Sentiweb in France). This approach to information gathering is being increasingly used by healthcare professionals, an example being the Global Public Health Information Network (GPHIN), an electronic surveillance system developed by Health Canada which has search engines that actively trawl the Internet for reports of communicable diseases in electronic discussion groups or on news wires. GPHIN has begun to search in English and French and will eventually expand to all official languages of the WHO. Another such system is HealthMap, developed by a team at Boston Children's Hospital in 2006. Data on emerging public health threats are made freely available via the Internet at www.healthmap.org/en and are also available from the mobile app, Outbreaks Near Me. The aggregated data provided by HealthMap are derived from a wide range of freely available sources including, among others, ProMED, GeoSentinel (clinician-based

sentinel surveillance of individual travellers), OIE (the World Organization for Animal Health [Office International des Epizooties]), FAO (Food and Agriculture Organization of the UN), Eurosurveillance and Google News. It is of note that in early 2014, HealthMap tracked early press and social media reports of a haemorrhagic fever in West Africa that was subsequently identified by WHO as Ebola.

The global response to disease

Public health threats posed by some disease outbreaks may extend beyond an affected state's national border and require coordinated international action. After convening an expert Emergency Committee, WHO may designate these as Public Health Emergencies of International Concern (PHEICs), allowing the implementation of temporary control measures. WHO may also coordinate a response using resources from the Global Outbreak Alert and Response Network (GOARN), which is



Fig. 1. Cases of multidrug-resistant TB in Europe in 2014. Dataset provided by ECDC based on data provided by WHO and Ministries of Health from the affected countries (data available at: <http://microb.io/2dGZ0Fj>).

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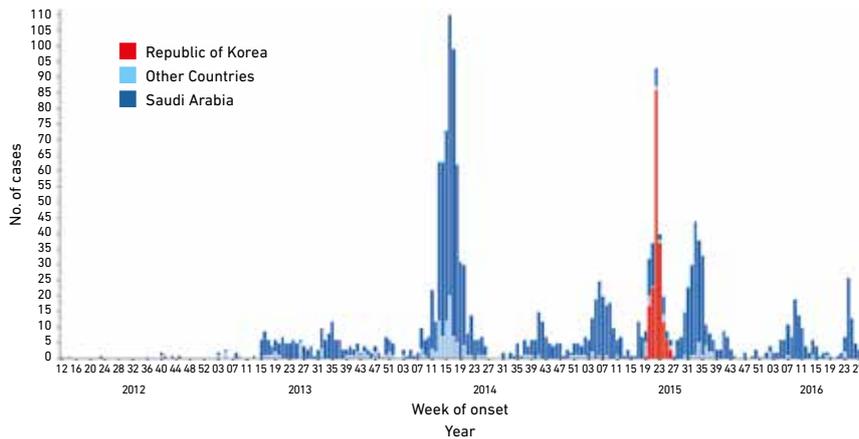


Fig. 2. Time trend for confirmed global cases of MERS-CoV reported to WHO as of 22 July 2016 ($n=1791$).

www.who.int/csr/disease/coronavirus_infections/maps-epicurves/en



Fig. 3. Global occurrence of Zika virus reported via HealthMap for the last week of July 2016.

www.healthmap.org

a collaboration of existing institutions and networks in different countries. A WHO team may be sent to instigate initial control measures and make an assessment of the response required. Rapid dissemination of information is important, and WHO alerts are made publically available via the Internet at www.who.int/csr/don/en.

Re-emerging and new infectious disease threats

Despite advances in medicine, public health continues to be threatened by re-emergence and international spread of infectious diseases thought

to have previously been under control such as tuberculosis (TB), which is now increasingly difficult to treat due to multidrug resistance (Fig. 1). In addition, recent decades have seen the emergence of new infectious agents such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome coronavirus (MERS-CoV) (Fig. 2), Ebola, Zika virus and chikungunya, as well as new variants of known pathogens such as influenza virus. We have also seen the emergence of new syndromes such as microcephaly associated with the Zika virus (Fig. 3) and hantavirus

pulmonary syndrome. Efforts to control the spread of these infections will require improved detection, diagnosis and reporting, as well as close international collaboration and sharing of information to trigger international responses. These will include mobilisation of healthcare personnel, and provision of clinical and travel advice aimed at mitigating the spread of disease.

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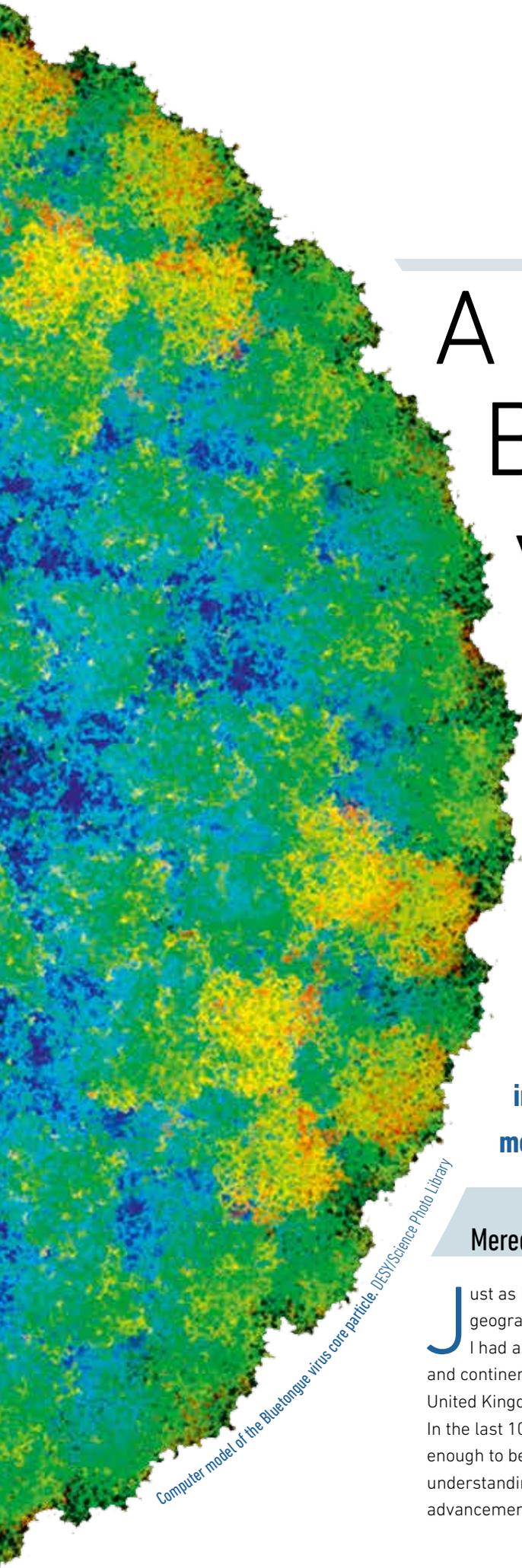
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A spotlight on Bluetongue virus?

In the late 1990s, there were rumblings that Bluetongue virus (BTV) was on the move. The 2006 summer outbreak changed the way that the European economic and scientific communities viewed its importance. It shifted from being a neglected disease confined to the tropical regions of the world to a potentially important threat to agriculture. Suddenly, BTV was sharing research priorities and the limelight with other important viruses of animals such as foot-and-mouth disease virus and avian influenza virus.

Meredith Stewart

Just as BTV had changed its geographical location in 2006, I had also moved across oceans and continents from Australia to the United Kingdom to study this virus. In the last 10 years I have been lucky enough to be involved with the increased understanding and technological advancements that have ensued due

to the impact of a highly pathogenic virus entering a new environment.

The importance of BTV

BTV is a member of the *Reoviridae*, a family that includes the diarrhoea-causing rotavirus. But, unlike rotavirus, which is transmitted via the faecal-oral route, BTV transmission occurs between

Computer model of the Bluetongue virus core particle. DESY/Science Photo Library



A biting midge (*Culicoides nubeculosus*) engorged with blood – a potential transmitter of Bluetongue disease.
Sinclair Stammers/Science Photo Library

ruminant animal hosts (e.g. sheep, cattle) via biting midges (*Culicoides* species) taking a blood meal. For those readers that live in Scotland or in Western Australia, you may be all too familiar with these swarming, biting insects that use you as their own personal summer smorgasbord. Classically, BTV is non-contagious;

therefore, without these biting midges BTV would not be able to spread from animal to animal. But there is a newly identified strain (BTV-26) that may be transmitted via direct contact.

The clinical symptoms of Bluetongue disease depend on viral strain, host species and even animal breed. In general, sheep are the most susceptible

to disease, in particular, breeds of European descent. Typically, the disease presents as an acute period of high fever (5–7 days), excessive salivation and sweating, laboured breathing, swelling of the face and, in ~10% of cases, a cyanotic (blue) tongue. Not all sheep develop clinical signs, but those that do rapidly lose condition, with the sickest generally

The emergence of BTV into northern Europe placed a spotlight on the BTV research community to rapidly respond and provide a solution.

dying within a week. Associated with the disease are severe increases to production costs, as the recovery of affected animals is slow, while high fever in sheep results in poor quality wool.

The European outbreak (2006–2008) is noteworthy as BTV displayed new characteristics. First, this novel strain, BTV-8, was exceptionally virulent, with fatalities in sheep reaching 40%. Furthermore, BTV-8 could also induce clinical signs in cattle. The virus also crossed the placenta and caused disease in the foetus; something that had only been observed with certain live BTV vaccine strains. From an epidemiological perspective, BTV-8 was being transmitted exclusively by European midge species that had not previously been shown to be capable of sustaining an outbreak.

The impact of the BTV-8 outbreak was devastating. In addition to direct losses, regions where BTV is endemic or where outbreaks occur are now subject to international trade restrictions; the economic cost of the 2007 BTV outbreak in France was \$1.4 billion and \$85 million in the Netherlands.

Changing locations

Historically, BTV had been confined to regions between 40° N and 35° S latitudes, including Africa, the Middle East, India, China, the United States and Mexico. Although BTV is also endemic in South-east Asia, Papua New Guinea,

northern South America and northern Australia, these countries are considered to be free of clinical disease by the World Organization for Animal Health. This is in part due to the particular sheep breeds present, or a lack of sheep present in the endemic regions of these countries. In Europe, Bluetongue disease was considered exotic with sporadic cases localised to the Mediterranean Basin until the late 1990s. Although outbreaks can sometimes be attributed to animal movement, encroachment into naïve territories is primarily due to the windborne dispersal of BTV-infected midges. This allows expansion of the virus over large geographical areas (e.g. from Indonesia to Australia). In Australia BTV spread has been predicted to be due to the climatic conditions (e.g. wet, warm springs), while in Europe the size of the midge population/susceptible animal populations are critical factors. Recently, an Oxford group showed that 38% infection of BTV during 2006 was due to midges moving upwind under their own power. These findings have implications for other viruses and pathogens spread by biting midges.

The increased incidence of BTV in new environments is a clear indication that the geographical location of BTV is expanding. The source of the outbreak of BTV-8 in northern Europe is still unknown. It may have been introduced by different mechanisms other than the wind-assisted movement of infected

Culicoides species. This includes the movement of infected livestock, use of live attenuated vaccine strains and the importation of midges with flowers or fresh produce. Furthermore, unlike the previous movements of the virus throughout Europe, BTV-8 expanded from Northern Europe (i.e. Belgium, France) into Italy and Spain, crossing the major physical barriers of the Swiss Alps and Pyrenees mountain range.

Traditionally, spread of BTV in Europe was linked to the geographical distribution of the African midge (*Culicoides imicola*), which has extended northwards as a consequence of climate change. The ability of the midge to be infected by BTV (vector competence) was always postulated to be a factor that hampered BTV's geographical spread. Infection of European midges (*Culicoides obsoletus* and *C. pulicaris*) was often associated with a lag time where other BTV strains had to 'adapt'. BTV-8 infection of the European *Culicoides* species did not display this lag time. These viral characteristics may have assisted the rapid spread throughout Europe.

Geographical change of BTV research

The emergence of BTV into Northern Europe placed a spotlight on the BTV research community to rapidly respond and provide a solution. The biggest factors identified with enabling BTV to spread throughout Europe were strategies to identify and control the spreading outbreak, and the lack of suitable vaccines. The use of live attenuated vaccines in Italy had proven to be troublesome. Just as the virus had dispersed, scientists like myself were travelling through Europe as part of a collaborative research network.

Importantly, diagnostic tests with rapid turnaround times were developed. This led to the identification of new types of BTV and a system to identify all circulating strains of BTV. The advancement in vaccine development was aided by molecular tools to manipulate the virus, and protein expression tools. The research group I belonged to was involved in developing and testing new vaccines with DIVA (discriminate between vaccinated and infected animals) potential to limit the impact of trade restrictions.

This network of scientists provided a greater understanding of virus–host interactions and factors that enabled BTV outbreaks to occur (weather, midge population, etc.). Importantly, these results aided in the rapid response to another midge-transmitted virus of sheep (Schmallenberg virus) in Europe years later. Although a wealth of knowledge has been generated, there are still big questions to be tackled, with the threat of a new outbreak always present.

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Chytridiomycosis as a cause of global amphibian declines

Thomas J. Burns, Mark S. Greener & Paul A. Hoskisson

Amphibians are remarkable creatures that have inhabited the Earth for over 350 million years, and exhibit some of the most amazing and diverse life histories. The planet is home to around 7,500 species of amphibian, which occupy an extraordinary number of ecological niches. They are often viewed as indicators of environmental health by ecologists due to their reliance on both aquatic and terrestrial environments to complete their lifecycles. Furthermore, their thin and highly sensitive skin, where much of their respiration occurs, makes them highly susceptible to environmental toxins, disease and radiation.

Beginning of the decline

In the mid-1980s amphibians began to decline at an alarming rate, with a number of species being considered as extinct. Much of this decline was attributed to habitat loss, climate change and environmental pollution. At first these declines were noticed in Central America and Australia; however, mass mortality events also began to

occur in what were considered to be pristine environments. In 1998 the major pathogen responsible for these declines was identified as the zoosporic nonhyphal eu chytrid, *Batrachochytrium dendrobatidis*. The eu chytrids are believed to be an early diverging branch within the fungal kingdom that use zoospores as the primary mode of dispersal, a trait which is believed to

have been lost in the higher fungi as new spore dispersal mechanisms evolved. Moreover, it is this zoospore stage of the chytrid lifecycle that is fundamental to amphibian pathogenicity.

The lifecycle of *B. dendrobatidis* begins as an aquatic spore with a single flagellum. These zoospores disperse within the environment, where they may come into contact with the thin,



permeable skin of amphibians. Upon contact with amphibian skin, the spores penetrate the skin and the zoospores encyst, absorbing their flagellum and forming a cell wall. Subsequently the cyst germinates, developing a small germ tube, which allows tissue and cell penetration. The fungal cells proliferate intracellularly and the germ tube gives rise to the sporangium. The infected cells are carried to the skin surface during epidermal differentiation, where the mature zoospores are released into the environment via discharge tubes. It is this process of growth and differentiation in the sensitive skin that

is highly damaging to amphibians and results in the pathogenic effects. *B. dendrobatidis* is known to infect over 500 species of amphibian and has resulted in global amphibian declines. Remarkably, there is huge variation in the pathogenic effects of *B. dendrobatidis*, with some species being highly sensitive, with devastating effects on the population, and with other species appearing to be unaffected by infection and potentially acting as environmental reservoirs for *B. dendrobatidis*. Genomic studies of *B. dendrobatidis* indicate that it has a complex evolutionary history with the population structure consisting of

multiple divergent lineages with no single evolutionary transition being linked to the observed global amphibian declines. This points to a multifactorial cause for global amphibian declines, perhaps linking evolutionary and ecological causes such as increased global trade of amphibians distributing *B. dendrobatidis* across the world, coupled with climate change and possibly other, as yet undiscovered, causes.

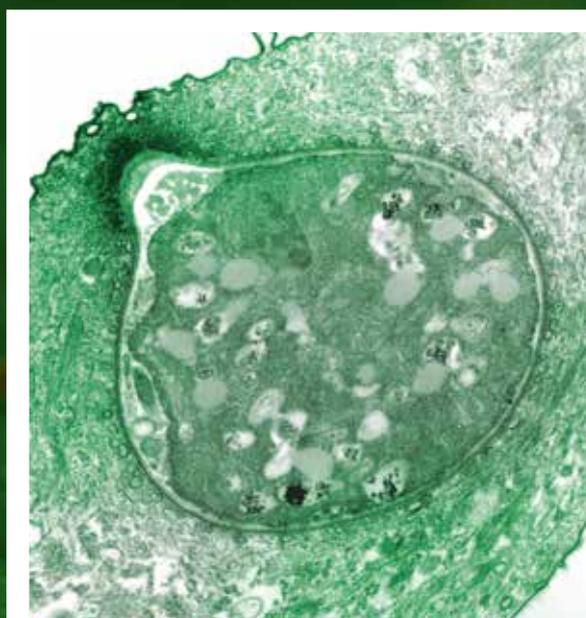
***B. dendrobatidis* – the first chytrid fungus**

B. dendrobatidis has been found on every continent where amphibians occur (all

Above Common frog (*Rana temporaria*). Paul A. Hoskisson

Below Glass frog (*Hyalinobatrachium orientale tobagoensis*). Paul A. Hoskisson

Inset *Batrachochytrium dendrobatidis* on the skin of an amphibian. Dr E. Davidson, Visuals Unlimited/Science Photo Library)



except Antarctica) and linked to their decline. In Europe, *B. dendrobatidis* is widely distributed and has been linked to declines in a range of species, with midwife toads (*Alytes obstetricians*) and natterjack toads (*Epidalea calamita*) being particularly affected. More recently, the emergence of a second *Batrachochytrium* species, *B. salamandrivorans*, has resulted in huge losses in fire salamander (*Salamandra salamandra*) populations in northern Europe. It would appear that *B. salamandrivorans* emerged in Asia and has coexisted with certain species of amphibian there; however global amphibian trade has resulted in its introduction to naïve amphibian populations in Europe with devastating effects. Whilst resulting in huge losses in salamander populations, *B. salamandrivorans* has so far been restricted to urodele amphibians (newts and salamanders).

Chytrid-mediated amphibian declines in Australia (in line with the rest of the world) date back to the late 1970s, with Queensland's gastric brooding frog (*Rheobatrachus silus*) being the first species to succumb to extinction. This species declined in the winter of 1979, and was last sighted in the wild in 1981. Prior to the identification of chytrid fungus in 1998, there was much debate on the cause of such dramatic amphibian declines around the globe, especially those that occurred in apparently pristine habitat. Australia was at the forefront of this debate, with observations of declines spreading northwards up the Queensland coast leading to early (and at that time unpopular) suggestions that a disease epidemic may be the cause of declines.

Australia was initially proactive in developing policy to combat chytrid



Fire salamander (*Salamandra salamandra*). Paul A. Hoskisson



Southern corroboree frog (*Pseudophryne corroboree*). Michael McFadden

It is clear that chytrid-mediated amphibian declines

are a complex problem, of which there is still much to

be discovered. Understanding the disease dynamics for

amphibian species which have experienced complex

chytrid-mediated declines will be a substantial challenge.

fungus, listing it as a 'key threatening process' in 2002 and drawing up a Threat Abatement Plan in 2006. Recently, there have been calls for more to be done; a recent review of chytridiomycosis management and the adequacy of conservation efforts in Australia highlighted seven species at immediate risk of extinction and a further 22 species at moderate or lower risk. With Australia's 238 species, that equates to > 10% of all Australian amphibian species facing extinction risk from chytrid.

Risk of extinction

Of the seven species identified as at immediate risk of extinction, three of these - the Baw Baw frog (*Philoria frosti*), the southern corroboree (*Pseudophryne corroboree*) and northern corroboree frogs (*Pseudophryne pengilleyi*) are temperate, sub-alpine specialists from south-eastern Australia. Unlike the tropical Queensland frogs, which declined rapidly as chytrid spread, these populations declined over a period of decades. Both Baw Baws and southern corroborees experienced an initial dramatic decline in population, distribution and density in the late 1980s/early 1990s, followed by a more gradual decline since. This suggests a more complex interaction with the chytrid pathogen. So, what were the driving factors in population decline for these species? Have they changed over time and how may they interact?

All three species are relatively long-lived, slow to mature and predominantly terrestrial. They make use of both

heath/bog and forest habitat, and lay their eggs in terrestrial nests within their breeding habitat, as opposed to a focal pond. These are not attributes that appear immediately conducive to the maintenance and spread of an aquatic pathogen, at least not at population densities existing in the wild today. Perhaps key to understanding their continuing decline is their co-occurrence with common eastern froglets (*Crinia signifera*), which is a non-susceptible species that may act as an environmental reservoir host of chytrid.

It is clear that chytrid-mediated amphibian declines are a complex problem, of which there is still much to be discovered. Understanding the disease dynamics for amphibian species which have experienced complex chytrid-mediated declines will be a substantial challenge, but one that will be essential for predicting and mitigating the impacts of chytrid on amphibian populations on a global scale.

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Cracking the genetic code of our cities: researchers around the world aim to map the urban genome

Sofia Ahsanuddin, Ebrahim Afshinnekoo & Christopher E. Mason

It is rare to say that one has lived through a revolution, but we are all living through one right now. High-throughput sequencing technologies have become cheaper and more cost-effective over the past decade, moving even faster than Moore's Law for computer power (doubling every 18 months). Because sequencers are modern-day 'molecular microscopes', scientists believe that we are currently experiencing a scientific revolution similar to the one sparked by Antonie van Leeuwenhoek's invention of the world's first light microscope in the 17th century.

The past few decades have witnessed a surge in microbiome and metagenomics studies, all of which are intent on elucidating the vast invisible world beneath our fingertips. With the advent of next-generation sequencing technologies, we are able to study this world like never before.

The birth of PathoMap

In 2010, Dr Christopher Mason, Associate Professor in the Department of Physiology and Biophysics at Weill Cornell Medicine, was suddenly struck by inspiration as he watched his daughter play with toys with her friends on the train. The infants unknowingly exchanged bacteria with one another as they drooled on their toys, passing them from hand to hand, and rolling them on



New York. Caia Image/Science Photo Library

the ground before repeating the cycle. These observations eventually gave birth to the PathoMap (www.pathomap.org) study in 2013, in which Dr Mason and his research team created a molecular portrait of the New York City subway system. Inspired by Dr Mason's daughter, the PathoMap study aimed to pioneer the field of metagenomics (study of all kingdoms' environmental DNA) and microbiome studies by creating the first baseline geospatial metagenomic map of a city's mass-transit system.

The PathoMap study's primary objective was to study the microbiome of a metropolitan environment. Since New York City's subway is the most highly trafficked transit system in the United States, it made perfect sense to sample all 468 stations to investigate the genetic

and microbial diversity present in each station. A team of volunteers collected and processed a total of 1,547 samples. Using next-generation sequencing technologies and bioinformatics to analyse the sequencing data, the research team was able to determine the taxonomic classification and functional diversity of the micro-organisms present on such ubiquitous surfaces as handrails, wooden benches, train seats, rubbish bins and floors. Most of the DNA uncovered from these surfaces matched bacteria associated with the skin microbiome. Altogether, the researchers found over 600 species of microbes riding the subway with fellow New Yorkers. Furthermore, while the research team found evidence of antibiotic resistance markers and

antibiotic resistant microbes, there was no evidence of virulence factors or pathogenicity in the samples. Interestingly, nearly half (48%) the DNA matched no known organism, which is a testament to the fact that we are only as good as our databases. As the field develops, our databases will become more refined and replete with accurate references that may impact the finality of taxonomic classification at species- and strain-levels.

PathoMap's implications for human health, illness and disease

Creating the world's first-ever metagenomics profile at the city-scale has tremendous implications for the future of public health and epidemiology. For one thing, it is the first step to creating futuristic real-time pathogen monitoring systems in urban spaces to prevent the rapid spread of epidemic and pandemic-scale disease outbreaks. The study may also help urban planners and engineers better utilise microbial ecology to design sustainable and healthy cities. Specifically, this study opens the door to incorporating the microbial world in our understanding of how building materials complement the urban microbiome. We are unknowingly building urban microbiomes each time we construct a new building or renovate a space. Studies like the PathoMap study suggest that it is crucial to incorporate a comprehensive understanding of the microbiome in order to improve upon environmental and human health. The research team was able to discover bacteria that digest toxic sludge, which may potentially help city planners and researchers formulate sustainable methods of revitalising 'Superfund' sites like the Gowanus Canal in Brooklyn, New York.



MetaSUB Global Sample Collection Map. For full interactive features, please visit www.metasub.org/interactive-map. The MetaSUB International Consortium and Landscape Metrics



Geospatial map of *Enterobacteriaceae*. Afshinneko *et al.*, 2015

The PathoMap study also provides a unique model of data collection and processing to the emerging field of participatory disease surveillance, whereby community members themselves report on illnesses that emerge in close proximity to them. The use of citizen science and crowdsourcing models has further closed the gap between science and society. Dr Mason and his colleagues believe that PathoMap is a testament to the power and potential of publically engaged scientific initiatives.

Inauguration of the MetaSUB International Consortium

The success of PathoMap led to the expansion of the project to other cities like Buenos Aires, Argentina; Tokyo, Japan; Cairo, Egypt; Lima, Peru; and Paris, France. In 2015, Dr Mason inaugurated the Metagenomics and Metadesign of Subways and Urban Biomes (MetaSUB) International Consortium (www.metasub.org) in an effort to create the world's first-ever longitudinal metagenomics profile of cities around the world. Since then, it has grown to include over 58 cities across 32 countries. Scott Tighe, one of MetaSUB's premier contributing members on developing extraction techniques for the consortium, said, "The scientific reward of benchmarking the microbial DNA content of global urban environments is an awesome undertaking." Different cities are profiling environments other than those found in the transit systems – Vienna has sampled the Danube Canal, Montevideo in Uruguay has sampled the city's beaches (MetaBEA) and sewage (MetaSEW) systems, and Tokyo plans to sample the city and university buildings. Gaston Gonnet, the Principal Investigator of MetaSEW and MetaBEA in Montevideo, remarks that "these types of projects are quite novel and the

possibility of exchanging information is very beneficial; it gives us new ideas and saves time and false starts.”

The MetaSUB Consortium has so far hosted two international meetings – one in New York City, USA, and the second in Shanghai, China – where collaborators discussed the latest updates in metagenomics research and standardised experimental protocols. Moreover, consortium members participated in ‘Global City Sampling Day (CSD)’ on 21 June 2016 in concert with Ocean Sampling Day (<https://www.microb3.eu/osd>) to map genetic and epigenetic stratification of antimicrobial resistance markers in the urban environment. Dr Leming Shi, co-organiser of the 2nd Annual MetaSUB Summit in Shanghai, commented on MetaSUB’s unique model of scientific collaboration. He said, “What impressed me the most is MetaSUB’s capability of engaging a mix of well-accomplished scientists, young college students, and graduate students under the same roof with the same objective of gaining a better understanding of ourselves by better understanding the environment we live in.”

Mapping human ancestral data in MetaSUB Sheffield, United Kingdom

In Sheffield, UK, Dr Eran Elhaik is working hard to piece together human ancestry data from metagenomic data found on public surfaces. Elhaik states: “One of the greatest difficulties in studying microbial ecology is their complex relationships with human populations. Inferring the geographical origins of humans from the genetic data collated during the swabbing process allows identification of the demographic forces that shaped the microbial communities. However, despite its great promise, due to technological

difficulties, we are only capable of studying the combined DNA of individuals or rather ‘communal DNA.’ Afshinnkoo & others already showed that when classifying this ‘communal DNA’ to four ethnicities, their proportions are correlated with the ethnicities in the Census data. We extended this approach by classifying the ‘communal DNA’ to twelve potential gene pools and applying the GPS algorithm, shown to infer geographical origins with high sensitivity (0.75) and specificity (0.99) (Elhaik *et al.* 2014). Compacting the 12 gene pools to four and applying GPS to the NYC subway data yields results that are in agreement with those of Afshinnkoo & others and the Census data. Our approach can thereby be applied to infer temporal population dynamics and study their effect on micro-organism communities.”

Exploring microbial diversity in MetaSUB Sydney, Australia

Rather than focusing on human ancestral data, Dr Aaron Darling and Dr Catherine Burke of the University of Technology Sydney, Australia, are focusing their efforts on delineating the taxonomic classification and functional diversity of microbes in the Sydney transit system. Dr Burke emphasises that her interests lie in exploring the effect of natural sources of air ventilation and exposure on microbial diversity in built environments because they are further correlated with positive health outcomes, like a decreased risk of asthma. Because Sydney’s city train stations are exposed to a variety of different environments, she and Dr Darling are interested in seeing the effect of these different exposures on the microbiome of each station, such as outdoors vs underground, and harbour vs further inland train stations.

She states, “Knowing how exposure to different environments affects microbial diversity in these public spaces could help inform their future design.”

The 2016 Olympiome

Along with the launch of Global CSD, MetaSUB is launching the world’s first ‘Olympiome’. Co-organised by Drs Emmanuel Dias-Neto, Milton Ozório Moraes, Fernanda Kehdy, and Christopher Mason, the researchers profiled Rio’s subway and other public areas before, during, and after the 2016 Rio Olympics. This initiative will better reveal how migration at large-scale public events impacts the microbiome and elucidate the genetic signatures that move between cities. Dr Dias-Neto said of the Olympiome project that it is “a very exciting project” because it is the “first time the microbiome will be studied in a big global mass event.”

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Further reading

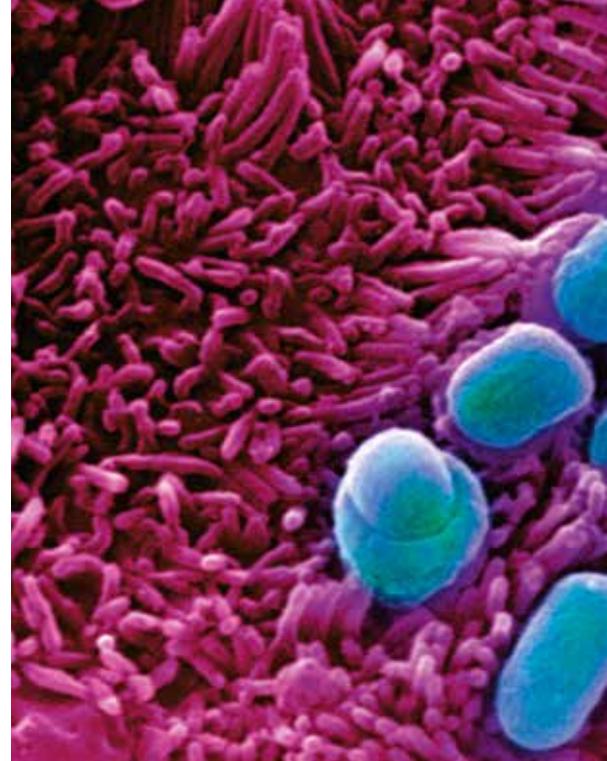
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Globalisation of antibiotic resistance

David M. Livermore

Travel always spreads disease. Bubonic plague reached Turkey in 1347 via the Silk Road, following an outbreak in 1330s China. By 1348, it raged in Italy, shadowing the gaiety of Boccaccio's *Decameron*. By 1351, half of Europe lay in plague pits. One hundred and fifty years later, the conquistadors took smallpox to the Americas, decimating local populations. They returned – many believe – with syphilis, which 'enjoyed' its first European outbreak in 1495 among Charles VIII's army, then besieging Naples. The French called it the 'Neapolitan disease' and carried it home. In England, it became the 'French pox' and in Tahiti, the 'British disease', imported by the Royal Navy.



Coloured scanning electron micrograph of *Escherichia coli* (blue) taken from the small intestine of a child. Stephanie Schuller/SPL

Exponentially growing air travel (Fig. 1) accelerates the spread of bacteria. Travellers sample the local microflora – often more resistant than at home – as they eat, drink and swim, returning home colonised. What are often picked up are *Escherichia coli* with extended-spectrum β -lactamases (ESBLs), which confer resistance to modern cephalosporins. Population carriage of these is much higher in Asia and the Middle East than in Europe, Australasia or North America (Fig. 2). There is also circulation – particularly in India, but also Brazil – of bacteria with 'carbapenemases', which are β -lactamases able to hydrolyse the last-reserve β -lactams. These include the KPC, OXA-48/181 and NDM enzymes. Producers are often resistant to all 'good' antibiotics.

Cross-continent colonisation

Colonising bacteria cross continents in the guts of returning travellers. Tangden and colleagues took rectal swabs from 105 Swedish volunteers, about to travel internationally, finding just one already with ESBL *E. coli*. One hundred of the remaining 104 provided a second swab on return, and 24 became colonised,

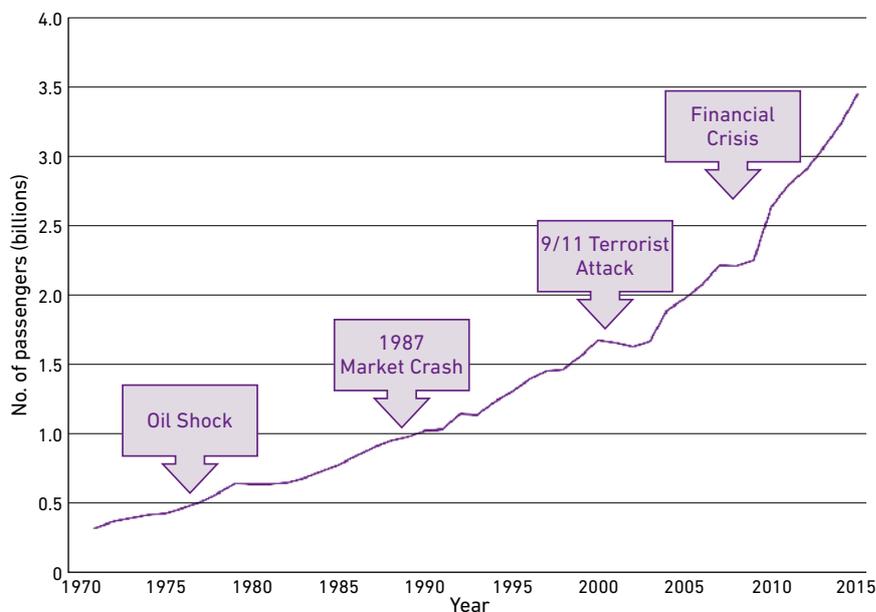
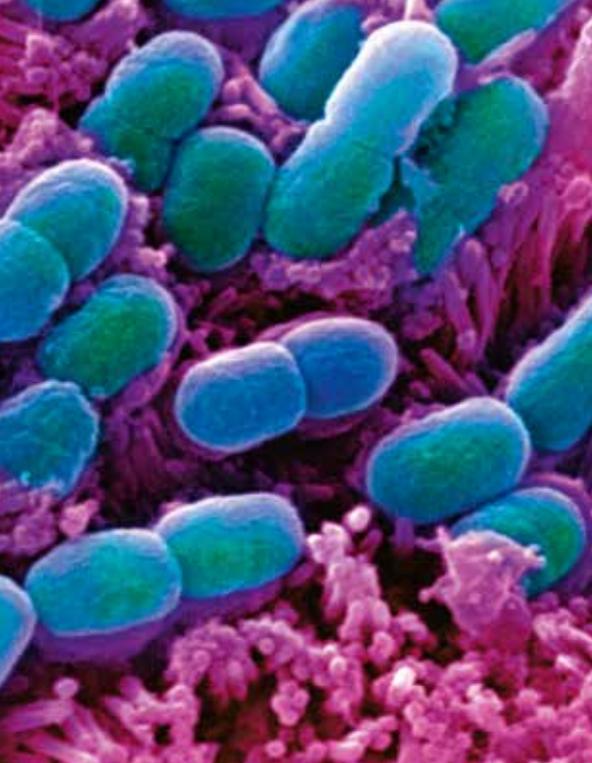


Fig. 1. The growth of passenger air travel. D. Livermore

including seven of eight who'd travelled to India and 10 of 34 who'd gone to East Asia. The ESBLs found were types prevalent in the countries visited – CTX-M-15 from India, CTX-M-14 from East Asia. Twenty-one of the 24 returned (!) for a third swab six months later and five remained colonised. Other studies have obtained similar results, and a meta-analysis found that travellers to South Asia stood an 88% chance of acquiring multi-resistant *Enterobacteriaceae*,

increased by antibiotic use or diarrhoea, which disturb the gut flora. One-way travellers bring resistant bacteria too: 35% of unaccompanied migrant children screened in Germany late in 2015 carried ESBL *E. coli*. Colonisation by carbapenemase producers is rarer, but occurred in 3/824 travellers from France, all visiting India. In a different surveillance approach, Petersen & others sampled the toilets of aeroplanes arriving in Denmark, finding the lowest

resistance gene burden in flights from Greenland and highest in those from South and East Asia (Fig. 3).

Colonisation is innocuous if the *E. coli* remains intestinal, but the gut seeds urinary and intra-abdominal infections. Pitout, in Canada, found that infections with cephalosporin-resistant *E. coli* mostly involved strains with ESBLs prevalent in countries visited.

Some travellers are hospitalised overseas following accident or illness;

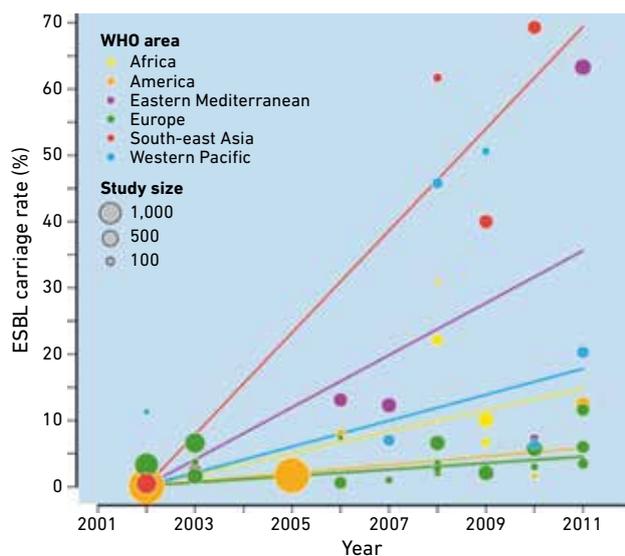


Fig. 2. Gut carriage rates of ESBL-producing *E. coli* by time and place. Reproduced from Woerther et al. (*Clin Microbiol Rev*, doi:10.1128/CMR.00023-13)

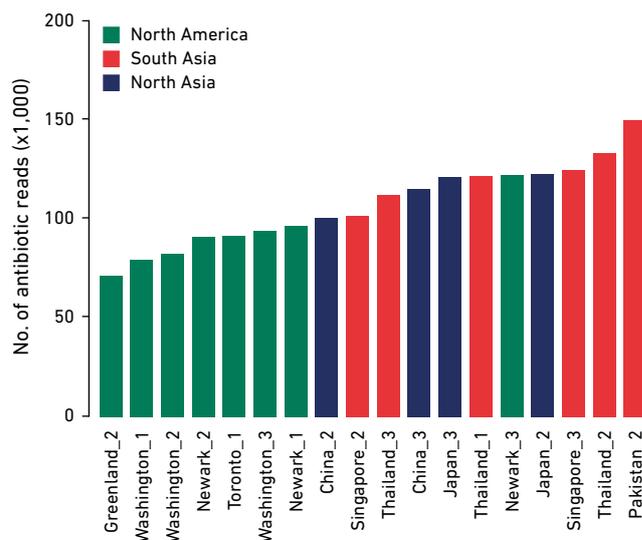


Fig. 3. Burden of resistance genes in toilet waste from aeroplanes arriving in Denmark. Reproduced from Petersen et al. (*Sci Rep* 5, doi:10.1038/srep11444)

others travel specifically seeking medical services. Elderly UK residents with family ties to India or Pakistan divide lives and healthcare between countries. Middle-Eastern patients come to private London hospitals, whilst 'corporate' hospitals in India draw patients from Europe, Africa and the Middle East. In 2010, 63,000 UK residents travelled abroad for treatment including many to India (Fig. 4), which, in total, drew 1.27 million medical tourists in 2012, generating \$1.8 billion in revenue.

Whilst many of the hospitals attended by medical tourists and accident victims provide excellent care, the fact remains that vulnerable patients are moving between low- and high-resistance countries. Moreover, by their nature, hospitals concentrate antibiotic selection pressure. At a medical college in northern India, 50% of intensive care patients were colonised with ESBL producers and 3% with carbapenemase producers. At Rawalpindi, Pakistan, 27% of inpatients and 17% of outpatients

were colonised by *Enterobacteriaceae* with NDM ('New Delhi Metallo') carbapenemase in 2010.

NDM ('New Delhi Metallo') carbapenemase

NDM carbapenemases are interesting because we saw their early globalisation. They were first recognised in Sweden in 2008, carried by urinary *Klebsiella* and gut *E. coli* from a patient transferred a day earlier from New Delhi, India. In the subsequent 20 months, Public Health England received 29 *Enterobacteriaceae*, of multiple species, with NDM enzymes. These were from 25 patients, at least 17 of whom had visited the Indian subcontinent and 13 been hospitalised there, for reasons ranging from a road traffic accident to kidney transplants (Pakistan) to 'tummy tuck'. Most were susceptible only to colistin and tigecycline. Publication was followed by a controversy in the Indian press about the enzyme's name and a flurry of further international reports, many again

describing patients who had visited the Indian subcontinent (Fig. 5). Reviewing the first 250 UK patients in 2013, we obtained a travel history for 100, finding half with travel to the subcontinent. Nevertheless the link is weakening: Public Health England now regularly sees NDM isolates from UK care home residents with no travel history, and there have been a few outbreaks in UK hospitals. Imported resistance is changing to low-level endemic...

Occasionally, a single import allows sharp expansion. *Enterobacteriaceae* with OXA-48 carbapenemase entered several European countries with casualties from the Libyan 'Emergency' of 2011. One became the index patient of an outbreak in a UK intensive care unit. Even starker was a Colombian patient who received a liver transplant in Israel, acquiring a sequence type (ST)258 *Klebsiella pneumoniae* with KPC carbapenemase. Back in Medellin he became the index case for a hospital outbreak, with 32 patients infected and 52 colonised.

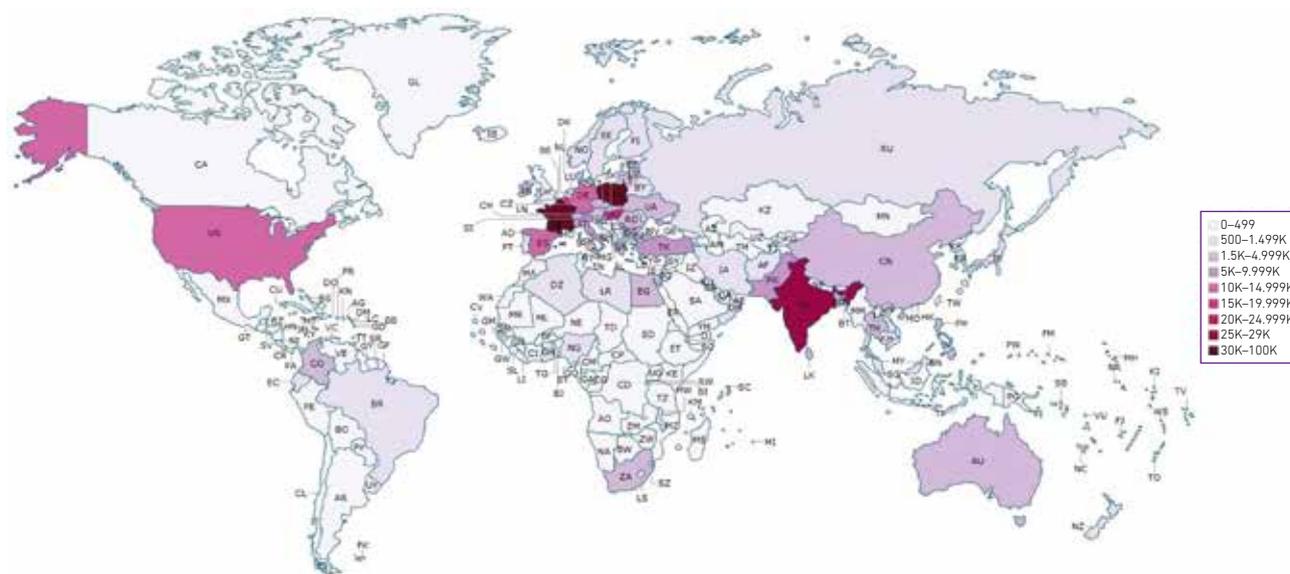


Fig. 4. Who went where from the UK for hospital treatment, 2001–2010. Reproduced from Hanefeld *et al.* (*PLOS ONE*, doi:10.1371/journal.pone.0070406)



Fig. 5. Reported cases of patients with NDM *Enterobacteriaceae*, 2008–2012. Dots coloured red indicate that at least some cases have epidemiological links to the Indian subcontinent. Adapted from Johnson & Woodford (*J Med Microbiol* 62, 499–513, doi:10.1099/jmm.0.052555-0)



Fig. 6. Countries where ST258 and related *K. pneumoniae* with KPC carbapenemases have been reported. D. Livermore

KPC carbapenemases have a strong association with *K. pneumoniae* ST258 and its variants (Fig. 6), and the global spread of this combination of 'high-risk clone' and resistance likely reflects successive transfer events, as from Israel to Colombia, though most remain undocumented. Other high-risk clones have globalised too, notably *E. coli* ST131 with CTX-M-15 ESBL, but its story is more complicated as, unlike ST258 *K. pneumoniae*, this lineage often occurs without ESBLs and occasionally acquires different ESBLs besides CTX-M-15.

What can be done?

Can the globalisation of resistance be halted? The simple answer is 'No'. You

can't stop people travelling or quarantine them. There is no reliable decolonisation strategy, and the duration of carriage is variable. Travellers who drank only bottled water and followed scrupulous hand hygiene were as likely to acquire ESBL *E. coli* as those who omitted these precautions, doubtless because others, who were less fastidious, prepared their food. Nevertheless, two approaches should be encouraged. First, it is vital to encourage countries with high antibiotic resistance to improve sanitation, reducing the circulation of resistant bacteria, and also to improve antibiotic stewardship and hospital infection control. The main beneficiaries will be for the local population, but the traveller

will gain too. At the same time, healthcare providers in developed countries should recognise patients with a history of travel to high-resistance countries, when they are being admitted to hospitals, adapting empirical treatments and infection control precautions until the patient is confirmed *not* to be carrying unusually resistant bacteria.

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The Great Pox

The 3rd of August 1492 marked the start of one of the most significant periods of global exploration, travel and migration. Setting sail from Palos on the Portuguese coast, Christopher Columbus, sponsored by King Ferdinand and Queen Isabella of Spain, headed westward bound for the Canary Islands. From the Canaries, Columbus continued his voyage. Thirty-five days after setting sail, he reached the Bahamas. His first landing point, on a small island, known as San Salvador, was used by Columbus as a base to explore and map the islands of this New World, before he and his crew returned to Spain in the spring of 1493.

Colourised light micrograph of
Treponema pallidum. James
Cavallini/Science Photo Library

Laura Bowater

As we still see today, large migrations of human populations are often accompanied by devastating outbreaks of disease. Over time, isolated populations can build up specific immunity patterns to indigenous diseases but they are often susceptible to new infections. Columbus's exploration of this new world was no exception. Shortly after his crew's arrival, the indigenous population was decimated by epidemics of influenza and smallpox that swept across the continent. The evidence suggests that this was a mutual disease exchange; by 1495, Columbus and his crew arrived back in Europe and they brought the 'Great Pox' (as opposed to the 'Small Pox') with them. This 'Great Pox' soon gained notoriety because of the severity and location of its physical symptoms:

"boils that stood out like acorns, from whence issued such filthy stinking matter that who so ever came within the scent, believed himself infected"

[Von Hutten (1519), translation from Major (1945) p31(5)].

Today we know this disease as syphilis thanks to Girolamo Fracastoro, the famous 16th century mathematician, physician and poet from Verona, who described a dreadful plague sent by a vengeful sun god to strike down the mythical shepherd Syphilis in his poem *Syphilis sive morbus gallicus*. This name has stuck to this day.

The Age of Discovery

Europe in 1495 was mid-Renaissance and experiencing a resurgence of literature, art, sculpture and architecture. But this was also a time of turmoil and change. Shortly after Columbus returned to Europe, the French troops



By Doctor James Tilborgh, Famous through Germany, and Holland, Brabant, France and Italy, for Curing the FRENCH POX, and all Venereal Distempers; Living at present at the Black Swan in St. Giles's in the Fields, over against Drury-Lane End, where you shall see at Night three Lanthorns with Candles burning in them upon the Belcony. Where he may be spoke with all alone, from Eight of the Clock in the Morning, till Ten at Night, desiring you to be careful for your own benefit not to mistake the place because there is a new person that is lately come over and hath presumed to make use of the Bill and Peice which formerly I did make use of. And further without any name, which is the cause I have altered my Peice. And I desire nothing for my labour and pain till the person be cured, and wish you to be careful and not be abused.

This is to give notice by these Papers, That there is a very expert famous outlandish Doctor, and Citizen of Hamburgh, who is lately arrived here in London, and hath brought by Gods blessing, a wonderful Art with him, which he hath found through long seeking for, and travelling through many Kingdoms, yet not without great trouble and charge. *viz.* The right way of Curing the Pox, otherwise called *Morbum Gallicum*, with all its dependants, which no man can so soundly Cure as he; which he hath stewn to many thousands. And because it is the best time of the year to Cure such Diseases, he hath caused these Bills to be Printed

FIRST, He Cures the French Pox, with all its dependants, *viz.* The Running of the Reins, Pains in the Groin, and in making of water, Shankers, Buboes, Sockloats, Spanish Kraagen, Boils and Scabbs about the Head, Holes in the Throat and Neck, and rotting of the Palate and Grissels of the Nose and Gums, whereby the Nose and the Palate often-times comes to fall, and by that means Men are bereaved of their speech all their

A 17th-century handbill advertising a cure for syphilis (here called the 'French Pox') and other venereal (sexually transmitted) infections. British Library/Science Photo Library

of King Charles VIII were marching to besiege Naples in order to create a Mediterranean base to launch a Crusade. This was the start of the First Italian War. Soldiers and mercenaries were recruited from across Europe, along with more than 800 camp followers. It wasn't long before the great pox emerged within their ranks. This 'French disease', as the great pox was soon rebranded, spread remorselessly across a wide swathe of the European continent. Recognising no

borders and travelling eastwards into India, China and Japan, and south into the African continent, it collected several new names along the way. These names had one thing in common – an inherent desire to attribute this terrible disease to foreigners and aliens. The French named it the 'Neapolitan disease', the Russians the 'Polish disease', the Polish and the Persians called it the 'Turkish disease', and the Turkish called it the 'Christian disease'. Further afield,

the Tahitians named it the 'British disease' and in Japan it was known as the 'Chinese pox'.

Syphilis: the bacterial disease

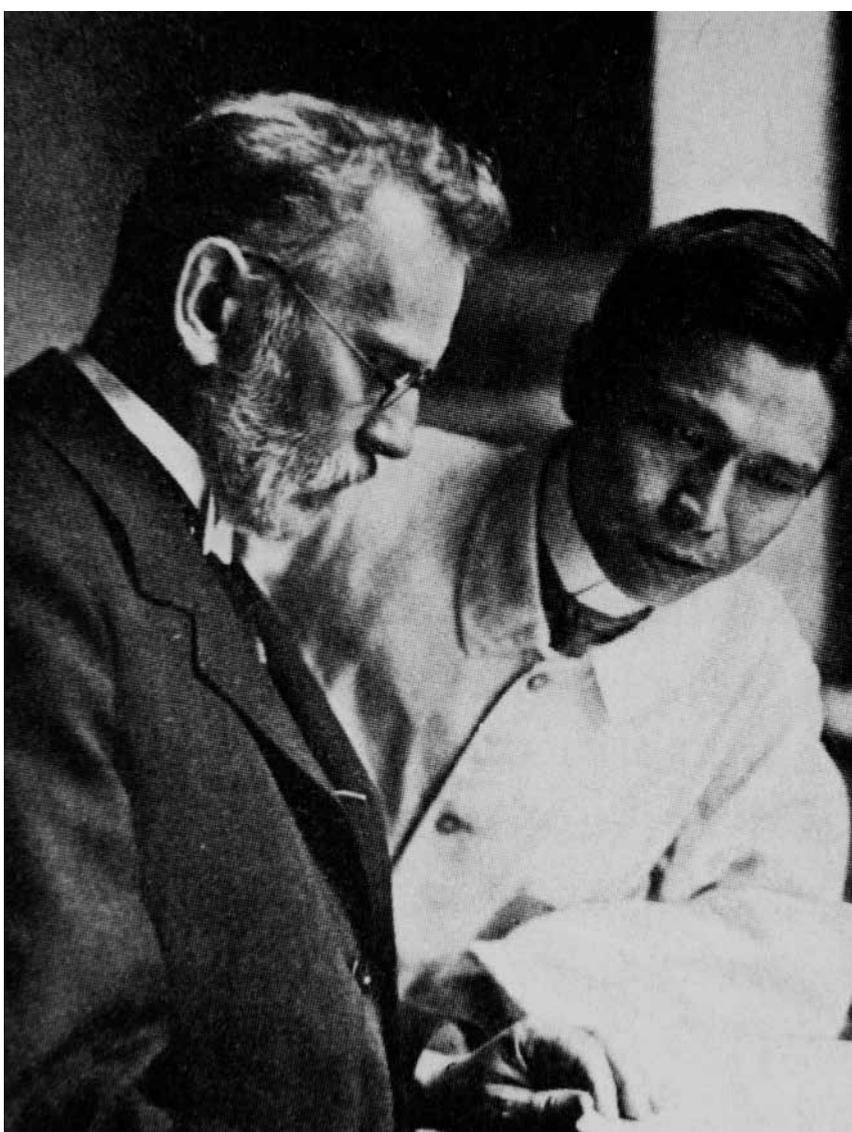
Syphilis is a sexually transmitted infection; the more sexual partners an individual has, the more likely they are to catch the disease. In the pre-antibiotic era syphilis was an extremely common disease that ravaged populations. In 1905, more than 400 years after the disease arrived in Europe, two German scientists, the zoologist Fritz Schaudinn and the dermatologist Erich Hoffmann, finally identified the bacterial agent responsible for this devastating disease. *Treponema pallidum* is a spirochaete, a delicate corkscrew-shaped bacterium that enters the body through micro-traumas and abrasions in mucous membranes.

The disease erupts in three stages. Primary syphilis, the first stage of the disease, manifests as a 'chancre' (or ulcer) appearing at the initial site of the bacterial infection. Left to its own devices, this ulcer usually heals, but unfortunately this isn't the end of the infection; the disease re-emerges as secondary syphilis. The infected individual begins to feel unwell with a fever, a rash, and a sore throat. Once again, these symptoms can appear to improve spontaneously but they can be relapsing until finally the disease retreats, becoming latent and asymptomatic. Syphilis can lie latent and hidden for many years before emerging once again as tertiary or late syphilis. It is at this stage of the disease that the most severe symptoms appear. Syphilis damages the heart, causes gummy tumours that can appear in any body tissue including the bones, and causes neurological damage that can lead to mobility problems, dementia and insanity.

Syphilis can also be passed from mother to child. A pregnant woman infected with *T. pallidum* can transmit syphilis to her foetus via the placenta, and in a third of cases this can cause stillbirth and miscarriage. Infected mothers can also give birth to babies with congenital syphilis – a severe, disabling, and often life-threatening infection.

Syphilis treatment and cures: past, present and future

In 1516, Ulrich von Hutton, a German scholar plagued with syphilis, described one of the first treatments for this disease in his poem, *De Morbo Gallico*. Guaiacum, or *holy wood*, was brought from Central America to Europe in order to treat this noxious disease. It was not an effective cure, and alternative



Portrait of Paul Ehrlich (1854–1915) and Sahachirō Hata (1873–1938), the bacteriologists from Germany and Japan, respectively, who discovered the first cure for syphilis. Science Photo Library

In the UK, the numbers of infectious syphilis diagnoses are at the highest since the mid-1950s and this pattern is repeated on a global scale.

treatments such as sweat baths and mercury ointments and inhalations (sometimes both) soon became an accepted treatment. Although mercury had terrible side effects and many patients died of mercury poisoning, it remained the go-to drug for syphilis until 1910, when Paul Ehrlich, a German physician and Nobel prize-winning scientist, discovered the antisyphilitic effects of arsenic compounds. Ehrlich's approach to treating infectious diseases like syphilis was radical. Instead of focusing on ameliorating the symptoms of syphilis, he decided to target the disease-causing agent, *T. pallidum*, curing the patient and the patient's symptoms in the process. Ehrlich and his assistant, Sahachirō Hata, a Japanese bacteriologist, began to search for a 'magische Kugel': a 'magic bullet'. They focused on screening a raft of arsenic-based synthetic dyes by methodically testing the compounds on syphilis-infected mice. Compound 606 soon emerged as a clear frontrunner and it was quickly marketed globally as Salvarsan™ and later, the improved Neosalvarsan™. Was Salvarsan™ the magic bullet that Ehrlich had hoped for? Well not quite; although it effectively destroys *T. pallidum*, the drug's harmful side effects and complex treatment regime were significant issues. Eventually, a new treatment for syphilis emerged following the discovery of penicillin by Alexander Fleming in London, in 1928. By 1943, the production of penicillin had mostly moved to

the United States. It was against the backdrop of mass migration caused by the Second World War that John F. Mahoney, Richard C. Arnold and Ad Harris at the US Marine Hospital, Staten Island, successfully treated four patients with primary syphilis. Later in 1984, Arnold wrote about his earlier work:

"Syphilis was once a dreaded and dreadful disease involving millions of US citizens. Before the introduction of penicillin, the heavy-metal cure often caused thousands of deaths each year. The morbidity and mortality of the disease itself was horrendous, involving all ages from the fetus to the elderly."

During the golden era of antibiotic discovery, new alternative drugs to penicillin, such as doxycycline, azithromycin and clindamycin, also emerged to treat this disease. But sadly the optimism that the new antibiotic age would lead to the eradication of bacterial diseases like syphilis has been premature. Syphilis is not a disease of the past. On a worldwide scale, congenital syphilis is still a condition that affects pregnancy, causing serious health problems and death to babies. Current estimates indicate that in 2012, there were approximately 18 million cases of syphilis, with 5.6 million new syphilis cases in women and men aged 15–49 years globally. In the UK, the numbers of infectious syphilis diagnoses are at the highest since the mid-1950s, and

this pattern is repeated on a global scale. Worryingly, although penicillin and its derivatives still remain an effective cure, we already have strains of syphilis that are now resistant to the newer, alternative drug treatments, such as azithromycin and clindamycin. The 'Great Pox' is still with us and serves as a stark reminder that prevention is still better than the cure.

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Ian Atherton

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Writing your abstract

Here are some top tips to consider when writing your abstract:

Format

- Abstracts should be 200–250 words in length.

Title

- Make sure the title is informative – this is your chance to catch the reader's attention.
- Indicate the presenting author – this is usually (but doesn't have to be) the first author.

Background

- This should be around two sentences long, summarising how your work came about.

Methods

- This should be the second longest section of your abstract, outlining how you achieved your results.

Results

- This should take up the majority of your abstract, and detail your findings. Findings should be stated objectively.

Conclusion

- This should be two sentences setting your results in context with the wider research area. Why does your research matter?



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Our 2017 programme is packed full of symposia, forums, workshops, Prize Lectures, social events, professional development and plenty of networking. You can visit our website for a breakdown of the schedule, speakers and events but to give you a taste of what to expect, here's an overview.

Main symposia:

- Anaerobe 2017: Molecular, genomic and metagenomic insights into anaerobic infection
- Annual Meeting of Protistology-UK Society: Intracellular infection and endosymbiosis within protists
- Aquatic microbiology: New model organisms and new challenges
- Cell biology of pathogen entry into host cells
- Microbial circadian and cell rhythm
- Critical health challenges in medical mycology
- Epigenetic and non-coding RNAs
- Geomicrobiology
- Heterogeneity and polymicrobial interactions in biofilms
- Just passing through – virus infections of the tract
- Macromolecular machines
- Microbial cell surfaces
- Microbial genomics: From single cells to large populations
- Microbial mechanisms of plant pathology
- Regulation of RNA expression during virus infection
- Synthetic and systems approaches to microbiology

Prokaryotic forums:

- Environmental and Applied Microbiology Forum
- Microbial Physiology, Metabolism and Molecular Mechanisms Forum
- Prokaryotic Genetics and Genomics Forum
- Prokaryotic Microbial Infection Forum

Virus workshops:

- Antivirals and vaccines
- Clinical virology
- Evolution and virus populations
- Gene expression and replication
- Innate immunity
- Morphogenesis, egress and entry
- Pathogenesis

In addition to these sessions, we will have our Prize Lectures at the start and end of each day:

- Colworth Prize Lecture
- Fleming Prize Lecture
- Marjory Stephenson Prize Lecture
- Prize Medal Lecture

Plus, in 2017 there will be three ticketed evening events for exclusive access. These can be booked online when registering:

- Sunday networking event
- Quiz night
- Traditional ceilidh

And exclusive access to all of this:

- Professional development events
- Poster sessions
- Live at Lunch sessions
- Hot Topic discussions
- Flash poster presentations
- A large trade exhibition
- Networking and drinks receptions

While every effort has been made to ensure the programme is accurate, changes are unavoidable.

Visit www.microbiologysociety.org/annualconference for the latest version.



Ian Atherton

Focused Meetings

2016 Review

Molecular Biology of Archaea 5	The Dynamic Fungus	Molecular Biology and Pathogenesis of Avian Viruses	Irish Division Meetings	
1–3 August 2016	5–7 September 2016	27–29 September 2016	Host-Pathogen Interactions	Exploring the Microbe-Immune System Interface
London School of Hygiene and Tropical Medicine, London	Mercure Exeter Rougement Hotel, Exeter	Charles Darwin House, London	30 June–1 July 2016	1–2 September 2016
			Trinity College, Dublin, Ireland	Rochestown Park Hotel, Cork, Ireland

The Society has now completed its third year of Focused Meetings. The topics are always intriguing and offer a fabulous opportunity to present and listen to new research. These small and concentrated meetings have proved to be essential for scientists to network more closely within their field.

This year's Focused Meetings provided an exciting opportunity to bring together experts in microbiology from the UK, Ireland and all over the world. The programmes were designed to attract researchers from microbiology-related

disciplines and to inspire new collaborations. For the first time the Microbiology Society worked together with the Irish Society of Immunology to host a meeting that encouraged the exchange of ideas and findings between these two scientific disciplines.



The conference dinner at the Charles Darwin Centre, Natural History Museum, London. Thorsten Allers, University of Nottingham

Overall an excellent meeting, well selected talks, enough breaks to network! I was glad to be selected for a talk which gave me visibility and a good overview of the community, which is important for a last-year PhD student looking for a postdoc.

Elena Rensen, Institut Pasteur, France
Attended the Molecular Biology of Archaea 5 meeting

[The meeting] exposed me to new/different ideas in host-microbe interactions, and I met new people.

Leighton Pritchard, Computational Biologist,
The James Hutton Institute, UK
Attended the Host-Pathogen Interactions meeting



Delegates at the Host-Pathogen Interactions Focused Meeting in Ireland.

Excellent networking. Important new unpublished information was presented.

Harriet Knafle, University of Aberdeen Attended the Dynamic Fungus meeting



Delegates at the Avian Viruses Focused Meeting at Charles Darwin House.

Keep up-to-date with events, follow the Society on Twitter: [@MicrobioSoc](https://twitter.com/MicrobioSoc)

Dates for your diary – 2017 Focused Meetings

ISSY33 Exploring and Engineering Yeasts for Industrial Application

June 2017 – Cork, Ireland

Irish Division: Microbial Resources for Agricultural and Food Security

June 2017 – Belfast, UK

British Yeast Group Meeting 2017: The Versatility of Yeasts

September 2017 – Kent, UK

Irish Division: Antibiotic Resistance and One Health

September 2017 – Maynooth, Ireland

15th International Conference on *Pseudomonas*

September 2017 – Liverpool, UK

IMAV 2017: International Meeting on Arboviruses and their Vectors

September 2017 – Glasgow, UK

To register your interest in these meetings, email conferences@microbiologysociety.org. Visit our website for further information on our events: www.microbiologysociety.org/events.

Conference grant opportunities

The Society offers a number of grants to support members presenting their research at our Annual Conference, Focused Meetings and Irish Division meetings.

Society Conference Grants

Open to technicians, postdoctoral researchers or PhD students. This grant can also support those attending their first Society meeting, whether or not they are presenting.

Travel Grants

To support eligible members to present at any Society conference, who are not eligible for the Society Conference Grants.

For further information, including full eligibility criteria please visit: www.microbiologysociety.org/grants

Shape our events programme

Every year our programme of events is developed and driven from proposals submitted by our members. At this time of year we want you to start to consider your proposals for Annual Conference sessions for our 2018 event and to apply for your Society-Supported Conference Grants.

Annual Conference session

We welcome proposals from organisers who wish to deliver a session at our Annual Conference. Our Conference offers you a collective audience of over 1,200 delegates from around the world, allowing you the opportunity to share and develop your network in your specialist subject. These proposals are for our 2018 event and must be discussed with the relevant Division Chair in advance of submission. The Chairs and their contact details are listed on the Microbiology Society website.

Society-Supported Conference Grants

To ensure our members and the microbiology community has continuous access to a varied programme, we regularly work in collaboration with other organisations and session organisers to sponsor UK and international speakers. If you have an event that is taking place and are looking for sponsorship, you can apply for a Society-Supported Conference Grant. Grants are allocated in two phases each year: January and July. Grant applications must be seen and discussed with the relevant Division Chair in advance of submission to ensure your application is supported.

Decision-making process

All of the proposals and applications are submitted to the Scientific Conference Committee, which is made up of representatives from the Virology, Eukaryotic, Prokaryotic and Irish Divisions. This process ensures our programme of events covers a broad spectrum of microbiology.

Key dates

Deadline: **Friday 16 December 2016**
Notification date: **Monday 13 February 2017**

For further information and application forms visit: www.microbiologysociety.org/events

All Microbiology Society journals to move to continuous publication model

From January 2017, all Microbiology Society journals will begin publishing articles using a model known as continuous publication.

Currently, the Society's four print and online journals (*Microbiology*, *Journal of General Virology*, *Journal of Medical Microbiology* and *International Journal of Systematic and Evolutionary Microbiology*) are published in monthly print and online issues. This means that there can be a delay to final publication while the approved article waits for the issue to be ready.

With continuous publication (CP), as soon as an author has approved their copy-edited and typeset proof, the Microbiology Society's Production Team

will do a final check and then publish the article online. Each month, these will be grouped together into an issue online, which will also be printed and dispatched to subscribers.

The change means that readers will see the best version of the article as soon as possible. Authors can expect to see the final corrected proof of their article published online within approximately two weeks from acceptance. The uncorrected, author accepted article will no longer be published in favour of this higher-quality version. This change was supported by Microbiology Society authors; when surveyed, 61% said that they would prefer the first version of their article to be published in this format, while 17% preferred the raw, uncorrected version.

Of the move to continuous publication, *Journal of Medical Microbiology's* Editor-

in-Chief, Professor Pete Borriello, stated, "This is an exciting change for authors and readers alike. By taking away the wait for issues, articles will be published online in a better format much more quickly."

The Microbiology Society has launched two online-only, gold open access journals in the last two years, both of which have benefitted from using the CP model. The change to the print and online titles will harmonise the systems and workflows across the Society's portfolio and ensure that we can make the most of our online publishing platform.

Visit www.microbiologyresearch.org to find out more about the Microbiology Society's journals.

Rachel Walker

Head of Publishing Operations

Agar art competition in Nepal

Budding artists in Nepal have taken part in an agar art competition – the first to have been organised between the Microbiology Society and local host partner organisation, Amazing Microbiology Nepal.

Society Champion, Manoj Pradhan, is the person behind Amazing Microbiology Nepal, which is primarily a Facebook group sharing ideas but the group also organises events, workshops and conferences too. He said, "The main objective behind organising the agar art contest was to reach a wider audience and make them more aware not only of the Microbiology Society, but also the opportunities the study of microbiology brings for researchers, students and academics. I think we have achieved our goal." Manoj went on to say that the competition had already generated a lot of interest and that group members were busy answering many queries resulting from it.

The competition saw 51 entries from 12 different institutions

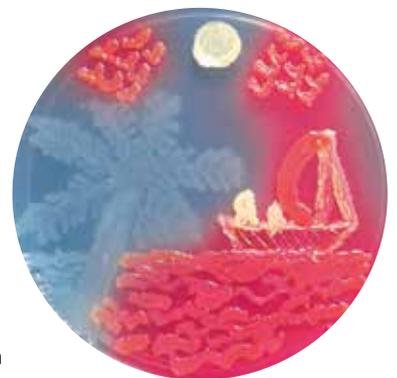
across Nepal. Entries were judged on both their creative and microbiological content. First prize (lower left) went to Nisha Pote from Dhulikhel Hospital; second prize went to Binita Adhikari from Nepalese Army Institute of Health Science, while third prize (above) went to Monika Maharjan from St Xavier's College.

The Society is delighted to have supported Manoj in this competition. Nepal has been through some challenging times recently and we are very pleased to have members in the country who can still find time to support initiatives like this.

Paul Easton

Head of Membership Services

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What do our authors really think of Microbiology Society journals?

Earlier this year, the Microbiology Society surveyed over 850 authors to find out about their experience of publishing with our journals. This was a first for the Microbiology Society and we would like to share the results with our members.

The survey was conducted in May 2016 across five of the Society's journals (*Microbiology*, *Journal of General Virology*, *Journal of Medical Microbiology*, *JMM Case Reports*, and *International Journal of Evolutionary and Systematic Microbiology*) and asked for feedback from anyone who had submitted an article to one of the journals in the last two years. We wanted to find out about authors' experiences and learn where we can improve.

We are pleased to report that there has been a great deal of positive feedback. When asked, 83% of respondents rated the submissions process either 'excellent' or 'very good'. On top of this, 81% of authors stated that they would submit to the journal again, and would recommend publishing with the Microbiology Society to a friend or colleague.

"Every step of the review process, including manuscript submission, was straightforward and easy to complete."

Journal of General Virology author

On average, our authors rated the peer review process 4/5. Our expert Editors and reviewers work

hard to maintain a fair and efficient peer review process, so we are delighted that this area has been rated so highly.

"My manuscript improved a lot thanks to the Editor contribution."

Journal of Medical Microbiology author

When asked about publication time, 86% of respondents were either 'satisfied' or 'extremely satisfied' with the speed of publication on accepted papers (first version online), while 78% of respondents were 'satisfied' or 'extremely satisfied' with the speed of publication to the final Version of Record.

Since the survey, Microbiology Society journals have moved to a new typesetter. We hope to see author satisfaction increase in this area as the Society moves to a continuous publication model in 2017 – for more information see page 186.

One area of concern for our authors was the open access payment system, which has now changed. Using a streamlined online payment system via Copyright Clearance Center, we hope to see author satisfaction improve over time in this area.

"The journal is run by a professional team that gave us the impression of high efficiency."

International Journal of Systematic and Evolutionary Microbiology author

The Society's Publishing Team are always looking for ways to improve the peer review process and author experience; delivering a personal approach, ensuring the best service during every stage of the process. To achieve this we aim to run the survey annually.

The Microbiology Society would like to thank all authors who took part in the author survey this year.

To find out more about the Microbiology Society journals, including information on how to submit, visit www.microbiologyresearch.org. If you've published in one of our journals and want to share your experience, please get in touch via email (journals@microbiologysociety.org) or Twitter ([@MicrobioSoc](https://twitter.com/MicrobioSoc)).

Diandra Roberts

Editorial Development Coordinator
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A close-up photograph of soil with numerous colorful, pill-shaped objects scattered throughout, representing a diverse microbiome. The colors include shades of blue, green, yellow, orange, and pink. The soil is dark brown and textured.

Policy

Exploring the potential of microbiome research

Steve Gschmeissner/Science Photo Library

Microbiomes – the microbial communities found in and on human, animal and plant hosts, and associated with other environmental niches – are a hot topic.

Driven by advances in high-throughput sequencing and meta-omic approaches, microbiome research is a rapidly developing area of microbiology. Not only researchers, but also industry, funders and other supporters and end-users of research are increasingly interested in the potential implications and applications of exploring and exploiting microbiomes, for example, for human and animal health, and improving agricultural efficiency and sustainability.

However, much fundamental research remains to be done to understand the composition, dynamics and functions of many microbiomes. One challenge this raises is ensuring policy-makers and the wider public are appropriately engaged and informed, without current research being interpreted out of context and oversold.

Importantly, there is growing international consideration among the research community and other stakeholders about the science and policy gaps and challenges that need to be addressed to progress fundamental and translational microbiome research.

Notably, the US White House Office of Science and Technology Policy have launched a National Microbiome Initiative, with federal agencies allocating \$121 million of funding, substantial private investment, and goals to support interdisciplinary research and develop infrastructure.

Given the widespread interest in microbiome research, and its associated scientific and societal opportunities and challenges, the Microbiology Society identified an important need for policy-makers and other stakeholders in the UK and Ireland to have access to appropriate scientific information and expert opinion about this rapidly emerging field. The Society has established a Microbiome Expert Working Group to oversee the development of an accessible, evidence-based report, which will consider current and future developments in microbiome research across human and animal health, agriculture and food, and the environment, and its public policy relevance.

The Microbiome Expert Working Group's first meeting was held in July in London at the British Academy.

Chaired by Professor Julian Marchesi, the multidisciplinary group of experts considered what defines microbiomes and microbiome research, potential opportunities for discovery and translation, and the scientific, policy and regulatory gaps and challenges that need to be addressed to realise these opportunities. Dr Mark Bale, Deputy Chief Scientific Adviser at the Department of Health, also spoke to the group about how microbiome research and the report could help inform public health policy-makers and advisers.

Over autumn, the Society is holding several multidisciplinary stakeholder workshops in the UK and Ireland. The workshops will further inform the report and aim to facilitate interdisciplinary networking and knowledge exchange between researchers, and with other stakeholders, such as representatives from funders, industry, regulators and public health.

The final report will be published next year. In the meantime, keep an eye on our e-newsletter for updates and activities linked to the project. We are also planning some allied communications and engagement activities, to provide the wider public with accessible, expert information about microbiome research.

Previous Microbiology Society expert panels have produced policy reports on food safety and security and sexually transmitted infections. For more information about these reports and the Microbiome Policy Project visit our website (www.microbiologysociety.org/policy) or get in touch by email (policy@microbiologysociety.org).

Paul Richards

Policy Officer

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Early Career Microbiologists' Forum: Your Executive Committee



Helen Brown

Chair

Dr Helen Brown

is a postdoctoral researcher at Cardiff University, investigating bacterial attachment to

metal implants and abiotic surfaces. She brings experience of working with several successful committees, and in particular understands how important the first few years of a researcher's career can be. Helen wants to provide more focused material for early career researchers at the Annual Conference, and develop a mentoring programme that is open to all Society members.

The Early Career Microbiologists' (ECM) Forum was established at the beginning of 2016, to enable early career members to have their say within the Society. With professional development opportunities tailored directly for them, and opportunities to bring the early-career viewpoint to all Society strategic priorities, the Forum have elected an Executive Committee to direct their work. The members of the Executive Committee were elected this summer, so we asked them to tell us more about who they are and what they want to achieve during their tenure.



Ian Martindale Photography

Communications Representative

Rebecca Hall is a PhD student in Mechanistic Biology at the University of York, investigating the microbiome of the tsetse fly. She brings a lot of enthusiasm for science communication and anything a bit geeky, and has experience writing for blogs and the student newspaper. Rebecca would like to engage ECMs more in terms of science communication, and explore ways in which budding writers could use the Society to get their work out to other microbiologists and the general public.



Sion Pickering

Conferences Representative

Dr Amy Richards is a Research Fellow and Lab Manager at The Roslin Institute, investigating the host-pathogen

interactions of *Staphylococcus pseudintermedius* and *Staphylococcus aureus*. She brings motivation, focus and objectivity to the Forum as well as event management experience. She wants to develop greater opportunities for ECMs to meaningfully present their research findings at conferences and organise specialist sessions that will equip ECMs for a career in academia.



Linda Oyama

International Representative

Dr Linda Oyama is a Postdoctoral Research Scientist at Aberystwyth University, investigating

rumen-derived anti-infectives as alternatives to antibiotic therapy. She brings an infectious personality to communicating science and is constantly involved in widening participation and in organising science events. Linda hopes to get more international ECMs involved in Society events and activities, and reach out to more ECMs outside the UK and Europe.



Andrew Day

Programmes Representative

Andrew Day is a PhD student at the University of Cambridge, studying

phage-host interactions. He brings a passion for communicating science and promoting the representation of early career microbiologists. Andrew would like to grow the Forum in size, identify key areas that will be the future focus in the field of microbiology and enact changes to increase the engagement of early career microbiologists.

Maria Fernandes

Professional Development Manager
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Schoolzone

International travel and the spread of disease

In recent history, diseases have spread across the globe and had drastic effects on human and animal populations' health. Before colonisation and the arrival of European settlers to countries across the world, indigenous people were only exposed to certain diseases that were present in their own country. The arrival of settlers meant the introduction of new pathogens that the indigenous people did not have natural immunities to.

As soon as a new disease is introduced into a population that has no antibodies for it, the disease can run rampant through the human or animal population and be devastating to its numbers. There are several ways diseases can be transmitted, including through the air, via a bloodborne route and by direct contact. As people began to explore the new world, for example, diseases spread through many different transmission routes and infected those without any antibodies.

Today, due to international travel, a person can carry a disease from one side of the world to the other in approximately one day. This is particularly worrisome as this is shorter than a lot of incubation periods of many diseases. This means that someone can travel through several countries or continents without knowing they are infected, allowing diseases to spread rapidly.

Although in many countries the mortality rate of diseases has decreased

due to advancements in vaccines, there is always the concern of re-emergence and the introduction of new diseases. To curb this, disease surveillance systems have to be implemented. Many of these systems are networks of local, regional and national health boards that report on diseases and feedback into a large network of World Health Organization (WHO) member countries.

Impact of disease spread to Australia

In Australia, colonisation had a devastating impact on the indigenous Aboriginal people who had lived there for thousands of years. The Aboriginal people were introduced to many European diseases from the early settlers, which had a huge negative impact on the population. These diseases included tuberculosis, measles and the common cold. A smallpox outbreak spread rapidly throughout the indigenous communities who did not have appropriate medicines to treat



Milky Way over Uluru, Australia. Babak Tafreshi/Science Photo Library

these diseases. Venereal diseases were also introduced that impacted fertility of some sections of the population and therefore reduced birth rate.

Another impact European settlers had on Australia when they arrived was the introduction of animals, including rabbits. After only a few years the rabbit numbers in areas of Australia had increased exponentially. By the 1920s there were over 10 billion rabbits across the country. This caused problems to the natural vegetation as rabbits would eat the seeds, meaning the plants could not regenerate. Australia's native burrowing species were also threatened by the increased rabbit numbers because they were in competition for food and stealing their existing burrows.

In a bid to decrease rabbit numbers, conventional methods of eradication were used. This included poison and

fumigation and ploughing of rabbit burrows. However, these methods were time-consuming and did not have a huge impact on population numbers due to the rate at which rabbits reproduce.

In the 1950s, as a means of biological control, the myxoma virus was introduced. This virus causes myxomatosis, a disease where infected rabbits develop mucus-filled lesions and die of haemorrhage within approximately 10 days. This method was initially extremely effective and the rabbit population was almost wiped out completely in some areas. However, over time, the disease's effectiveness was reduced as the rabbits began to develop a resistance to the virus. To combat this, a second biological control of rabbit calicivirus has been introduced to curb numbers. In a similar way to myxoma virus, rabbit calicivirus showed initial promise by eradicating large numbers of rabbits but once again the rabbits have developed immunity to the virus.

A rabbit with myxomatosis.
Ashley Cooper/Science Photo Library



How do diseases spread internationally? (Classroom activity)

This simple activity will demonstrate how diseases spread through populations when there is no immunity compared to when some immunity is present or acquired.

What you will need:

- Sheets of stickers, dots will suffice (at least two different designs).
 - A timer to keep track.
 - An area for the students to walk and move around freely.
1. Give one student (the 'carrier') a sheet of stickers.
 2. Set 60 seconds on the timer and have all students except the carrier student move around freely in the designated space. After 30 seconds, signal to the carrier student to start moving around and attempt to stick the stickers on to the other students. Advise the students not to move towards or run away from the carrier and just walk about the space as they were before.
 3. After the first minute, count the number of students who have a sticker attached to them. This is

- the number of students who have become 'infected'.
4. Remove all the stickers from the students and make three students disease carriers. Repeat steps 2 and 3. How many more students were infected with the disease when there were more disease carriers?
5. This time, before repeating steps 2 and 3, place a sticker of a different colour on two students. After the 60 seconds is up, count the number of students who have been infected but discount anyone with a sticker of a different colour. This represents people with immunity to the disease (either through vaccination or acquired immunity). How does immunity affect the number of students with the disease?
6. Repeat the process again but place a sticker of a different colour on six students. How many are infected now with a higher number of students with immunity?
7. Continue these steps until all students are immune.

Questions to consider

- Which round of the activity represents the introduction of disease to new settlements?
- How can diseases be prevented from spreading?
- How do different levels of immunity affect the spread of disease?
- What other preventative methods could be used to prevent disease spread?

Hannah Forrest

Public Affairs Administrator
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Outreach

Antibiotics Unearthed goes back to the forest

Citizen science project travels the UK

After a successful series of pop-up events in August 2015, the Antibiotics Unearthed Team were out at Forestry Commission sites again this summer, crowdsourcing for new antibiotics.

Antibiotics Unearthed, inspired by the Small World Initiative in the USA (www.smallworldinitiative.org), gives the general public, students and educators in the UK and Ireland the opportunity to work with scientists as part of a global initiative to discover new antibiotics from soil bacteria. The pop-up events encourage members of the public to get engaged with the topic of antibiotic

resistance and be involved in research looking for new drugs.

This summer we visited two Forestry Commission sites: Garwnant Visitor Centre in the Brecon Beacons and Kielder Castle Forest Park in Northumberland. People visiting the event could take a sampling kit around the forest with them, collect a soil sample and prepare a spread plate of

It is a privilege to be able to involve the public in the hunt for new antibiotics as part of my PhD. Their overwhelming support is encouraging in the face of antibiotic resistance.

Ethan Drury, PhD student
Antibiotics Unearthed

their sample when they returned to see the bacteria present in the soil, before depositing the sample in our soil bank, which was then sent to the University of East Anglia for analysis.

Visitors to the stand were welcomed by a team of expert volunteers, who talked with them about searching for new antibiotics in the soil, the methods used to look for new medicines and the threat of antibiotic resistance. We also had microscopes on the stand with plates containing mixed soil communities, and several strains of *Streptomyces*, which are the source of many antibiotics in common use, kindly provided by Dr Paul Hoskisson at the University of Strathclyde.

Three hundred samples were submitted by visitors to the forests, who are being kept up-to-date with the analysis of the samples at the University of East Anglia via email and social media. Ethan Drury, a PhD student match-funded by the Society and based at the UEA, is analysing the samples to look for new antibiotics. He also carried





out detailed interviews with visitors to the event, as part of his research into best practice of public engagement and measuring the impact of long-term engagement with scientific research.

All ages of visitors enjoyed collecting their sample, and prepping it ready for further analysis. We are really pleased to see the enthusiasm from people who are following the analysis online. Results of the experiments have been shared on the Society's website and social media. Even if you didn't manage to join us in the forests, please check out the website and Facebook page and see if you can spot any potential antibiotics on our samples.

If you would like to find out more about the project, please contact the Antibiotics Unearthed Team on antibioticsunearthed@microbiologysociety.org.

www.microbiologysociety.org/AntibioticsUnearthed
[@MicrobioSoc](https://www.facebook.com/antibioticsunearthed) #AntibioticsUnearthed

Hear from one of our volunteers about the project

I'm an undergraduate studying a Microbiology BSc in Aberystwyth University. Previously, I worked from home running my own small business while also raising my children. I've returned to study as a mature student to change my career path. I'm interested in pathogens and natural products and I'm planning to do a PhD once I've completed my degree.

When I first heard about the Microbiology Society's citizen science project to try to find new antibiotics I was intrigued. I really like the idea of getting ordinary people involved in this important issue. For the Small World Initiative, I researched and presented a poster on a technique with the potential use for antimicrobial discovery that is easy, fast and accessible to the public. This was a great experience and it was wonderful to hear all the informative talks, read the posters from the other students and to build my own confidence in presenting.

The Antibiotics Unearthed pop-up event was also really enjoyable. I

volunteered because I wanted to gain more experience as well as continue to help with the project. It was nice to be doing something outdoors in a different environment. It was an opportunity to meet other volunteers interested in antibiotic discovery from a variety of backgrounds too.

It was a family-friendly couple of days, with children and adults of all ages engaging. It was good to be involved and learn from people how much they understood and whether they were aware of the problem of resistance and the need for new drugs. I like the way the event brought together members of the public, students and professionals with a wide range of levels of expertise and interests to share.

Promoting awareness and understanding of the issue of antibiotic resistance is essential. Being involved in communicating this through public engagement has been a thoroughly enjoyable and rewarding experience.

Eleanor Furness

The Antibiotics Unearthed Team would like to thank the Forestry Commission, and especially Brian Prosser at Garwnant and Jennifer Watson at Kielder Castle, for hosting us. Thanks to Dr Paul Hoskisson for providing plates of *Streptomyces* cultures for the stand; and

Professor Laura Bowater, Dr Richard Bowater, Dr David Whitworth and Professor Nigel Brown for volunteering on the stand. We would also like to thank all of our volunteers for giving up their time to come and engage with the public and making the events such a success!

Theresa Hudson

Education and Outreach Manager
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Membership

Membership questionnaire – key insights

I am currently going through the results of the questionnaire members have kindly been completing over the past weeks. We've had a very good response and the challenge now is to take these findings and use them to create a more memorable and engaging membership experience. Our goal is to make membership the single 'must-do' action for those working in or studying the subject and ensure we remain the organisation of preference for the duration of your professional life. It's not an easy challenge, but one we are determined to work towards.

I have chosen three questions to highlight that I believe are significant for us working within the Society and for you too, as members.

How did you first hear about the Society?

Overwhelmingly, the answer here was from a tutor, teacher, colleague or friend. In other words we were recommended, face-to-face. The importance of a personal recommendation to organisations like ours cannot be overstated. We rely on our existing members to spread the word to non-members. This implies, of course, that members feel positively enough towards us to do it! Fortunately, many of you do and we thank you for this.

With a new academic year underway, now is the ideal time to have those conversations with students, friends and colleagues, to spread the word and encourage others to join. To help in this, we have prepared a simple-to-use toolkit to convey the benefits of membership

to a wide range of potential members. Components include a short 10-page presentation about the Society; and three posters that can be displayed on a departmental notice board. These can be downloaded from our website (www.microbiologysociety.org/toolkit) or sent on request.

If we could enhance three aspects of Society membership, what would they be?

The three most popular responses were:

1. Improve local opportunities to socialise and network.
2. Support opportunities to improve your professional development.
3. Improve career enhancement tools and services.

Local opportunities to socialise and network were referenced strongly across all membership categories. These were equally identified by members who were established in their careers, as it was by those who were still studying. But we need to explore this further – what do we mean by 'networking', and what is 'local'? Is networking to a postgraduate student the same as it is to someone who is established in their career? And if it's different, what makes it different? Is 'local' the area you work in? Or is it the town nearby? Or even the country a short distance away? Again, we need to understand more about members' perceptions of these concepts. Also, are members asking for something that we don't currently do, or is it that it is happening, but they are simply not aware

of it? There is a lot to consider here and we will be exploring this further in the weeks to come.

Choose the five most important Society benefits to you

As you might expect, career stage and personal circumstances drive the response to this question. But interestingly, when looked at across the Society, the two most important benefits were not tangible 'things'; they were intangibles. 'Building knowledge and understanding' and 'building my network' were perceived as the two most important benefits of Society membership. Much of our work in future will revolve around improving our understanding of members' expectations in these areas and looking at how we can better meet them.

The areas above (and others too) were discussed in more detail at a series of membership workshops held across the UK in the autumn. Workshops were held in Glasgow, Manchester, Norwich and London and participants engaged in some lively debate to help bring clarity to many of the issues raised. Input from the workshops and the questionnaire has given us a better insight into what's important to members and prospective members.

If you weren't able to complete the questionnaire or take part in the workshops, but wanted to join the membership conversation, there is still time. Simply email me your thoughts and comments and I will ensure they are fed into the wider discussion. A summary is also available of the questionnaire – do contact me if you would like a copy.

Paul Easton

Head of Membership Services

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Obituary

Professor Julian Wimpenny

March 27 1936–January 7 2016

Emeritus Microbiologist and ingenious innovator, Julian William Thomas Wimpenny was an example of a true Renaissance man.

Julian, a leading microbiologist of his generation, was as adept at glassblowing as in devising, fabricating, and interfacing fermentation equipment; he was a consummate hands-on research laboratory scientist. Also a first-rate lecturer and supervisor for young students, he enthused and communicated these facilities to us all and to the successive generations privileged to work with him.

Pure monocultures of microbes growing in liquid suspensions never entirely satisfied him, and his application of his own novel techniques revolutionised and re-invigorated our discipline. This innovative approach propelled him from the traditional era of shake flask and continuous culture microbiology to his newly invented gradient plates and 'gradostat' devices, providing simultaneously multiple graded environments for selection and optimised growth of micro-organisms. Microelectrode measurements on bacterial colonies led to analogies with growth of tissues. Use of the constant depth thin-film fermenters led him to consider the problems of surface growth of mixed populations in biofilms in the real world of dental plaque and serious problems of microbial metal corrosion.

Microbial ecology, in laboratory and computer models, but also studies of spoilage in the food industry followed, and developed into exciting ideas about 'extremophiles' in space. Julian's last

written works were a comprehensive review on biofilms and a survey of the limits to microbial life.

Julian instigated the Computer Users' Group of the then Society for General Microbiology, and the Biofilm Club; his infectious enthusiasm always ensured the success of new enterprises.

Born at Lowestoft, where his father was the Director of the Fisheries Laboratory, Julian was a boarder at the Leighton Park Quaker School then spent a year at the Sorbonne. At Emmanuel College, Cambridge, he read Life Sciences and his PhD was on the isoniazid inhibition of *Mycobacterium tuberculosis* at Guys' Hospital Medical School. For the two years, a seminal study (regulation by O₂ of *Escherichia coli* metabolism) at Dartmouth College, New Hampshire, followed. Julian then joined the newly-established Microbiology Department at Cardiff, as Honorary Lecturer in 1965.

Initially, Julian was at the Oxford Biochemistry Department (MRC Group for Microbial Structure and Function: Director – Professor David E. Hughes). Others in this group were at Newport Road, Cardiff, and were well served by MRC equipment from Oxford due to the generosity of Professor Sir Hans Krebs. The Group (Wimpenny, Lloyd, Coakley, Venables and Griffiths) was incorporated into the College after five years, and with members of the Microbiology (Botany) sub-department, Hill, Williams (Eddington) and Cally, this team led



Lee Wimpenny

Cardiff Microbiology to train a host of industrially-, environmentally- and medically-based scientists, including 45 future professors. Apart from sabbaticals in Germany and Indiana in the USA, Julian's entire academic career was spent at Cardiff.

Living in Monmouthshire, Julian enjoyed pottery, gardening, and the cultivation of fruit trees; he also kept bees. A handsomely produced Millennium Volume, *Trellech 2000*, was his pride and joy. An expert with pen and paintbrush, the Wye Valley Arts Society exhibited his paintings widely. He loved music and remarked that Radio 3 alone was worth the TV/radio licence. He retired as Professor from the Cardiff School of Biosciences in 2006. We miss his friendship, jovial company and wisdom; he leaves us with many fond memories.

A dedicated family man, our sympathies reach out to Lee, Ross, Joshua and Anna, and Bethan, his 'Welsh granddaughter'. Also to Jan, his first wife, Nicola and Kirsten, and Nicola's daughters, Jaycey and Caitlin, his 'American grandchildren'.

David Lloyd & Lee Wimpenny

With acknowledgement to Dr J. Barbara Evans for her help.

An extended version of this obituary is available on the Cardiff University website: <http://microb.io/2bw9Bw6>.

Membership Q&A

This is a regular column to introduce our members. In this issue, we're pleased to introduce **Ipek Kurtböke**.

Where are you currently based?

The University of the Sunshine Coast, Australia.

What is your area of specialism?

Bacteriology with specific emphasis on actinomycetology.

And more specifically?

Biodiscovery from *Actinomycetes*. Searching for industrially important compounds from these organisms such as antibiotics and enzymes.

Tell us about your education to date.

I obtained my BSc from the Middle East Technical University, in Ankara, Turkey (1982), one of the leading universities in Turkey where the language of instruction is in English. After that I did three years of postgraduate research at the University of Milan, Italy (1983–1986), where my interest in antibiotic-producing actinomycetes grew deeper in the laboratory of Professor Locci, who was part of the International Actinomycete Group. After that I moved to the UK to do my PhD at the University of Liverpool (1986–1990). Since early childhood I was encouraged for academia and scholarly work starting at home by my parents and grandparents and later by distinguished teachers. All of them had significant

impact on my educational development contributing from different angles. I gratefully remember all of them.

Where did your interest in microbiology come from?

After the completion of my BSc degree, I obtained my first graduate employment at Eczacibasi Ilac A/S in Istanbul, Turkey (1982–1983). The company was then Turkey's leading pharmaceutical company and was producing antibiotic gentamicin under Shering, USA, license. Following the discovery of the first potent antibiotic from actinomycetes (streptomycin), there was a global interest in this field, and gentamicin was another potent antibiotic produced by an actinomycete species. A career path was evolved for me in the field of actinomycetology, allowing me to work with the then leading scientists in this field, like the late Professor Stan Williams at the University of Liverpool, who supervised my PhD studies. His laboratory and research was then one of the leading ones in the field of biodiscovery, including links with GlaxoSmithKline and Xenova Group pharmaceuticals. Both at the University of Milan and University of Liverpool I had opportunities to take part in their industrially-linked research and become familiar with industrial and applied processes. I benefitted greatly from these experiences and incorporate



them into my teaching related to applied microbiology and biotechnology.

What are the professional challenges that present themselves and how do you try to overcome them?

At the scientific level: the changing world of microbial ecology with new advances such as the metagenomics. Careful interpretation of the huge data generated to reveal true functional diversity of the micro-organisms, as well as their taxonomical status, is

required. Knowledge generated at the eco-taxonomical level and their sound interpretation forms the basis for applied processes. At the professional level: tertiary education has to protect its foundational principles, one of which is scholarship. Current trends should not alter these principles, as true advancements can only derive from scholarly knowledge generation. I try to emphasise and make the younger generation aware of the traditional values. Tertiary education is not only gaining a well-paid job at the end of their studies but a scholarly transformation in their thinking which is important for the advancement of mankind.

What is the best part about 'doing science'?

Science teaches us to be factual, analytical, objective and critical. Koch's Postulates have to be justified in the scientific approaches with a rationale.

Upon my arrival to the University of Liverpool, I was introduced to the Microbiology Society (then SGM) in 1986 and became a member in 1987. Over the last nearly 30 years I read with great interest *Microbiology Today*, which has always been contemporary and visionary. I have also become a member of the Microbiology Australia Editorial Board in 2004 and since then guest edited six special issues, including the special issue on 'Actinomycetes' (Vol. 25, Issue 2, 2004, <http://microb.io/2dB8QA2>), which was contributed by distinguished UK scientists as well. I am very happy to be able to connect both societies in 2017 to produce a joint special issue on an important topic of microbial diseases of travel.

Continuous questioning and the desire to better the best take the scientist into a mature level of understanding of life's facts and develop tools to deal with them.

Who is your role model?

Experts I have encountered in the field, like the late Professor Stan Williams, Professor Arnold Demain, Professor William Fenical, Professor Julian Davies, Professor David Hopwood.

What do you do to relax?

At the moment I am extremely busy with teaching and research activities. But, if I have time, I love swimming. I grew up with the pristine waters of the Mediterranean Sea and miss it greatly. Australian oceans are too rough for me (I cannot surf!). I also like cycling, walking and visiting art galleries. The Queensland Gallery of Modern Arts (GOMA) in Brisbane has been a great place to escape when I have time. I also watch Turner Classic Movies, which contribute towards my understanding of my grandparents' and parents' generations – providing insights into their way of life and their changing way of life from World War I to World War II and then to the 1950s and 1960s.

What one record and luxury item would you take to a desert island?

Hamac and Verdi operas. My mother was an opera singer (Turkish State Opera and Ballet), and so I grew up listening to opera and Turkey's leading opera singers who were friends of my mother. In later years, I was fortunate to attend many performances at La Scala when I was in Italy. I was frequently in the audience watching

the Liverpool Philharmonic and Manchester Hallé Orchestras when I was in the UK. I also used to take the train to London to go to the Barbican Centre and would return to Liverpool on the last train.

Tell us one thing that your work colleagues won't know about you.

Science has taken me from Turkey (motherland) to Italy, to the UK (1986–1990) and to Australia (1990–2016) with fascinating experiences shaping me in a truly multicultural way. I benefit greatly from all these experiences and incorporate them into my teachings to encourage my students to broaden their horizons and encourage them to take part in the Global Opportunities program that the University of the Sunshine Coast offers.

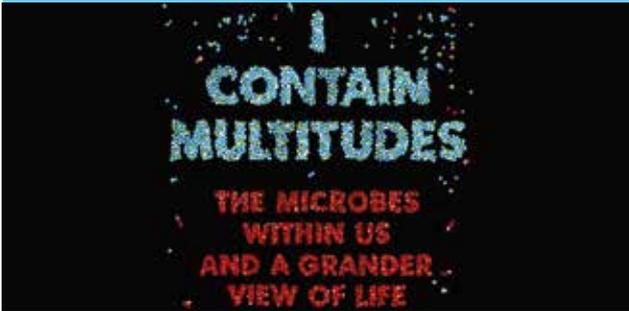
If you weren't a scientist, what would you be?

Maestro (perhaps a second Toscanini!). Although my mother was a musical person I was encouraged into science and academia by my late father, who was a colonel of the Turkish Army and was fascinated by the post-Second World War advancements in science (biochemistry, genetics, molecular biology...). I cannot play an instrument but the artistic background from my mother is always there, perhaps helping me be creative, which is required in science, and the discipline required probably comes from my father.

If you would like to be featured in this section or know someone who may, contact Paul Easton, Head of Membership Services, at p.easton@microbiologysociety.org.

Podcast – *Microbe Talk*

The Society has produced its regular podcast for several years, which you can find by searching for 'Microbe Talk' wherever you get your podcasts from. In a recent edition, we've interviewed the journalist Ed Yong about his new book *I Contain Multitudes*, sure to be high on many critics' end of year Top Ten lists. During the summer we also interviewed Professor Didier Pittet, who is leading on the WHO's drive to reduce incidences of healthcare-acquired infections, through the use of alcohol-based hand gels.



YouTube channel – Microbiology Society

We have a popular YouTube account that you can find by searching for 'Microbiology Society YouTube'. On our channel you'll find interviews with our Prize winners, educational videos, and information on the latest research. Recently, we've posted a video explaining the science behind CRISPR-Cas (using scissors and plasticine!) and one detailing a day at our Antibiotics Unearthed outreach event.

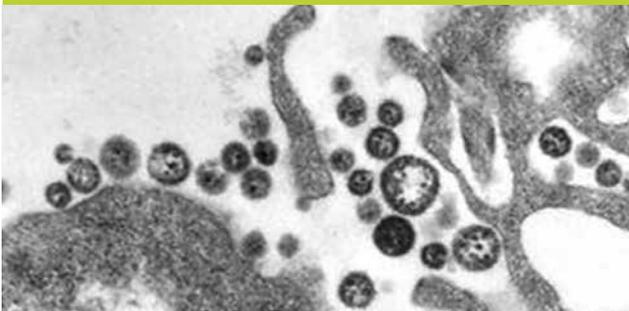


The latest from the Microbiology Society

Find out what you may have missed from the Microbiology Society. This is a roundup on some of the latest from each of our channels, with details of where you can find them.

Blog – *Microbe Post*

The blog continues to go from strength-to-strength. Starting in the summer, we began a series about emerging infections of humans, animals and plants called *On the Horizon*. We've learnt about efforts to control Lassa fever in Sierra Leone, a bacterial pathogen attacking olive trees in Italy, and an obscure virus found in Bangladesh. In other posts, we learnt about the effect that antibiotics have on cow belches and published a series of opinions on open data.



Twitter and Facebook – Microbiology Society

The Society's Twitter account and Facebook page are the best place to get the most up-to-date information about our activities, including this short video about phages. You can find us on Twitter **@MicrobioSoc** and on Facebook by searching for the Microbiology Society or go direct via this link:

www.facebook.com/MicrobiologySociety.



The Microbiology Society is producing more content than ever before – don't miss out!

Reviews

Holding Hands with Bacteria: The Life and Work of Marjory Stephenson

Written by S. Štrbáňová

Springer Briefs in Molecular Science,
Heidelberg: Springer-Verlag (2016)

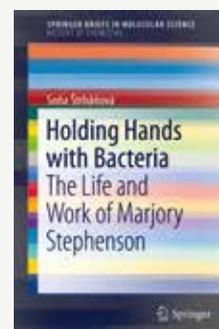
£37.99 ISBN 978-3662497364/ISSN (printed)
2191-5407/ISSN (electronic) 2191-5415

When a science reaches maturity, those interested in its early days can sometimes find the history hard to access. Štrbáňová deserves the thanks of all microbiologists for her readable and scholarly biography of Marjory Stephenson, a gifted pioneer of their subject.

Stephenson spent most of her career working in association with F. G. Hopkins at the Institute of Biochemistry, Cambridge. Hopkins allowed his colleagues free rein in selecting research

projects, and Stephenson chose to work with micro-organisms (mostly bacteria but occasionally yeast). Over 25 years she: elucidated several important reactions specific to bacteria; made, with her students, fundamental contributions to the study of 'enzyme adaptation' (induced enzyme synthesis); published *Bacterial Metabolism*; was instrumental in founding the Society for General Microbiology and was unanimously voted as President by its inaugural committee; and became one of the first women to be elected to the Royal Society. Sadly, she died when she was only 63.

The biography shows that Stephenson was not only an outstanding scientist but also vivacious, witty, cultured and generous, both with her time and her money. She cared deeply for her students and was active on behalf of refugee scientists. Stephenson suffered gender discrimination –



her laboratory was never officially recognised as a Unit and she was not designated Director, and her university awarded her the title of DSc in 1936, but not the degree itself. Štrbáňová paints for her readers an absorbing portrait of a brilliant and deeply lovable woman with the grace and self-confidence to take such slights in her stride.

Michael Yudkin

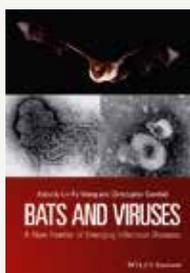
University of Oxford

Bats and Viruses: A New Frontier of Emerging Infectious Diseases

Edited by L. Wang & C. Cowled
Wiley Blackwell (2015)

£100.50 ISBN 978-1118818732

It is believed that about three-quarters of emerging infectious diseases are zoonoses, and bats are an important reservoir of a very wide range of viruses. Bats are unique in a number of ways



that are relevant to the transmission of infectious diseases between themselves and to humans. They live very close together in vast communities, they are able to fly, and they are present in every environment where humans live. Studies have suggested that bats harbour more viruses (in all major virus families) than other mammals, including life-threatening ones like rabies, Ebola, MERS, Nipah and Hendra. Despite harbouring so many potentially dangerous viruses, experimentally and naturally infected bats only very rarely display symptoms of disease. The co-evolutionary history of bats and viruses, spanning 65 million years, has probably resulted in the establishment of a state of equilibrium, allowing both viruses and their hosts to co-exist in a disease-free state. Therefore, bats not only

represent a reservoir for numerous viruses, but also a 'melting pot' for the emergence of new viruses resulting from recombination and re-assortment. This relatively small book contains a vast amount of useful information, describing the features of bats that help to explain how they serve as a viral reservoir and also vessels for the creation of new ones that may pose threats to humans in the future. It is obviously a highly specialised book, but it will be a very interesting and valuable text to students and researchers in terms of its presentation of bat biology, and the current and potential future threats to public health.

Christopher Ring

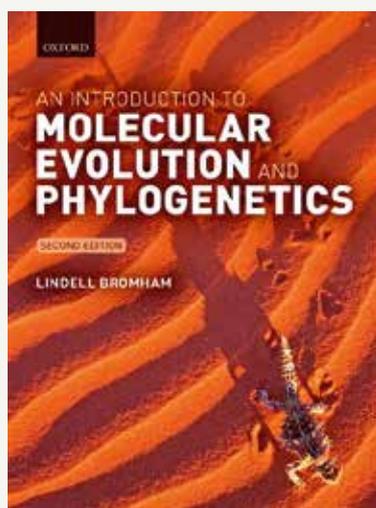
Middlesex University

An Introduction to Molecular Evolution and Phylogenetics

Written by L. Bromham

Published by Oxford University Press (2016)

£38.99 ISBN 978-0198736363



Innovative is the keyword when describing *An Introduction to Molecular Evolution and Phylogenetics* by Lindell Bromham. A highly engaging and well-organised book, it achieves what others haven't: breaking down complex information to an audience with little or no prior phylogenetics knowledge without making the reader feel overwhelmed or patronised. The author has

chosen to explain concepts by using real examples of published research (each one of them topical, captivating and, yes, even fun). In addition to this, little sections on 'role model scientists' relevant to each chapter appear throughout the book and are sure to inspire the next generation.

While this book is best suited for undergraduates at the beginning of their university career (making it the perfect companion for lecture planning), it will equally be as useful to both postgraduate bioinformaticians coming from a non-biological background and those trained in life sciences. Personally, coming from a veterinary medical sciences background, I certainly appreciated the author's approach of leaving algorithms and complex equations out of the book, making this piece even more approachable.

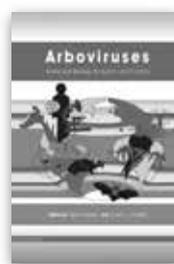
Finally, even though this manual does not have a particular microbial focus, all information is applicable and useful for bacterial and viral molecular epidemiology and phylogenetics.

Mario Afonso

University of Liverpool

Books on Vector Borne Microbes

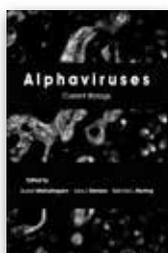
From Caister Academic Press



Arboviruses

Molecular Biology, Evolution and Control
Edited by: N Vasilakis, DJ Gubler
xii + 398 pages, April 2016

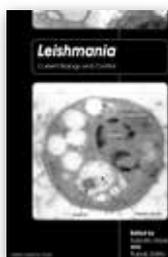
"a thorough and compelling review ... an outstanding book" (*Am. J. Trop. Med. Hyg.*)



Alphaviruses

Current Biology
Edited by: S Mahalingam, L Herrero, B Herring
x + 184 pages, January 2016

"up-to-date review of the field" (*Aus. Vet. J.*)



Leishmania

Current Biology and Control
Edited by: S Adak, R Datta
x + 242 pages, January 2015

"an excellent reference" (*Doodys*); "a useful guide" (*Fungal Diversity*)

Also of Interest

- **Gas Plasma Sterilization in Microbiology:**
"a nice state of the art compilation" *Doodys*
- **Virus Evolution**
"highly informative" *Microbiol. Today*
- **Epigenetics: Current Research and Emerging Trends**
"this is one text you don't want to miss" *Epigenetics*
- **Advanced Vaccine Research Methods for the Decade of Vaccines**
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Full Details at: www.caister.com

Comment

The voyages of Zika virus

Derek Gatherer

The announcement in May this year from the World Health Organization, that the Zika virus outbreak that began in October 2015 in the Cape Verde Islands off the west coast of Africa was an American variant of Zika virus, confirmed that Zika has now circumnavigated the world.

Unlike the first human circumnavigators in the 16th century, who sailed the world from east to west, Zika travelled in the opposite direction, heading east out of Africa to South-east Asia, then across the Pacific Ocean, through the Americas and finally back across the Atlantic to Africa. Zika was discovered by accident in 1947 in macaque monkeys caged in Uganda's Zika forest as part of a yellow fever monitoring study. A relative of yellow fever in the genus *Flavivirus*, and spread in much the same way by mosquitoes of the genus *Aedes*, Zika simply joined the growing list of obscure tropical viruses of no clinical importance, registering barely a dozen mild cases of fever and rash in humans over the next 60 years.

Obscure no more

Then in 2007, the isolated Micronesian island of Yap became the location of the first epidemic in humans. Subsequent

serological investigation showed that the majority of the population of a few thousand were infected, and that most of them reported no symptoms. Zika's potential for disseminated transmission was amply illustrated, but it wasn't until 2013 that the clinical implications of this became clearer. In that year, an even bigger outbreak occurred in Polynesia, infecting tens of thousands and adding an unwelcome new symptom to Zika's clinical description – Guillain-Barré syndrome, an auto-immune paralysis. Even then, there were no fatalities, and it wasn't until Zika completed the trans-Pacific leg of its journey, arriving in Brazil during or before the 2014 World Cup, a wave of foetal microcephaly cases trailing nine months in its wake, that the world finally realised the seriousness of this new pandemic, with the WHO declaring a Public Health Emergency of International Concern (PHEIC) on 1 February 2016.

Out of Africa

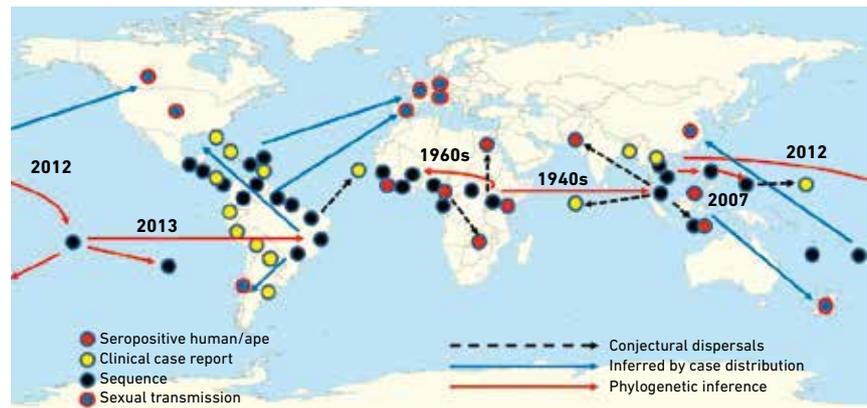
Why Zika should suddenly cause so much trouble after decades, perhaps centuries, of obscurity, remains a mystery. We have good grounds to believe that Zika originated in Africa, for the classic population genetic reason – which also applies to human immunodeficiency virus (HIV) and hepatitis C virus (HCV) – that the African strains are more genetically diverse than the non-African ones, indicating an accumulation of variation over a longer period of time. Diversity within the Asian and American strains is comparatively small and Bayesian phylogenetic analyses have dated Zika's emergence from Africa in the early- to mid-20th century. Zika's sporadic appearances in Africa have been in a belt from Uganda, through the Central African Republic to Nigeria and Senegal in the west, and its first isolation outside of Africa was in Malaysia in the 1960s. Just as earlier slave trade movements probably exported Zika's relative yellow fever from Africa across the Atlantic to the Americas, it is easy to imagine later colonial migrations, possibly administrative, commercial or military, carrying Zika from the British colonies in East Africa to those in South-east Asia. The fact that it didn't reach the Americas along with yellow fever in the 18th century suggests that Zika was rare in West Africa at that time, and indeed we have no up-to-date information on Zika's incidence in Africa now, except for a handful of serological studies conducted mostly before 1980 which suggest that between 6% and 60% of the African population are exposed to Zika at some point in their lives. In Asia, the corresponding figures are lower: less than 15% at all sites tested, again consistent with a relatively recent arrival from Africa.

Increased virulence or lack of herd immunity?

We cannot currently reconstruct much concerning Zika's pre-history until we can obtain more genome sequences from both Africa and Asia, and Zika is so far proving a difficult virus to isolate and sequence. A short viraemia and odd compositional content mean that we simply aren't accumulating genomes as fast as we did with Ebola at the height of the West African outbreak in 2014–15. To a certain extent, however, quality is better than quantity. Most of the Brazilian and other Latin American Zika genomes are very similar, and the really interesting differences are likely to occur away from the leaves of the phylogenetic tree and down in the branches where Asian Zika diversified before setting off across the Pacific. Here is where the crucial genetic differences will be found if it is the case that Pacific/American Zika's apparently novel properties – wider range of symptoms, possibly a greater transmissibility, Guillain-Barré and microcephaly associations – are due to evolution of the virus. On the other hand, it is perfectly possible that strain differences are inconsequential genetic drift and that what we are really seeing in the Americas is simply yet another example of an introduced pathogen wreaking havoc in a population with no previous exposure. The Native Americans of colonial times suffered terribly from the introduction of smallpox, influenza, yellow fever and even cold viruses from the Old World, and Zika may simply be doing what many viruses tend to do when they enter a host population with no herd immunity.

What now for Africa?

The answer to this question will also have consequences for Africa. The Zika



Zika circumnavigates the world. The pattern of spread has been deduced from phylogenetics (red arrows), epidemiology (blue arrows) or by informed guesswork (dotted arrows). Underlying map, Vardion, Wikimedia Commons; arrows, circles and dates added by author

outbreak in the Cape Verde Islands is confirmed by the WHO as being of Brazilian origin, and has been associated with microcephaly. If the islanders have never been exposed to Zika before, we might regard this as a similar situation to Brazil. On the other hand, if African Zika has circulated in Cape Verde, we must wonder why it has not produced a cross-protective effect against the American strain. Meanwhile, Guinea-Bissau has just become the first mainland African country to report an outbreak in recent times. The strain involved is of African origin and not, unlike the strain in Cape Verde, an import from Brazil. What happens there may forewarn us of what might happen elsewhere in Africa. The crucial question is – can African Zika also cause microcephaly? We may soon have an indication from the macaque monkey model of Zika infection used in the vaccine development programme. The current experimental Zika vaccine is based on American strains (Brazilian and Puerto Rican), so if it protects against infection with an African strain, the converse will probably apply and we are unlikely to see a similar epidemic of microcephaly in Africa as we have recently seen across tropical Latin America.

Zika Down Under

Meanwhile, Zika continues to be detected more sporadically in South-east Asia.

The lower epidemiological intensity and absence, so far, of microcephaly complications suggests that South-east Asia, perhaps like Africa, has the herd immunity that the Pacific and Americas lack. Since the climate of Indonesia, and also some *Aedes* mosquito species, is shared by the tropical northern Australian coast, Zika might have been expected to have already arrived in Australia. However, what is different is the absence of a wild monkey species in Australia, which may deprive Zika of the animal reservoir it needs to maintain itself in an area where the human population is mostly immune. In Africa, red-tailed monkeys have been shown to be a Zika reservoir, and in Brazil, Zika has already been detected in marmosets and capuchins. Of course, Australia, like all countries, could also see Zika spread by sexual transmission. This is climate- and mosquito-independent, but we still have no idea if it is sustainable.

Derek Gatherer

Faculty of Health & Medicine, Lancaster University, Lancaster LA1 4YG
d.gatherer@lancaster.ac.uk

Read more about Zika in the article *Pregnancy, the placenta and Zika virus (ZIKV) infection* by William Rawlinson on page 170 of *Microbiology Australia* included at the back of this issue.

Announcing a new collaboration between *Journal of General Virology* and the International Committee on Taxonomy of Viruses (ICTV).

From January 2017, *Journal of General Virology* will publish 'ICTV Virus Taxonomy Profiles' – a new series of concise review-type articles that summarise the individual chapters from the ICTV's online (*10th*) *Report on Virus Taxonomy*.

Written by ICTV study groups comprised of leading experts in the field, these reviews will provide overviews of the classification, structure and properties of individual virus orders, families and genera. These summaries will become the “go-to” place for researchers looking for up-to-date taxonomic information on viruses.

The Microbiology Society will publish these short, citable profiles freely online, while the full chapters will be available to all through the ICTV website. This has been made possible thanks to a five-year Biomedical Resources grant from the Wellcome Trust.

Look out for the first virus taxonomy profiles, which will be published in January 2017 on the *Journal of General Virology* website.

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MICROBIOLOGY
SOCIETY

Microbial diseases of travel

Microbial diseases of travel



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The November 2016 special issue of the *Microbiology Australia* is the first joint one with the Microbiology Society of the UK. Deciding on an appropriate theme for this issue, the 'Microbial Diseases of Travel' was a relatively straightforward task and a direct 'fallout' from the geographical distance that separates our two societies; In the recorded history of mankind, travel has been one of the most effective means of disseminating infectious diseases throughout and among different populations. Explorers carried with them, many infectious agents such as influenza, measles, small pox, typhus and yellow fever resulting in devastating consequences for the indigenous populations that they encountered on their travels. Nowadays, with the current explosive rates and speed of travel the consequences of carrying infectious agents continue to be significantly detrimental to human, animal and crop populations even with our understanding of effective public health measures. Exposure to disease causing agents carried on wild animals can also be a potent force in the emergence of disease on travellers' return to their home country. In addition, migratory animals and birds can bring disease into far away countries as illustrated by the avian influenza.

Climate and environmental changes can also lead to the emergence of microbial diseases, which may not have been seen at a particular geographical location previously. Moreover, diseases such as brucellosis, HIV/AIDS, leishmaniosis and TB are known to have prolonged and variable incubation periods. As a result their clinical manifestations may appear long after the return from travel. As a direct consequence, it does not take a lot of imagination to see that tracking the source of infection can be difficult in some cases.

Due to the 'abrupt and dramatic changes in environmental conditions' such as changes in the altitude, temperature and humidity, travellers might also become more prone to diseases. The most commonly encountered microbial-mediated disease affecting travellers is called 'travellers' diarrhoea' and can be caused by many different foodborne and waterborne infectious agents. Prolonged

shedding of infectious agents via the faecal-oral route can also happen, resulting in dissemination of the infectious agents along the travel path. Understanding the modes of transmission and corresponding general precautions can reduce the risks of infections. WHO lists these factors as:

- Foodborne and waterborne diseases
- Vector-borne diseases
- Zoonoses (diseases transmitted by animals)
- Sexually transmitted diseases
- Blood-borne diseases
- Airborne diseases
- Diseases transmitted via soil

At the destination or along the travel path, the risk of becoming infected depends on the sanitary and preventative measures taken, including vaccination. However, there are still some infectious diseases including some deadly ones, spread via travel, that have not generated effective vaccination programmes. A list with some of the diseases and causative agents associated with travel, where no vaccine are currently available is highlighted in Table 1.

The WHO uses the following criteria for classifying specific infectious diseases that involve potential health risks for travellers

- diseases that have a sufficiently high global or regional prevalence to constitute a significant risk for travellers;
- diseases that are severe and life-threatening, even though the risk of exposure may be low for most travellers;
- diseases for which the perceived risk may be much greater than the real risk, and which may therefore cause anxiety to travellers;
- diseases that involve a public health risk due to transmission of infection to others by the infected traveller.

The mode of travel can also be another factor in the increase or downgrade of infection risk. Most modern aircraft are fitted with high-efficiency particulate air (HEPA) filters and ventilation rates are controlled to recycle cabin air so that its quality is ensured. Well maintained HEPA filters trap dust particles and are adept at trapping bacteria and fungi. Transmission of infectious agents may occur between closely sitting passengers, as a result of personal

Table 1. Diseases and causative agents commonly encountered by travellers.

Disease	Causative agents
Amoebiasis	Parasitic amoeba
Angiostrongyliasis	Parasite
Anthrax	Bacterium
Brucellosis	Bacterium
Chikungunya	Virus
Dengue fever	Virus
Giardiasis	Parasite
Haemorrhagic fevers	Virus
Hepatitis C	Virus
Hepatitis E	Virus
Histoplasmosis	Fungus
HIV/AIDS	Virus
Legionellosis	Bacterium
Leishmaniasis	Parasite
Leptospirosis	Bacterium
Listeriosis	Bacterium
Lyme borreliosis (lyme disease)	Bacterium
Lymphatic filariasis	Parasite
Malaria	Parasite
Onchocerciasis	Parasite
The Plague	Bacterium
SARS (severe acute respiratory syndrome)	Virus
Schistosomiasis (Bilharziasis)	Parasite
Trypanosomiasis	Parasite
Typhus fever	Bacterium
Zoonotic influenza	Virus

hygiene decisions and shared fomites. If infectious diseases are to be avoided then the best advice is to strictly adhere to safety precautions and committed personal hygiene practices. An example is the transmission of Tuberculosis in air travel and the preventative measures are highlighted in the WHO Guidelines for Prevention and Control.

It is not just air travel that can spread disease: sea travel is also an effective ‘transmission’ environment with gastrointestinal disease outbreaks from contaminated food or water, norovirus infections, legionellosis, varicella and rubella all being reported.

Another concerning risk might derive from poorly stored seafood under unchilled conditions (e.g. mackerel, tuna, bonito, sardines, marlin and butterfly kingfish), which might result in ‘scombroid (histamine) poisoning’. Bacterially converted histidine to histamine might lead to severe reactions and even death and once the fish is contaminated with this toxin freezing or cooking will not be effective in removing the toxin. Paralytic shellfish poisoning (PSP) and saxitoxin (STX) poisoning as a result of dinoflagellate algae contamination of the shellfish can also be another risk to be aware of for travellers.

In this joint issue our articles will cover some of the diseases of travel such as syphilis, avian influenza, dengue and mosquito-transmitted viruses, Zika as well as antibiotic resistant bacterial infections and food borne diseases involving human beings. Related to plants and animals articles will cover Chytridiomycosis, blue tongue, decline in bees, crop diseases. Disease surveillance and biosecurity aspects are also included. Australia and the UK have historic links and extensive travel history and we are overjoyed to put a joint issue together and thank all the contributors, Editorial Boards of the both journals and Editor-in-Chief of *Microbiology Australia* Ian Macreadie and the Digital Communications Manager, Microbiology Society, UK, Ruth Paget for their support during the production.

Reference websites referred to in the above article are:

- <http://www.who.int/ith/diseases/en/>
- <https://wwwnc.cdc.gov/travel/diseases/>
- http://www.who.int/tb/publications/2006/who_hmt_tb_2006_363.pdf

Biographies

Dr Kurtböke has been working in the field of biodiscovery and has been a member of the international actinomycete research community since 1982. She currently conducts research and teaches in the field of applied microbiology and biotechnology and is senior lecturer at the University of the Sunshine Coast (USC), Queensland. She has also been an active member of the World Federation of Culture Collections (WFCC) including serving as the Vice-President of the Federation (2010–2013).

Laura Bowater is a Professor of Microbiology Education and Engagement at the Norwich Medical School in the University of East Anglia with a special interest in antibiotics and antibiotic resistance. Laura is currently completing her tenure as Editor in Chief of *Microbiology Today* and this joint venture with the Australian Society for Microbiology will be her final issue in this role.

Travel and tuberculosis



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Australians frequently travel to countries with a high incidence of tuberculosis (TB). What risk does TB pose to travellers and what can be done to mitigate this risk?

In the year ending June 2016, 9.7 million Australian residents left Australia visiting one or more countries for a short term period¹. Of the 10 most common short term destinations, six were countries with TB incidence rates of >40 per 100 000, a threshold in common usage to define 'high incidence' (Table 1)², contrasting sharply with the low TB incidence in Australia (5.3 per 100 000). Three of these destinations, China, Indonesia and India account for 45% of the world's total number of notified TB cases. A significant

burden of multi-drug resistant (MDR) TB is noted in India and China and to a lesser extent Indonesia (Figure 1). While risks of TB to travellers have recently been reviewed comprehensively elsewhere³ this short overview seeks to address key questions in understanding TB in the context of travel.

Table 1. Top 10 countries of destination for short term Australian travellers (in order of frequency)

Country	TB incidence per 100 000 (2014) ²
New Zealand	7.4
Indonesia	399
USA	3.1
United Kingdom	12
Thailand	171
China	68
Singapore	49
Japan	18
Fiji	67
India	167

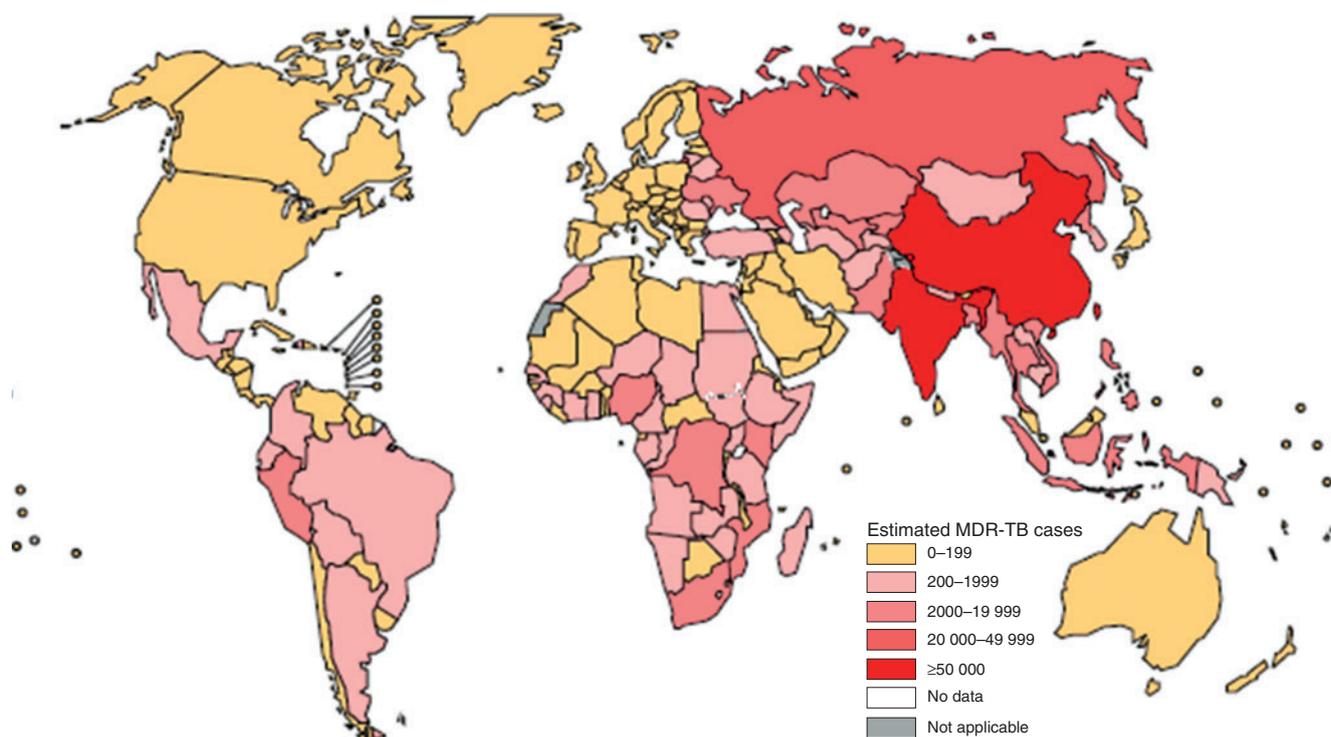


Figure 1. Number of MDR-TB cases estimated to occur amongst notified pulmonary TB cases, 2014 (reproduced from World Health Organization², figure 4.6, p. 64).

Assessing the risk

The likelihood of acquiring TB is determined by the probability of encountering one or more infectious cases and the cumulative duration of exposure. Host factors increase the risk that asymptomatic infection, (latent TB (LTB)), will progress to active disease and how severe that disease may be. In addition disease is most likely to manifest in the 2–5 years following acquisition.

The risk of acquiring infection for travellers, as assessed by tests for LTB such as the tuberculin skin test (TST) and interferon gamma release assays (IGRA), broadly is proportionate to the TB incidence in country of destination and the duration of stay. However this is not always the case and risk is substantially affected by variations in TB incidence in-country, living circumstances during the period of travel and activities pursued during travel. Participation in healthcare in countries of high burden is particularly acknowledged as both a risk for contracting TB and for the TB strain to be drug resistant. ‘Medical tourism’, seeking elective surgery overseas, is commonly to countries of high TB burden and may present additional risks of nosocomial or community transmission of TB.

Travellers previously treated for TB remain at risk of a new infection in communities with high rates of TB transmission.

Some of the most devastating manifestations of TB such as miliary TB and meningitis are more likely to occur in children under the age of five years and especially those less than age 2. Young children accompanying their migrant parents to countries of high TB burden to visit relatives and friends may be exposed to a significant risk of TB, especially if a household contact has untreated tuberculosis, regardless of the risk of TB as determined by overall country incidence.

Getting there and getting about

While the confined space of an aircraft may suggest an ideal environment for the spread of TB by respiratory aerosols, this is not the case. There are no published cases of active TB which have been demonstrated to have been acquired during plane travel. A recent systematic review provides evidence that infection may be transmitted on aeroplanes but 14 of 21 publications assessed did not find any evidence of transmission even when the index case was AFB smear positive⁴. Only one publication provided substantial evidence that TB infection (without disease) had been transmitted during air travel⁵. Modern passenger aircraft have sophisticated air flow management with HEPA filtered air efficiently being removed from the cabin in a downward direction (Figure 2)⁶. International convention considers only those passengers in the same row as an

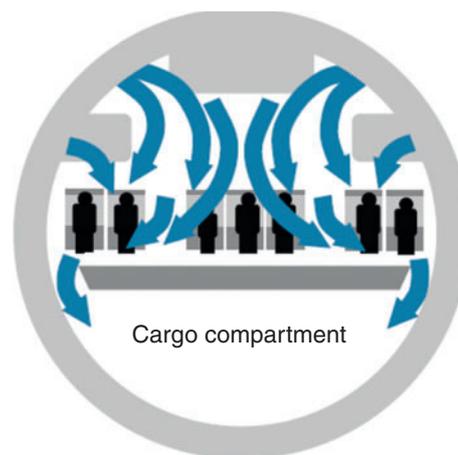


Figure 2. Cabin airflow (reproduced from European Centre for Disease Prevention and Control⁶).

index case and 2 rows in front and two rows behind to be potentially at risk⁴. Contact tracing is not generally embarked upon unless the flight duration is 8 hours or longer. Compared to most countries, relatively few international flights to and from Australia and New Zealand are of shorter duration.

While TB transmission in public ground transport may well occur, duration of exposure is short and the risk is difficult to quantify as passenger identity and detailed records of passenger seating is not usually recorded⁷. Crowded waiting rooms, especially if poorly ventilated could be a particular risk.

Prevention

TB prevention strategies should focus foremost on those with the greatest risk of mortality or long term disability. As such, prevention of TB in travelling children should have the highest priority. Although no longer used routinely in Australia, BCG vaccination in early childhood reduces the risk of disseminated disease and TB meningitis by >70%. The *Australian Immunisation Handbook*⁸ recommends BCG vaccination for children, especially under the age of 5 who will be travelling and staying in countries with an annual TB incidence of 40 or greater per 100 000 population for a prolonged period. At the current time such an effective preventative strategy is not easily implemented as there is no registered BCG product available in Australia (as of 1 January 2016) and there is variable usage between State and Territory jurisdictions of ‘BCG 10’, a vaccine manufactured in Poland and not registered in Australia by the Therapeutics Goods Administration. This vaccine shortage is in the context of a global shortfall in BCG vaccine supply⁹, a situation which is unsatisfactory and remains unresolved.

In the absence of BCG vaccine, post travel testing for LTB is an alternative and also applicable to older children and adults where BCG is generally not recommended. Two to three months

following return from a prolonged stay in one or more high TB burden countries, the TST or IGRA can be performed to assess whether LTB is present. While a pre-travel test can strengthen the conclusion that exposure has been recent, this is not necessarily required in young children from low TB burden settings such as Australia. If there is evidence of LTB, then treatment ('chemoprophylaxis') should be offered. For children, a three months course of isoniazid and rifampicin is well tolerated and effective. Isoniazid for 6–9 months is the most commonly used regimen in adults. The use of rifapentine-containing regimens is difficult as the agent is not registered in Australia.

Special situations

Once acquired, the risk of TB disease in HIV infected persons is generally estimated as 10% per annum as opposed to 5–10% lifetime risk for immunocompetent persons. While this risk is mitigated by immune maintenance or restoration by highly active antiretroviral therapy, HIV infected travellers should be counselled about their risk. Suggestions to use isoniazid as a pre-exposure prophylaxis for short-term travellers¹⁰ are not supported by evidence and may unnecessarily cause harm by hepatotoxicity, particularly in older subjects.

The risk of progression from latent to active TB is increased in pregnancy and is associated with a risk of congenital TB, increased risk of foetal loss as well as harm to maternal well-being¹¹. While drug susceptible TB can be treated in pregnancy with standard therapy, some of the drugs used to treat MDR-TB are considered to be potentially teratogenic and pregnant women should consider changing their travel plans if their destination involves a prolonged stay in a community where the risk of MDR TB is high. If this is not possible, avoidance of congregate settings and non-essential visits to healthcare facilities would be prudent.

Travellers working in healthcare overseas where TB risk is increased should be educated regarding personal protective equipment use and have a baseline TST. While there is no unequivocal evidence that BCG administration to adults prevents TB, BCG can be considered for TST negative healthcare workers who are likely to work in a setting of high MDR/XDR TB burden¹². For immunocompromised people including those living with HIV and in pregnancy, BCG is contraindicated.

As IGRA tests, unlike the TST, are unaffected by prior BCG, they can be used to assess LTB in healthcare workers who are TST positive at baseline. TST negative HCWs who do not receive BCG can be monitored by TST periodically during deployment or after return. Serial IGRA testing in HCWs who are initially IGRA negative is

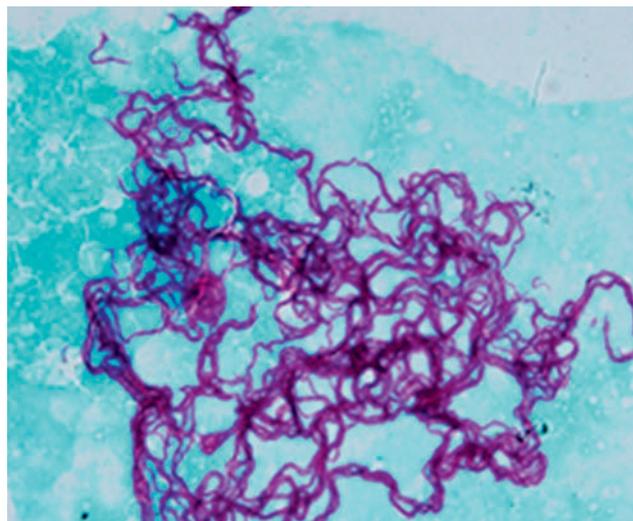


Figure 3. Typical cording of *M. tuberculosis* isolated from liquid culture (photo courtesy of Dr Sushil Pandey).

complicated by spontaneous conversions and reversions and some authorities advise against its use in this setting¹³.

Post travel assessment

It is important that active TB is considered diagnostically at the first point of contact with the health system if a returned traveller who has visited a high TB burden country presents with TB symptoms, especially >2 weeks of cough, fevers and weight loss in adults and fevers, cough, lymphadenopathy, failure to thrive or neurological disturbance in children. Chest radiography and sputum AFB smear and culture for mycobacteria (Figure 3) and, where drug resistance is suspected, rapid molecular tests such as Xpert MTB/RIF are the mainstay of the diagnostic approach. Tests of LTB should not be used to diagnose or exclude active TB as both false positive and false negative results are problematic. In contrast, evidence of recent acquisition of LTB should prompt either initiation of chemoprophylaxis or regular clinical and radiological review for at least 2 years. Australia has a well co-ordinated network for TB control and expert advice on treatment and prevention of TB can be readily obtained.

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Biography

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Avian influenza. Why the concern?



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Avian influenza normally has little impact on poultry and wild birds but since 1996, highly virulent viruses have emerged and continue to circulate in many countries. The results of these viruses have been devastating in domestic poultry and they have also spilled over into humans, infecting and killing hundreds and raising the opportunities for the virus to further adapt and possibly cause a future influenza pandemic. This article briefly details these events and discusses the consequences of these viruses continuing to circulate and cause disease.

The year 2016 marks a milestone for avian influenza, often referred to as ‘bird flu’. It is now 20 years since the outbreaks of highly pathogenic avian influenza (HPAI) in farmed geese in the Guangdong Province of southern China¹. These viruses are now recognised as the progenitors of the zoonotic H5N1 avian viruses that

caused global concern in Hong Kong in 1997 with 18 human cases and 6 deaths and led to extensive poultry culling and changes to live bird markets (Figure 1). These viruses continued to evolve and rapidly spread from China throughout Asia resulting in a HPAI panzootic (a global disease epidemic in animals) event which continues to this day. The ‘H’ in H5N1 refers to the serotype of the haemagglutinin protein and the ‘N’ is the serotype of the neuraminidase protein. H and the N proteins are both abundant on the surface of the influenza virus and play key roles in the attachment (H) to cells and the release (N) from infected cells. The H protein has a proteolytic cleavage site (PCS) where host proteases cleave the protein into two subunits HA1 and HA2, an essential step in producing infectious virus. Only strong proteases present in the respiratory tract of mammals and birds, and the gastrointestinal tract of birds, cleave the H of low pathogenicity influenza viruses (LPAI). However, in HPAI the H protein acquires

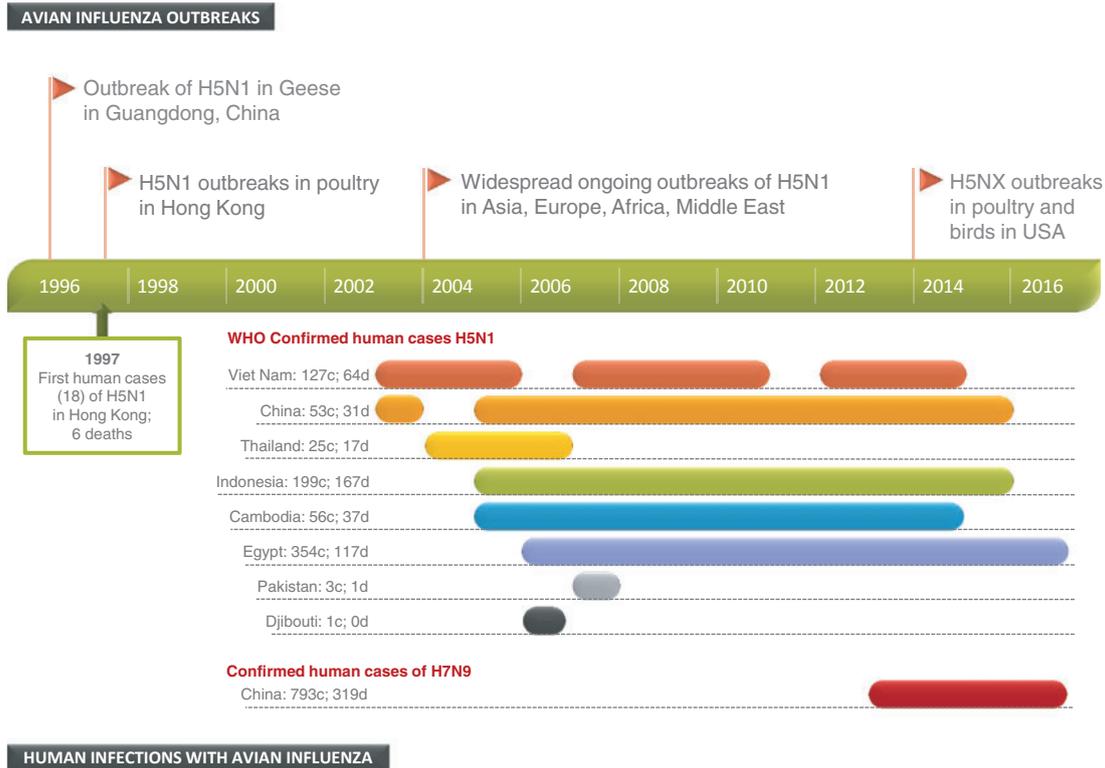


Figure 1. Timeline showing the spread of main countries affected by avian H5 viruses since 1996 and the cases of human H5/H7 infection (c = cases, d = deaths) reported to WHO.

an insert of additional basic amino acids at the PCS allowing proteases in many organs to cleave the protein and virus to spread widely in the body. These HPAI viruses can be extremely deadly in some poultry species especially chickens and can lead to high mortality in flocks within a day or two of infection. HPAI viruses with the multi-basic PCS have been restricted to the avian influenza H5 or H7 types to date. The majority of influenza viruses circulating in avian species lack this insert and therefore do not cause significant disease in birds (including most H5 and H7 viruses).

The H5N1 HPAI problem

So what's the problem 20 years on? Essentially it is the ongoing persistence of HPAI and its wide geographical spread (Figure 2) that have resulted in millions of birds being infected along with some humans, mostly through contact with infected poultry. The consequences of this panzootic have been dramatic, with millions of birds culled or dying from infection with H5N1 viruses. While human infections have been much fewer to date (854 human infections reported to WHO as of 19 July, 2016), the outcomes have been severe, with 450 deaths, fortunately without sustained human to human transmission². The lost food supply and the costs and effort in vaccinating or culling birds, monitoring outbreaks and treating infections during this period have been enormous. Concomitantly has been the ongoing threat that these viruses, either by mutation, genetic reassortment or a combination of the

two, might generate a virus that is more transmissible between humans and could cause a major human pandemic. Reassortment, where two or more influenza viruses infect the same cell resulting in a mixture of virus genes in the progeny can produce the most dramatic changes resulting in a unique virus. This has happened scores of times since 1996, most recently in North America and China where the H5 viruses have expanded their N type repertoire with HPAI H5N2 and H5N8 outbreaks in chickens and turkeys in North America and both avian and human infections in China with H5N6 from 2014–16, leading to these viruses being now referred to as H5Nx viruses. To date these viruses have retained their avian characteristics and have only occasionally infected humans: for example, there have been 14 cases of human infection with H5N6 reported in China since 2014.

A new problem, H7N9 LPAI

Adding to this mix of H5 viruses have been other avian influenza viruses that have also caused significant human infections. The most serious of these recently have been H7N9 LPAI infections, first detected in March 2013 in Southern China that have since recurred annually, with at least 793 human cases and 319 deaths, mostly associated with exposure to H7N9 infected birds especially with elderly men at places like live bird markets (Figure 3). As with H5 HPAI, these sporadic human H7N9 infections from birds and the continued endemic circulation in live bird markets and farms

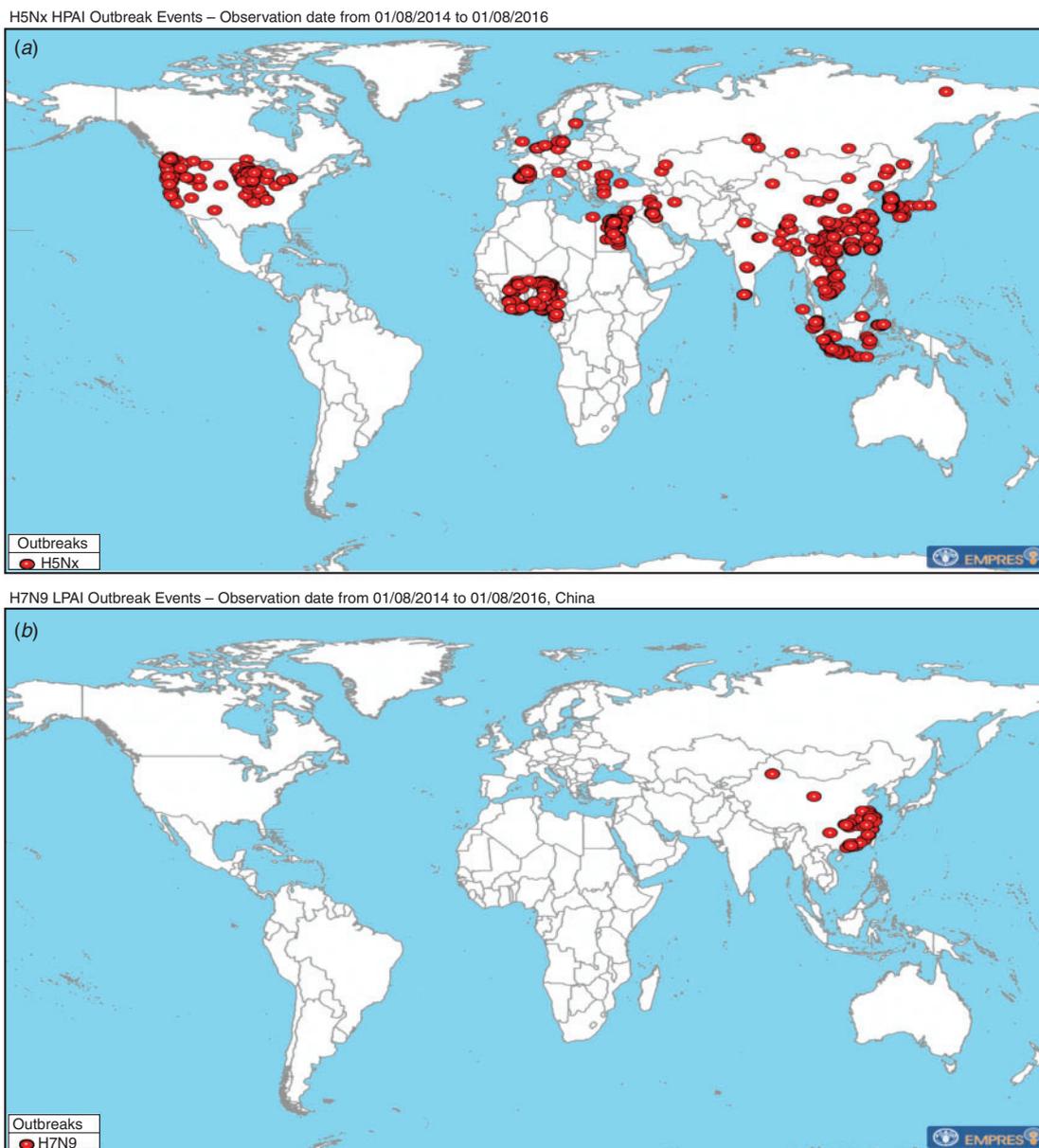


Figure 2. Red markers show outbreaks of (a) A(H5N1) and A(H5Nx) HPAI or (b) A(H7N9) LPAI in birds in the last 2 years (figure produced by Ahmed Al-Naqshbandi, Animal Production and Health Division-Animal Health Service, FAO, using the EMPRES database: <http://empres-i.fao.org/eipws3g/>).

in China, mean that the public health risk from exposure to these and potentially novel reassortant viruses remains a great concern. Other influenza A subtypes such as H9N2, H10N8 and H6N1 have also been implicated in human infections in China, some of which have been fatal, while others such as H7N7 cases in the Netherlands, have been associated with much milder human infections. As endemic LPAI viruses such as the Chinese H7N9 and H9N2 viruses have little pathogenicity in poultry, there is little warning of their presence, resulting in increased risk of human exposures.

The big questions that still remain today

Can these viruses be eliminated or controlled in poultry and if not, will any adapt and increase their tropism for humans, leading

to widespread outbreaks or a potential human pandemic of unknown severity? Thankfully the H5N1/H5Nx HPAI viruses have so far failed to become more transmissible in humans, with only a few possible clusters of H5N1 human-to-human transmission and there has been little increase in the number of human cases even with ongoing poultry outbreaks and human exposure. This is supported by testing in ferret models of influenza where H5Nx viruses did not transmit from infected to naïve animals even when co-housed, nor could they be transmitted to ferrets via virus infected aerosols. The situation for recent Chinese H7N9 viruses is less clear cut. Similar to H5Nx, there have been few human secondary infections or infection clusters recorded to date, but ferret studies demonstrated that these H7N9 viruses were easily transmitted by close contact and even by aerosols, although still not



Figure 3. A typical live bird market in Asia (photo supplied by Paul Selleck).

as efficiently as human seasonal influenza A viruses. The possible emergence of a virus variant of these or other subtypes that is able to replicate and transmit by the aerosol route more efficiently in man, would be an immediate pandemic concern since modern air travel means that infected persons can easily and quickly spread their infections at a global level before transboundary infectious disease mitigation strategies can be effectively implemented. This was highlighted by the rapid worldwide spread of the 2009 pandemic H1N1 virus that emerged from swine. The establishment of the Asian lineage H5N1 HPAI in the poultry of many other countries in Asia and Africa (Figure 2), and the recent emergence of related H5Nx viruses affecting birds in several Southeast and East Asian countries and further afield in Europe and North America, also demonstrate the potential for their widespread distribution by either cross-border poultry trade or carriage by migratory wild waterbirds.

Some possible answers?

To help manage the risk of these avian influenza viruses becoming a threat to mankind, various systems have been developed to assess avian and swine influenza viruses. One such system, IRAT (Influenza Risk Assessment Tool), was developed by the Influenza

Division at CDC, Atlanta, USA. This assessment takes into account a number of factors that may be important in avian influenza viruses making the 'jump' from being an avian virus to becoming a human virus. These include both virus and host characteristics, such as virus' H receptor specificity, pathogenicity in man and in animal models, background levels of immunity in the human population, transmissibility in man and in animal models, the number of infected birds and many other factors. These factors are combined and influenza virus types are ranked by plotting them according to their potential risk to achieve 'sustained human-to-human transmission' (emergence risk) and potential 'for significant impact on public health' (impact risk). In a recent publication³ from a small number of existing avian influenza viruses tested in the IRAT model, the Chinese H7N9 virus achieved the highest score (above H5N1 and a swine virus H3N2v) and this risk factor had increased slightly since a previous assessment in April 2013. This is not to say that an H7N9 outbreak is imminent but these rankings are meant to help guide public health measures such as early vaccine development and to also encourage virus control in the avian population, or to introduce measures to avoid human infection.

In addition to these risk assessments, researchers are exploring the factors that allow interspecies transmission but limit human transmission. A recent study with an H7N9 isolate suggests a 'genetic bottleneck' during infection of ferrets, and possibly humans, whereby the virus becomes less fit and therefore unlikely to be easily transmitted⁴. However, until we fully understand the mechanisms that allow ongoing human to human transmission it would be prudent to try to eliminate from poultry flocks those viruses with the highest risk to man (e.g. H7N9) and those of greatest risk to the domestic poultry population and to the global food supply (e.g. H5Nx HPAI) by targeted culling, effective poultry vaccines or in the future breeding poultry genetically resistant to HPAI. Meanwhile it remains important to maintain surveillance for novel influenza viruses in animals and humans and plan measures to combat any emerging virus in the human population, including appropriate vaccines and effective anti-viral drugs.

Acknowledgement

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Biographies

Professor Ian Barr is the Acting Director of the WHO Collaborating Centre for Reference and Research on Influenza based at the Doherty Institute in Melbourne. He joined the Centre 16 years ago and has previously worked in commercial, research and academic scientific positions. The Centre is one of six in the world that supports a WHO-led global human influenza surveillance network.

Dr Frank Wong is a Research Team Leader with the CSIRO Australian Animal Health Laboratory. Frank is the current World Organisation for Animal Health (OIE) expert focal point on avian influenza for Australia. He is also a contributor to the Joint OIE/FAO Network of Expertise on Animal Influenza (OFFLU), and currently represents OFFLU at the World Health Organization (WHO) vaccine consultations on zoonotic influenza viruses for pandemic preparedness purposes. He also serves as a Steering Committee member of the Wildlife Health Australia National Avian Influenza Wild Bird Surveillance Program. Altogether, Frank has more than 15 years' experience in the molecular characterisation of microbiological pathogens.



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Dengue and the introduction of mosquito-transmitted viruses into Australia



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Dengue virus outbreaks involving 100s of cases periodically occur in north Queensland, the area of Australia where the primary mosquito vector, *Aedes aegypti*, occurs. This article summarises the ecology, history, current situation and control of dengue virus transmission in Australia and examines the threat posed by newly emergent arboviruses, such as Zika and chikungunya viruses.

Dengue viruses

Each year, across tropical and sub-tropical regions of the world, an estimated 390 million people are infected with one of the four serotypes of dengue virus (DENV). The DENVs are single-strand positive sense RNA viruses of the genus *Flavivirus*, which also includes mosquito-borne viruses such as yellow fever (YFV), Zika (ZIKV), Japanese encephalitis (JEV) and West Nile (WNV) viruses. About a quarter of infections with DENV are symptomatic. So called 'classic dengue fever' is characterised by fever, rash, headache, and muscle and joint pain. Severe and potentially fatal disease occurs in about 1% of cases of DENV infection. This is characterised by plasma leakage with or without haemorrhage.

The DENVs are predominately transmitted between humans by the mosquito, *Aedes aegypti*, which has adapted its lifestyle to human habitation. Biological traits of this species that enhance its ability to serve as a vector of DENVs are: (1) it feeds almost exclusively on humans; (2) multiple blood feeding behaviour whereby a single female can bite several times to obtain a bloodmeal, thus potentially infecting numerous people; (3) adaptation to use man-made containers, such as tyres and potplant bases, as larval habitats; and (4) it prefers to feed and rest indoors.

The Asian tiger mosquito, *Aedes albopictus*, can also efficiently transmit DENVs and has driven outbreaks in locations where

Ae. aegypti is absent or are in low numbers. However, *Ae. albopictus* does not share the same anthropophilic ecology as *Ae. aegypti* and so outbreaks caused by this species are generally not of the same magnitude as those driven by *Ae. aegypti*.

Dengue in Australia

The DENVs are not endemic to Australia, but are intermittently introduced by infected travellers. Disease attributed to DENV infection has occurred historically in Australia since the 1800s. Early outbreaks involved 1000s of cases and whilst primarily focussed in northern Queensland, transmission extended as far south as Gosford in New South Wales. For instance, the 1904–05 epidemic in Brisbane infected 75% of the population and was associated with 94 deaths. One of the largest and most widespread epidemics occurred in 1954–55 and it was estimated that at least 15 000 people were affected in Townsville alone. Following this epidemic, outbreaks of dengue ceased in Australia for 26 years, coinciding with a contraction in the geographical range of *Ae. aegypti*. This contraction was due to a decline in rainwater tank usage via reticulation of water supplies, improved sanitation, use of residual insecticides by homeowners, and the invention of the motor mower and the resulting improvement in the maintenance of domestic backyards.

DENV reappeared in 1981, causing an outbreak across multiple localities in north Queensland. The frequency of dengue outbreaks has increased dramatically in the last 25 years. This increase can be attributed to a number of factors, including (1) epidemic DENV transmission in neighbouring countries; (2) increased arrivals from dengue active countries into international airports in Cairns and Townsville, which were opened in the mid-1980s; and (3) high populations of *Ae. aegypti*. Tourists taking advantage of low cost flights to Bali, fly-in, fly-out workers to Papua New Guinea and family visits have accounted for a considerable proportion of imports into Cairns in recent years. Although there have been almost 50 outbreaks in this time, they are usually of short duration and involve less than 100 cases. Larger outbreaks sporadically occur, involving 100s of cases, often across multiple locations and over several months (Figure 1). The largest outbreak in 50 years occurred in Cairns in 2008–09 when almost 1000 cases of DENV-3 were reported. The explosiveness of this outbreak was attributed to unseasonably hot weather and above average rainfall leading into the wet season, coupled with delays in case notification and

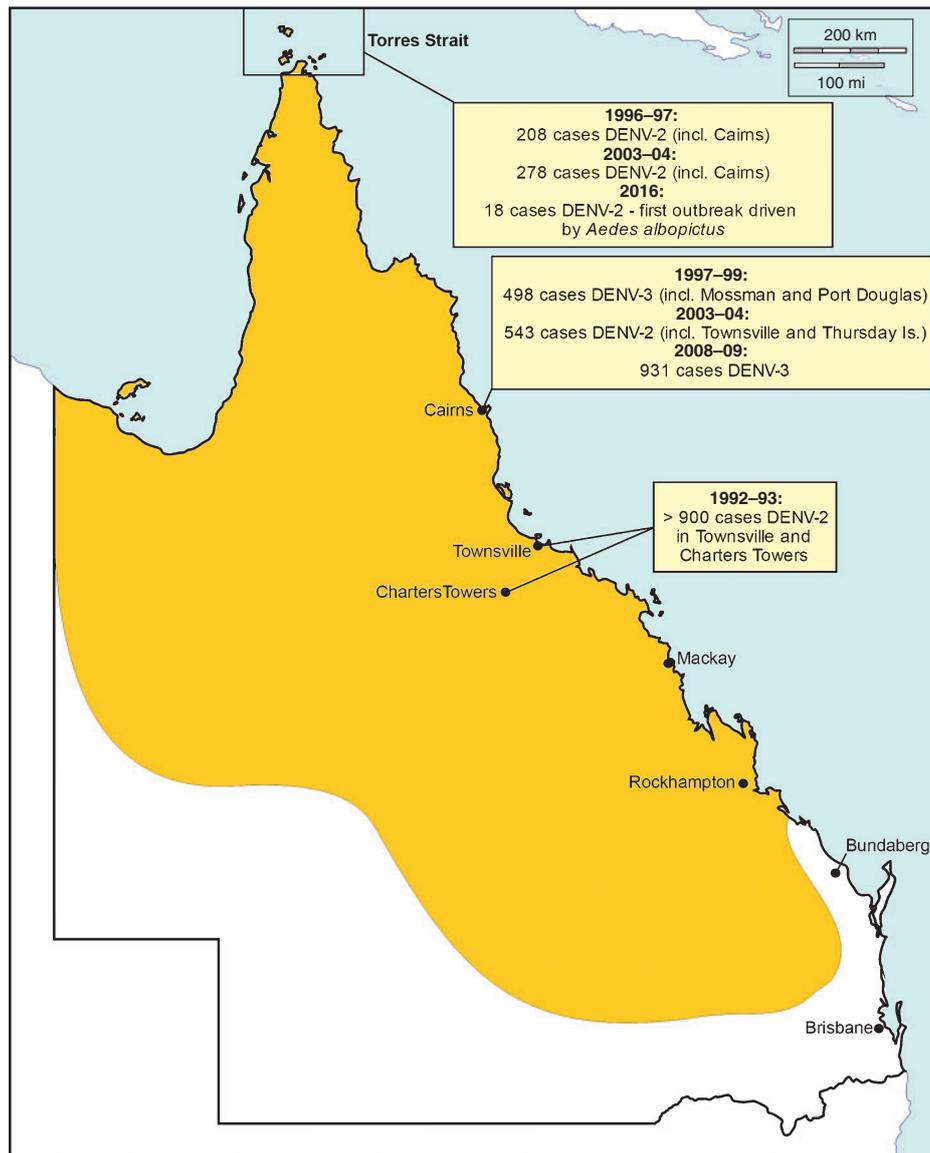


Figure 1. Map of Queensland showing the current range of *Aedes aegypti* (shaded gold) and significant dengue outbreaks since 1992. The locations in parentheses also reported cases that were linked to the primary epicentre of the outbreak. The distribution of *Aedes albopictus* is restricted to the Torres Strait.

a shortened extrinsic incubation period of the DENV-3 strain in *Ae. aegypti*.

Dengue control in Australia

In the absence of an effective DENV vaccine or specific antiviral treatment, the primary disease control strategy is suppression of *Ae. aegypti* and/or *Ae. albopictus* populations. This involves elimination of containers in which larvae develop by removing them or treating them with methoprene, an insect growth regulator which interferes with mosquito metamorphosis. Adult control is also implemented during episodes of local transmission and involves targeted spraying of indoor resting places of *Ae. aegypti* with residual pyrethroid insecticides. Considerable success has been achieved in the control of *Ae. albopictus* in the Torres Strait

when harbourage spraying of resting sites with pyrethroids has been used to supplement larval control. The success of interventions to limit local transmission is dependent on timely notification of suspected cases. Delays in case notification can result in a second generation of cases before control measures are initiated, which contributes to the rapid acceleration of some dengue outbreaks.

Although they are effective, chemical-based control methods are relatively expensive, labour-intensive and there is the potential for mosquitoes to develop resistance to the insecticide being applied. A promising control strategy that had its first field evaluations in north Queensland in 2011 is the release of *Ae. aegypti* trans-infected with the endosymbiotic bacterium *Wolbachia*. *Wolbachia* reduces the ability of the mosquito to transmit DENVs. Field releases in the Cairns region and Townsville have been very successful,

reaching almost 100% fixation of *Wolbachia* within the *Ae. aegypti* population. Encouragingly, strong DENV blocking within the mosquito continues at least one year post release. Because this technology is still in its infancy, it is too early to determine the effect of *Wolbachia* releases on the frequency and magnitude of DENV transmission amongst the human population in north Queensland.

The global march of other *Aedes*-transmitted viruses

Although local transmission of DENVs occurs all too regularly, Australia has so far been spared from the spectre of chikungunya virus (CHIKV) and ZIKV, which are also transmitted by *Ae. aegypti* and *Ae. albopictus*. CHIKV causes crippling arthralgia and has undergone a global expansion since 2004 that has afflicted millions of people on multiple continents. ZIKV has gone from causing an obscure non-specific febrile illness to being associated with neurological disease syndromes including Guillain-Barré syndrome (a form of paralysis) and congenital birth defects, most notably microcephaly, during its march through the western Pacific and South America. Despite over 550 and 66 imported cases of CHIKV and ZIKV, respectively, being notified in Australia as of August 2016, local transmission has not been reported. This is likely because most cases have been reported outside of areas where *Ae. aegypti* and *Ae. albopictus* exist and comprehensive control actions have been rapidly undertaken in response to notified cases in north Queensland.

Restricted to Africa and South America, YFV causes episodic outbreaks of acute haemorrhagic disease which have the potential to

spread to other areas of the world, as evidenced by 11 imported cases into China from an outbreak in Angola that began in December 2015. However, the risk of a YFV epidemic occurring in Australia is expected to be low, as travellers from endemic areas must be vaccinated against the virus.

The future

Due to the presence of *Ae. aegypti* and infected travellers, the DENVs will continue to be a threat to north Queensland. Current control programmes have undoubtedly limited the severity of DENV outbreaks and the *Wolbachia*-based approach may provide an alternative to the use of insecticides in the future.

Any geographical expansion of *Ae. aegypti* or the establishment of *Ae. albopictus* in temperate regions could render populated cities of eastern Australia, such as Brisbane and Sydney, receptive to outbreaks of DENVs, CHIKV or ZIKV. Comprehensive surveillance to detect the presence of these two species and rapid response protocols are essential to prevent their establishment.

Biography

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Pregnancy, the placenta and Zika virus (ZIKV) infection



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Zika virus (ZIKV) infections have been recognised in Africa and Asia since 1940. The virus is in the family *Flaviviridae* and genus *Flavivirus*, along with Dengue, Japanese encephalitis virus, Tick borne encephalitis, West Nile virus, and Yellow fever virus. These viruses share biological characteristics of an envelope, icosahedral nucleocapsid, and a non-segmented, positive sense, single-strand RNA genome of ~10 kb encoding three structural proteins (capsid C pre-membrane/membrane PrM/M, envelope E), and seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5). ZIKV has three known genotypes; the West African (Nigerian cluster), East African (MR766 prototype cluster), and Asian strains. Virus sequencing from the most recent South American outbreak suggests this virus is related to the 2013 French Polynesian isolates of Asian lineage.

ZIKV like other flaviviruses is arthropod-borne (arbovirus), with more recent evidence for sexual transmission, persistent presence in semen¹, and higher rates of acquisition due to a higher reproductive number than Dengue virus (DENV)². Infection with ZIKV is usually asymptomatic (~80% of cases) or causes mild disease similar to less severe DENV. However, ZIKV has emerged as a major public health threat globally due largely to substantial recent outbreaks in areas of large gatherings, and observed association with fetal neurological damage including microcephaly in the Americas and elsewhere (reviewed in Marrs *et al.*¹). Countries involved in the most recent outbreaks are summarised in the associated paper here. As a result of the risk to pregnant women, Australian public health authorities (and those in many other countries) recommend pregnant women defer travel to high risk countries. However, if exposure is likely, these women should prevent mosquito bites,

have their sexual partners avoid mosquito bites, and post exposure avoid pregnancy for 8 weeks (summarised in Marrs *et al.*¹), or possibly longer.

Clinical outcomes of mother to child transmission and diagnostic difficulties

Mother to child transmission (MTCT) of ZIKV has been documented via placental infection and damage, with increasing evidence of fetal ZIKV microcephaly. The number of infected mothers, compared with number of infected fetuses (i.e. rate of MTCT), is unclear, although in one Brazilian study, of 88 pregnant women with rash before 38 weeks gestation, 82% had ZIKV and 12/42 (27%) had fetal abnormalities on ultrasound compared with 0/16 women without ZIKV³. However, this is likely a significant overestimate due to the method of collection, the nature of the clinic and the lack of confirmed transmission on amniocentesis. A case control study of association between ZIKV and microcephaly showed ZIKV present in mothers of 24/32 cases of microcephaly compared with 39/61 mothers of controls ($p = 0.12$), and that in the babies, 13/32 with microcephaly compared with 0/16 of the controls had ZIKV infection⁴. These rates compare with rates of MTCT in maternal cytomegalovirus (CMV) infection of 32% in primary infection and 1.4% during reactivation⁵, and for rubella of 80% to 25%, depending upon gestation⁶. Effects on the fetus for all these infections depend upon many factors, including maternal immunity, gestation of infection, and viral characteristics.

Identification of mothers infected with ZIKV is predominantly via symptoms, serology, and molecular testing of the acutely infected person. Diagnosis is confounded by the low rate of symptoms (in ~20% of adults), technical difficulties with serology cross-reactivity, and the brief period of viraemia in some infections. Serology diagnostic problems occur due to co-circulation of other flaviviruses (particularly Dengue virus) in ZIKV affected areas. Cross-reactivity between ZIKV and Dengue virus occurs⁷, falsely negative tests for ZIKV may result if high levels of antibody are present to other flaviviruses (such as occurs following vaccination for Yellow fever virus), and acute ZIKV infection may result in false positive Dengue NS1 antigen tests⁸, further confusing diagnosis. Molecular testing using nucleic acid tests such as PCR is definitive if positive, although the duration of viraemia makes identification difficult when combined with low rates of symptomatic infection.

A major concern is whether MTCT occurs in ZIKV-infected asymptomatic women resulting in unexpected fetal damage. This occurs in murine models where ZIKV tropism for cells at the maternal-fetal interface is the likely source of transplacental transmission⁹, and is consistent with human cell studies *in vitro*¹⁰. Prolonged maternal viraemia, and excretion of ZIKV in urine for 5–6 weeks following infection provides opportunities for improved diagnosis¹¹, but also the possibility of continuing risk of ZIKV transmission either to other adults or MTCT during asymptomatic phases of an infected mother¹. ZIKV has been found in breast milk in three case reports of mothers infected <3 days from delivery¹², although MTCT transmission via breast milk has not been documented.

Placental and fetal infection

Most microcephaly is thought to arise from first trimester (T1) infection, although sampling difficulties occur with the high rate of asymptomatic infection. ZIKV has been detected in fetal brain tissue from microcephalic infants, in amniotic fluid taken from mothers of affected infants¹³, and from central nervous system tissue of affected microcephalic infants¹⁴. These are mainly observational data with minimal controls, albeit with autopsy and ultrasound data being consistent with microcephaly resulting from ZIKV infection during pregnancy¹⁵. ZIKV has been known to be neurotropic in animals for 60 years, with more recent murine experiments demonstrating replication in embryonic brain targeting neural progenitor cells, with consequent cell cycle arrest, apoptosis and inhibited neural progenitor cell differentiation^{9,16}. This is presumed to result in the microcephalic phenotype via neuronal cell death¹⁶. This is consistent with observations that African ZIKV strains infect neural precursor cells in murine models (summarised in Klase *et al.*¹⁷).

Mother to child transmission (MTCT) studies often use models from T2 or T3 placentae, which differ from T1 placentae in structure, cell components and surface markers. Studies of infection of explanted placentae in other viral infections such as with CMV show neonatal neural malformation and intra uterine death may be caused partly through Th1 cytokine-induced placental damage^{18,19}. The placenta is a complex organ that changes significantly over pregnancy, and comprises some unique cells with differential susceptibility to viral infection (Figure 1). ZIKV infects isolated placental primary cells and human placentae cultured *ex vivo*, with mid pregnancy (T2) chorionic villi (cytotrophoblasts, endothelial cells, fibroblasts, Hofbauer cells) and amniochorionic membranes (amnion epithelial cells, trophoblast progenitors) infected¹⁰. As MTCT requires virus to traverse the placenta, the role of trophoblasts (either as differentiated syncytiotrophoblasts or cytotrophoblasts) is likely to be key, similar to the key role they have for MTCT

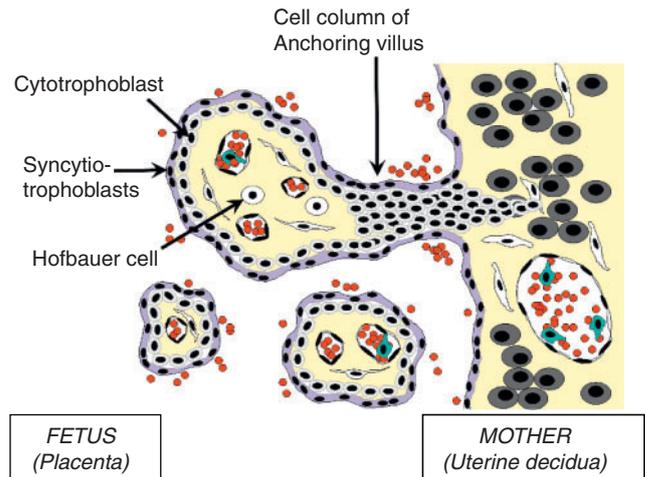


Figure 1. Possible sites of Zika virus infection of the human placenta. Cytotrophoblasts (CTB) form the inner layer of villi, fuse into multinucleated syncytiotrophoblasts, or give rise to extravillous trophoblasts (EVT), which invade and migrate into maternal uterine decidua (that is from left to right in the figure). Viruses infect different cell types, with ZIKV shown in *ex vivo* explants to infect CTB, endothelial cells, fibroblasts, and Hofbauer macrophage-like cells in the villus core on the uterine decidual side (Tabata *et al.*¹⁰).

of other viruses¹⁸. Placental inflammatory response to ZIKV may be important in fetal neurological pathology, although this remains to be proven in humans.

Early gestation (T1) infection with ZIKV has been associated with miscarriage, intrauterine growth restriction, and microcephaly¹⁴, and although causation is likely, it is still to be proven. These changes result from direct infection of the fetal neuronal tissue, although placental infection may contribute to the more generalised fetal pathology as occurs with other viruses causing similar fetal pathology, possibly through virus-induced cell cycle dysregulation²⁰. The presence of receptors and cell entry cofactors on these cells (Axl, Tyro3, TIM1) which are known also to be bound by other flaviviruses (DENV – Tyro3, Axl, Mertk) suggest a common mechanism of entry may exist²¹. These receptor tyrosine kinases are from a family known to clear apoptosed cells and interact with the innate immune system. Interventions that prevent ZIKV binding to these may provide therapeutics that can be trialled in mouse models or human placental explant models where reduced placental damage may reduce fetal injury⁹.

Future studies

ZIKV infection remains a disease clinically of either no symptoms, or relatively mild presentation with fever, myalgia, eye pain, and/or fatigue associated with a maculopapular rash. The major complication of fetal injury, particularly microcephaly and death *in utero*, need to be addressed with further research. Good murine and human placental explant models exist¹⁸, and candidate targets for ZIKV cell binding inhibition have been identified¹⁰. Vaccines for

related flaviviruses are now licensed in some countries (DENV – the live recombinant Denvaxia from Sanofi Pasteur) or undergoing trials. If continued spread of ZIKV occurs either within currently infected countries, or to other naïve populations, enhanced vaccine development needs to be considered, as suggested by some commentators. If so, such a vaccine will need to prevent MTCT and address the issue of cytokine/immune-dependent injury to the fetus, transplacental transmission of ZIKV^{10,18}, with the potential to significantly reduce the risk of congenital ZIKV abnormalities, as has occurred with the successful use of vaccines for rubella virus. Finally, all sources of ZIKV transmission to pregnant women should be avoided, including via blood products, as these may be infected despite being from asymptomatic individuals²².

Acknowledgements

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Biography

Professor William Rawlinson, AM, is Director of Serology and Virology Division (SAViD), Director of the NSW State Organ and Tissue Donor screening laboratory, Director of a State Reference Laboratory for HIV, and Deputy Chair Serology Quality Assurance Program (QAP) RCPAQAP. He is a clinician scientist recognised internationally for translational research into congenital malformation of infectious causes, particularly with cytomegalovirus (CMV). His work in emerging infections include inaugural Chair of the Australian Biosecurity Quality Assurance Program (QAP) RCPAQAP, which collaborates nationally and internationally with the WHO to provide proficiency testing for biothreats and emerging pathogens, including Zika virus.

Read more about Zika in the article **The voyages of Zika virus** by Derek Gatherer on page 206.

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From zero to zero in 100 years: gonococcal antimicrobial resistance



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The threat of antimicrobial resistance (AMR) in bacteria has been escalated to a rightful seat on the global health agenda. In September 2016, for only the fourth time in United Nations (UN) history, the UN General Assembly in New York will meet to focus on a health threat – antimicrobial resistance. Other diseases afforded this level of consultation at the UN were human immunodeficiency virus (HIV), non-communicable diseases and Ebola virus. There are grim

predictions for the future in terms of AMR and health security that span income settings. These predictions challenge the premise that minor bacterial infections of childhood are innocuous, and threaten to halt the medical advancements dependant on antibiotic therapy. Those with compromised immune systems, whether endogenous or induced, will be at highest risk. The development and spread of AMR has been, and will continue to be, fanned by

the relentless selection pressure of exposure to antibiotics whether used appropriately, unnecessarily or suboptimally, in human health, animal health and agriculture. The distribution of antibiotic resistant bacteria is facilitated by travel and transport. Antimicrobial resistance will affect those in the community and the hospital.

A well-documented example that demonstrates the development and spread of AMR involves *Neisseria gonorrhoeae* (Figure 1). The expansion of AMR to each successive therapeutic recommendation has left limited options for treatment of this once easy-to-treat infection. International travel remains a major factor in the dissemination of drug-resistant *Neisseria gonorrhoeae* strains and this has been highlighted most recently by the global spread of strains with resistance to extended spectrum cephalosporin antibiotics, the so-called last single dose therapy. Now a combination of two antibiotics are generally recommended for the treatment of gonorrhoea, ceftriaxone and azithromycin, and resistance to both has been documented^{1,2}. Resistance to azithromycin is typically caused by alteration of the 23S ribosomal RNA gene (the drug target), but may also arise via mutations causing increased activity of efflux pumps (which pump drugs out of the cell)³. Resistance to cephalosporin antibiotics is characterised by a mosaic penicillin binding protein-2 (PBP-2) (this mosaic PBP-2 occurs as a result of integration of DNA sequences from other bacteria producing a changed drug target). Mosaic PBP-2 strains belonging to multi-locus sequence type 1901, first reported in Japan at the turn of the millennium, have become a successful clone in several continents. Whilst genetic data are lacking to confirm what happened with the previous first-line antibiotic classes, it is likely that a similar global

transmission event was responsible for limiting the use of fluoroquinolones in the early 1990s.

Many questions remain regarding how to best deal with AMR in *Neisseria gonorrhoeae*. A gonococcal vaccine remains elusive and other primary prevention strategies, such as *safer sex* behaviour change strategies have not prevented the spread of gonococcal AMR. Many regions of the world remain unaware (particularly at the population level) of the nature and extent of gonorrhoea prevalence and the incidence of antimicrobial resistance. In addition, international travel continues to threaten AMR containment and border screening is not a realistic option for preventing spread of AMR. For these reasons, ongoing monitoring of AMR, both at national and global levels, remains the central tenet of the public health response to the threat of untreatable gonorrhoea. In our opinion, this can only be achieved through combined use of both bacterial culture and molecular AMR testing strategies. Culture based surveillance remains optimal for detecting new resistance mechanisms. However, mechanism and strain-specific molecular assays add rapid, important and clinically relevant data for situational analysis and to inform treatment guidelines, to monitor the effect of interventions and to provide data in countries or remote areas with limited laboratory capacity.

Gonococcal diagnostic and AMR testing strategies in remote and regional communities of Australia provide an ideal fine scale example of the above. These communities represent one of the few globally where penicillin can still be used for treatment of locally acquired gonorrhoea. Penicillin is an ideal treatment option as it is orally administered, and can be stored without need for refrigeration hence there is considerable motivation to maintain

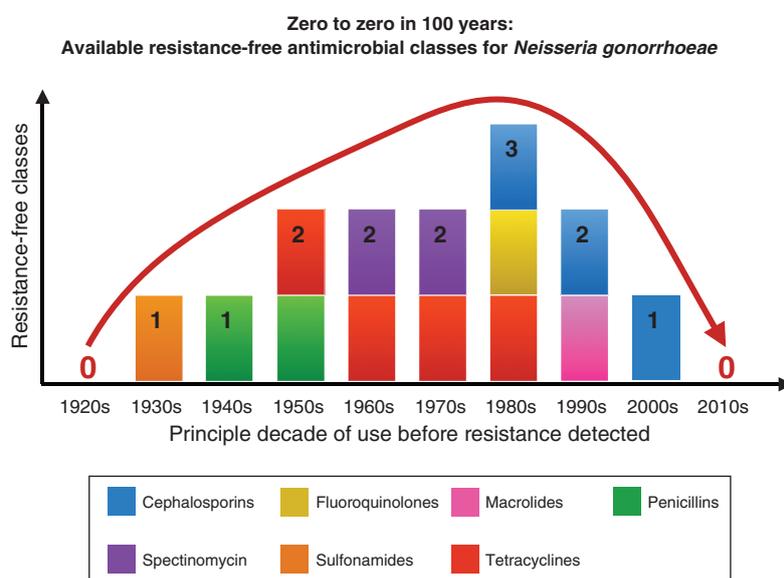


Figure 1. Gonococcal antimicrobial resistance over the past 100 years. Bars indicate the number of clinically tested antimicrobial classes available for *Neisseria gonorrhoeae* treatment.

this therapeutic option. IncurSION of penicillin resistant strains from elsewhere in Australia, where resistance rates exceed 40%, or from international travellers, is an ever-present threat. Optimal surveillance is pivotal to identify such incursions and initiate rapid public health interventions. Whilst gonococcal culture is promoted, the majority of infections (~90%) are diagnosed by molecular based testing. To facilitate surveillance locally, an in-house polymerase chain reaction (PCR) assay has been developed and implemented to screen for penicillinase-producing *Neisseria gonorrhoeae* (PPNG) strains. This approach has a key benefit: rather than simply responding to emerging trends in aggregate data, the assay provides immediate results at an individual level that can readily be acted upon.

The recent incursion of the ceftriaxone resistant A8806 strain into Australia exemplifies how the dual culture-molecular approach supports public health initiatives to contain gonococcal AMR⁴. The A8806 isolate was first identified by culture (highlighting the importance of maintaining bacterial culture). After the phenotypic AMR profile was established using conventional culture-based techniques, the isolate was sequenced, and a strain-specific PCR method developed. The PCR was utilised in clinical practice to determine the spread and prevalence of the A8806 strain across the two states where the infected patient had travelled. We are currently investigating an outbreak of azithromycin resistance in Australia, and further intend to use molecular assays to gauge the extent of the outbreak. Increasingly the availability of genome sequencing is facilitating the identification and characterisation of such clusters, permitting tracking and tracing of AMR strains and investigation of transmission dynamics.

The WHO's *Report on global sexually transmitted infection surveillance 2015* shows that in many regions where disease rates are high there is limited data to determine the scope and extent of AMR⁵. This is a function of a number of factors including limited resources and syndromic management of patients. Paradoxically, best resourced settings often test relatively few gonococcal isolates for AMR, due to a preference for nucleic acid tests which do not characterise AMR profiles of well documented resistance genes. Gonococcal antimicrobial susceptibility testing remains expensive and technically difficult. Strategies are required to strengthen local laboratory capacity and capability, to increase the number of isolates for testing, with all options available to gather timely and reliable information considered.

A population-based approach that identifies those at risk for gonococcal infections, possibly linked to other health interventions, such as HIV screening of high risk people, may be reasonable. Containing gonococcal AMR should be program oriented, linking

patient and contact management with the best treatments to prevent disease and reduce transmission. Merging cutting edge molecular technologies that can diagnose known and emerging AMR determinants with new ways of case finding, and bringing effective treatment to patients and partners in a timely fashion will improve health outcomes. Thus a strategy that focusses only on the acquisition of AMR data and which is isolated from other components of an active program to ensure treatment and elimination of transmission is bound to fail. Such programs may entail a shift in thinking regarding how AMR is diagnosed, how and what patients are identified, and the criteria for which treatment guidelines are modified.

Critically *N. gonorrhoeae* infects only humans and can therefore be potentially eradicated. Future success in the current context will rely on adaptive thinking, exploiting both new and pre-existing technologies to gather information and inform health care strategies. However, primary prevention must remain the principle focus.

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Biographies

Professor Monica Lahra is the Director of the Division of Bacteriology and Director of the World Health Organization Collaborating Centre (WHO-CC) for STDs, at Prince of Wales Hospital, Sydney, Australia. She is also Director of the National Neisseria Network and conjoint Professor at The University of New South Wales. Professor Lahra leads the team at the WHO-CC Sydney to coordinate national and international networks for laboratory surveillance of pathogenic *Neisseria*, including antimicrobial resistance surveillance using phenotypic and genotypic testing.

Professor Jo-Anne R Dillon is Professor and Head of the Department of Microbiology and Immunology, College of Medicine and a Research Scientist at the Vaccine and Infectious Disease Organization – International Vaccine Centre (University of Saskatchewan, Saskatoon, Canada). Her major research interests include the biology and molecular epidemiology of sexually

transmissible diseases, in particular *Neisseria gonorrhoeae* and the surveillance and molecular biology of antimicrobial resistance. Dr Dillon has extensive academic and public sector administrative leadership experience, has led several national and international scientific organisations, and has consulted nationally and internationally in the area of STIs and public health. Dr Dillon has authored numerous publications with a special focus on international trends in antimicrobial resistance, molecular typing of bacterial pathogens and the cell biology of *Neisseria gonorrhoeae*. She is a Fellow of the Canadian Academy of Health Sciences.

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Professor David Lewis, FRCP (UK), is Director of the Western Sydney Sexual Health Centre and Professor at the University of Sydney. He is also the Discipline Leader for STI/HIV within the Marie Bashir Institute for Infectious Diseases and Biosecurity. David's research interests focus on gonorrhoea, genital ulcer disease, STI care in resource-poor settings, outreach STI services and men's sexual health. He serves as the current President of the

International Union against STIs (IUSTI). David frequently assists the World Health Organization as a Technical Advisor in matters related to STI treatment guidelines, the proposed 2016–2025 STI strategy, point-of-care diagnostic tests and the Gonococcal Antimicrobial Susceptibility Programme (GASP).

Dr Teodora E Wi, MD, FPSVI is currently the Medical Officer, Human Reproduction Team, Department of Reproductive Health and Research, World Health Organization (WHO), Geneva, Switzerland. In WHO HQ she is leading the development of STI guidelines, antimicrobial resistance in *N. gonorrhoeae* and interventions for key populations, in addition to providing technical support to regional and country offices of WHO. She has over 20 years of experience in HIV and STI programming. She was the acting team leader for HIV/AIDS and STI, Western Pacific Region Office, WHO. Prior to WHO, she was the Director, STI Capacity Raising, Family Health International (FHI) India under the Avahan India AIDS Initiative of the Bill & Melinda Gates Foundation (BMGF).

Associate Professor David Whiley is based at The University of Queensland Centre for Clinical Research and Pathology Queensland. His research is principally focused on the development of novel molecular diagnostic and typing tools for infectious diseases. He has a particular research interest in *Neisseria gonorrhoeae*.

Foodborne disease associated with travel



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The most important determinant of developing foodborne disease is travel destination. The risk is proportional to regions where there is a high level of unsanitary water supply, lack of food hygiene, lack of food safety regulation, fluctuating electricity supply and lack of education. In medium to high risk regions a travel kit, designed to prevent, minimise or treat the effects should be carried.

After a decade of comprehensive work gathering data to estimate the world burden of foodborne disease the World Health

Organization (WHO) has produced a report in which it has calculated that 600 million people develop foodborne disease after eating contaminated food each year. The report also determined which regions and countries had the highest incidence and which foodborne pathogens caused the majority of outbreaks¹. This has great significance on the varying degrees of danger of developing a foodborne disease when travelling in these regions because the most important determinant of risk is travel destination. Risk also depends on the season of travel².

Diarrhoeal disease represents more than 50% of global foodborne disease¹. Traveller's diarrhoea (TD) is defined as the passage of three or more loose or unformed bowel actions accompanied by at least one of nausea, vomiting, and abdominal cramps, and may be further complicated by fever or blood in stools². Depending on the destination and season of travel, the chance of developing TD when travelling can range from 30% to 70%².

According to the US Centers for Disease Control and Prevention (CDC) there are generally three grades of risk of developing TD². The general division can be seen in Table 1.

The GeoSentinel network, the global surveillance network established in 1995 between the International Society of Travel Medicine and the CDC, has categorised the risk of travellers developing microbial gastrointestinal infections into very high, high, medium, moderate and low risk regions and has analysed the specific microbial pathogens causing gastrointestinal infections in each region³. Travellers to regions with high and very high morbidity due to foodborne disease were 200 and 800 times more likely to develop a gastrointestinal infection, respectively, than travellers to low or moderate morbidity such as Northern America and Europe³.

The number of people travelling from developed to high risk regions such as Africa, the Americas and Asia increased by 60% from 2000 to 2007, and it is estimated this will continue to increase at a rate of 6% per year³. Currently over 100 million travellers from non-tropical regions will visit a developing country each year and 60% of travellers who visit tropical and subtropical regions will develop diarrhoea and health problems^{1,3}.

The risk of developing foodborne illness when travelling is proportional to regions where there is a high level of unsanitary water supply, lack of food hygiene allowing cross contamination, lack of food safety regulation when producing and storing food, fluctuating electricity supply for effective refrigeration, and lack of education and literacy¹.

Table 2 shows the general percentages of microbial pathogens that account for TD². The symptoms of TD are commonly nausea,

Table 1. Three grades of travel destination risk²

Risk	Region
High	Africa, Asia (not Singapore), Middle East, Mexico, Central and South America
Intermediate risk	Eastern Europe, South Africa, and some of the Caribbean islands
Low risk	United States, Canada, Australia, New Zealand, Japan and countries in Northern and Western Europe

vomiting and diarrhoea but depending on the infective agent may be more severe with fever and bloody diarrhoea. The most common bacteria associated with TD are *Campylobacter jejuni*, *Salmonella* spp., *Shigella* spp. and enterotoxigenic *E. coli*³. Other pathogenic *E. coli* are also common. The main intestinal virus causing TD is Norovirus. The main protozoal foodborne pathogen causing TD is *Giardia*² from contaminated water used to prepare food. Other protozoa are less common. In regions where the tradition or normal practice is to eat raw or undercooked meat, poultry and eggs, drink raw milk and eat fresh produce grown using contaminated unsanitary water supplies, there is a high risk of developing the above diarrheal diseases. Infection with the tapeworm (*Taenia solium*) occurs from eating raw or undercooked pork. Some pathogens are much more common in low-income countries. These include typhoid fever and foodborne cholera. Several foodborne pathogens may cause more serious illness affecting sites outside the gastrointestinal tract including systemic, neurological, muscular, and long-term disease sequelae affecting the kidney, liver, brain, bone and skin. Travellers who are old and young, pregnant women and those with weakened immune system may be more susceptible to serious disease¹. Some of these will be discussed further in information on specific regions, below.

The WHO African, South-East Asia and Eastern Mediterranean regions have the first, second and third highest burden of foodborne disease in the world respectively which will have major consequences for risk when travelling. The majority of cases are TD, caused by typical bacterial and protozoal agents and Norovirus. Tapeworm is also prominent, however some interesting facts have emerged from the WHO foodborne disease burden statistics in these regions that also have significance for travellers¹.

Half the global population who die of hepatitis A infection or typhoid live in the WHO South-East Asia region so both diseases must also be considered when travelling there. Hepatitis A is also prevalent in the Eastern Mediterranean region due to faecal contamination of food. This region has more than half the global cases of brucellosis and travellers could be infected from eating raw or under-pasteurised dairy products from infected cows, sheep and goats with poor domestic health regimes¹.

Table 2. The general percentages of microbial pathogens that account for Travellers Diarrhoea²

Microbial foodborne pathogen	Approximate percentage of TD
Bacterial pathogens	80–90%
Protozoal pathogens	10%
Intestinal viruses	5–8%

Unlike other regions diarrhoeal disease is not the dominant foodborne disease in the WHO Western Pacific region. This area has a high incidence of liver cancer resulting from the ingestion of mouldy grain contaminated with aflatoxin. This region also has a high rate of foodborne disease due to ingestion of parasites. Most of the world's population infected with Chinese liver fluke is in this region¹. As this parasite is contracted by eating raw or undercooked fish this should be avoided when travelling in this region.

In Central and South America, in addition to TD, toxoplasmosis and tapeworm are also important¹. The risk of hepatitis A and foodborne amoebiasis, cysticercosis, brucellosis, infection with *Mycobacterium bovis* and listeriosis, which causes complication in pregnancy and serious systemic illness in susceptible people, have been associated with travel infections in Mexico⁴.

The WHO European region has the lowest burden of foodborne disease. In first world countries non-typhoidal *Salmonella* is an issue, as it is in all regions. *Campylobacter* is also an important pathogen¹. However, Norovirus is five times more common. One of the most frequent causes of this virus in first world countries often relates to cruise ships. Between 2012 and 2016 there were 45 gastrointestinal outbreaks on cruise ships reported to the CDC of which 41 were attributed to Norovirus⁵. Because Norovirus symptoms include vomiting, often projectile vomiting, the close quarters of cruise ships favour the rapid spread of this virus via aerosols and poor food hygiene. However, the incidence of Norovirus transmission on cruise ships is diminishing since improved sanitation and food safety and hygiene regulations and strict quarantine of infected passengers has been implemented⁶.

Vaccination to hepatitis A, typhoid and cholera are available and should be considered when travelling to regions at risk of these diseases⁷. A travel kit, designed to prevent, minimise or treat the effects and symptoms of TD should be carried by travellers to medium and high risk regions. It should contain an alcohol based hand sanitiser. Often a probiotic or capsules of bovine colostrum, which can be bought over the counter, is used as a daily preventative, although studies have not proved their efficacy². Anti-motility agents, such as loperimide, help reduce the frequency of bowel movements and allow travel to continue. However, the CDC does not recommend using this treatment if the general

foodborne disease symptoms of TD advance to fever and bloody diarrhoea². It is important for a travel kit to include dehydrated sachets of oral rehydration salts for oral hydration therapy, to reduce lost fluids and electrolytes. Oral rehydration is one of the most important treatments of TD. An antibiotic is often included in the kit, as prescribed by a medical practitioner, due to the frequency of TD's being caused by bacteria, however, travellers may find it very difficult to distinguish between the symptoms of various foodborne disease, so inadvertent use of antibiotic therapy is not recommended. Carrying a treatment for parasites such as *Giardia* is also important².

When travelling in high risk countries many factors, such as restaurant hygiene, are out of the traveller's control. Although the 'boil it, cook it, peel it, or forget it' rule is still highly recommended in high and medium risk regions, the hygiene of kitchens and cross contamination in food preparation areas are often unseen by travellers unsuspectingly enjoying a meal in a local or traditional restaurant. Avoiding raw or undercooked meat, fish, poultry and dairy products, exercising care when selecting food to eat, and timely use of prophylactics and medications will decrease risk and give the traveller a better chance of enjoying a trip free of foodborne pathogen health issues.

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Biography

Prue Bramwell is a Senior Lecturer in the School of Applied Science at RMIT University. She has over 20 years' experience in food microbiology and has been an educator in the fields of food microbiology and food safety for over 15 years. Her research interests are in methods for the isolation and identification of foodborne microbes.

Future issues of *Microbiology Australia*

March 2017: Bat-associated Diseases

Guest Editor: Glenn Marsh

May 2017: Industrial Microbiology

Guest Editors: Ian Macreadie and Ipek Kurtböke

Australia's biosecurity procedures and preparedness



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There is sometimes concern expressed in Australia and other countries that we do not specifically test imported food for the presence of antimicrobial resistant (AMR) bacteria. How significant is this threat and how do the biosecurity measures taken by Australia address these?

Australia operates a biosecurity regimen that is risk and science-based. Australia is one of only a few countries that has a legislated and clearly articulated Appropriate Level of Protection (ALOP) achieved through managing the risk posed by imported goods to an acceptable level. These actions include prudent sourcing, certification and testing of food products to manage the biosecurity and food safety risk.

The challenge with imported food is determining if there is a demonstrable risk. We know that AMR is a global problem, one that is estimated to threaten 10 million lives a year and a cumulative US\$100 trillion of economic output by 2050 due to drug-resistant infections¹. What we don't know is the relative contributions of factors such as inappropriate dispensing of antibiotics to the human population, resistant infections acquired through travel or hospital stays, use of antibiotics in agriculture, environmental exposure through contaminated water and soils, and consumption or preparation of foods carrying AMR bacteria.

For foods to pose an AMR risk multiple factors are likely to be in play including²:

- The food animals or plants are treated with or exposed to an antibiotic,
- The antibiotic is of significance to human health,
- Bacteria in or on the food animal or plant need to have resistance to that antibiotic,
- The bacteria need to survive the various stages of food processing to the extent that they are able to transmit their resistance capability to bacteria in a human host,

- The bacterium must be able to cause disease in humans, or transfer its resistance to bacteria that can cause disease in humans, and
- The disease requires treatment with antimicrobials for which the bacterium is resistant, leading to treatment failure.

In practice these criteria are rarely always met and so the contribution of food, whether imported or of domestic origin, to human AMR is not yet quantifiable and could be quite minor.

Antibiotics are used to treat and prevent disease in livestock because it is generally recognised that sick animals pose a food safety risk to humans and that livestock should be afforded good health on ethical and animal welfare grounds. Access to antibiotics for veterinary therapeutic use in Australia is controlled.

In Australia and many other countries, most food is produced without the use of antibiotics, there is some minor use in horticulture and use in livestock agriculture is largely confined to intensive rearing systems. While some livestock are provided with antimicrobials for growth promotion purposes, generally these are antimicrobials that do not impact on human health but in some countries this is not always the case. In Australia antibiotics available for growth promotion are regulated through the registration process.

Probably the most effective measure to prevent transmission of AMR through food is good food hygiene. Any good food processing and preparation process should work to reduce the number of bacteria carried forward at each step and ideally be completed with a kill step of cooking the food to remove any residual bacterial contamination. In human medicine, infection prevention and control (IPC) is an essential element contributing to any AMR strategy. Likewise, breaking the chain of transmission through good agricultural practices and good food hygiene is equally important in the food production system. If bacteria in the gut, or on the hide, of an animal can be prevented from spilling onto the meat then the risk of AMR transmission is effectively minimised. Likewise, preventing transfer of bacteria on ready-to-eat horticultural products reduces the risk of AMR transmission. Good food hygiene not only prevents exposure to AMR carrying bacteria, it also prevents food poisoning and the demand for antimicrobials.

In 2009, Australian farms produced 93% of the total volume of food consumed in Australia³. Over the past 20 years there has been a steady increase in the value of food imports averaging 4.8 per cent

per year⁴. Australia's food imports are generally processed, high-value products. We live in a connected world and foods from around the world are readily available in Australia. Steps are taken at airports to prevent travellers bringing in foods that pose biosecurity (and food safety) risks, but nothing can be done to address the possibly greater risk posed by the travellers themselves who may be carrying AMR bacteria from environmental exposure, contaminated food, infection or medical treatment as part of their travel.

Australia's biosecurity measures work to support our food safety objectives. We source from countries of compatible disease status and apply risk management measures (such as treatments and testing) to address potential risks. All imported food must meet biosecurity requirements before being allowed into the country and is subject to risk-based inspection at the border. To manage other biosecurity risks Australia does not import livestock and this has the side benefit of not introducing resistant bacteria through live animals into our national herd. Furthermore, chicken and pig meat imported into the country are either cooked, or further processed upon arrival, and fresh beef can only come from a few select countries.

As previously mentioned, Australia does not currently conduct AMR tests on foods at the border, just as domestic foods are not routinely tested for AMR. To conduct testing at the border in the absence of a demonstrated scientific risk and without similar testing of domestic foods would be inconsistent with our international obligations and place Australia in a vulnerable position with trading partners. Likewise, Australia would question or challenge any country that commenced testing our exported foods for AMR in the absence of a demonstrable scientific risk and an official control program.

We do not know how much of the AMR observed globally and within Australia can be attributed to food. This is acknowledged in Australia's AMR strategy, which has identified a comprehensive literature review as a key first step. The likelihood is that food's contribution is small, but it needs to be identified and possibly quantified so that measures can be devised to manage any unacceptable risk. The existing guidance⁵ provided by Codex Alimentarius is valuable and is currently being reviewed.

Global interest in the increasing threat of AMR has been conveyed by consumers to the food production and retail industry with a rising number of food outlets introducing antibiotic requirements on animals sourced by their suppliers. Australia is well placed to respond to this new demand given our strong controls over critical antibiotics, our largely extensive livestock agricultural production system, and our nimble and responsive industry and government assurance systems.

As AMR is an emerging threat we do not yet have all the answers, nor all the tools. It is thought that food may contribute relatively little to this threat, but our prudent national strategy recognises the gap in our knowledge and seeks to fill this through a comprehensive literature review. Meanwhile, Australia's biosecurity system will continue to manage the risk, appropriately informed by research and experience with this rapidly developing global issue.

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Biography

Mark Schipp was appointed Australian Chief Veterinary Officer in 2011. In 2012 he was elected to the OIE Council and in 2015 was elected Vice President of the OIE General Assembly. He is chair of Wildlife Health Australia management committee and chair of Animal Health Committee. Together with the Chief Medical Officer, Dr Schipp chairs the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance. Previously Dr Schipp has held positions responsible for animal derived food product inspection, market access and export certification. Dr Schipp served two terms overseas as Agriculture Counsellor in Seoul, South Korea and in Beijing, China. Mark is a biology and veterinary graduate of Murdoch University. After graduation he worked with the Western Australian Department of Agriculture.

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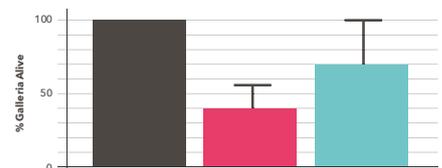
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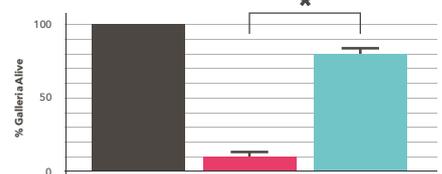
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Fig 1.

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