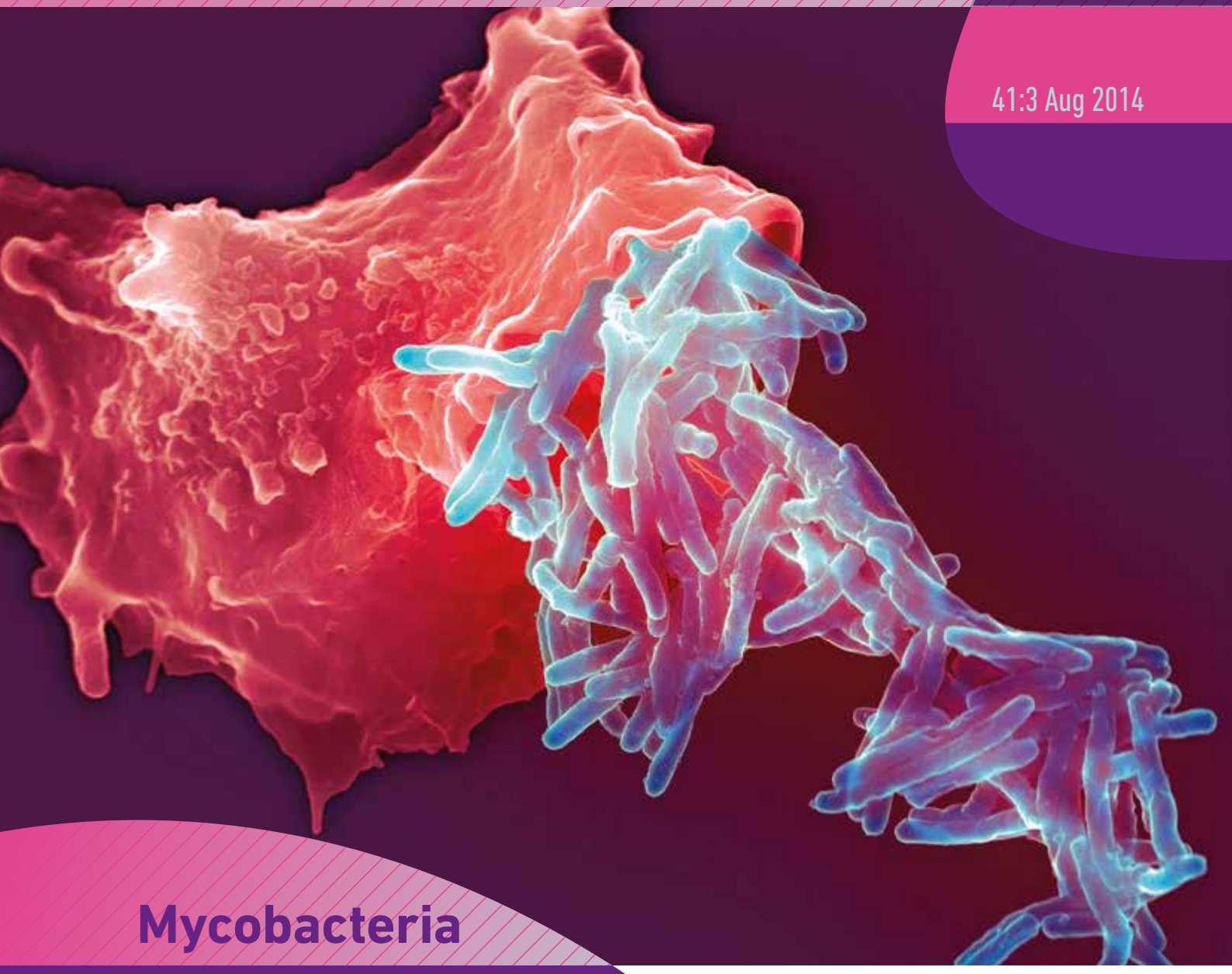
Microbiology TODAY

41:3 Aug 2014



Mycobacteria

Mycobacterium avium Complex
An (in)sensitive pathogen – *M. tuberculosis*
A new vaccine against tuberculosis
Mycobacterium leprae: the cause of leprosy
Mycobacterium ulcerans and Buruli ulcer

SOCIETY FOR GENERAL MICROBIOLOGY

Editorial

This edition of *Microbiology Today* focuses on *Mycobacteriaceae*, a family of bacteria that have been closely entwined with human health and disease throughout the world and across the millennia. Tackling diseases caused by mycobacteria calls for a global perspective. It is clear that even with the rapid advances in health care that our generation is experiencing, these diseases are still adversely affecting communities and societies across the globe.

Mycobacteria are usually slender, curved rods that personify the old adage of the 'exception that proves the rule'. They can be classified as Gram-positive bacteria but they do not stain as Gram-positive bacteria should. Instead they are distinctive bacteria that share the common property of a thick, lipid-rich cell wall that tightly retains carbol fuchsin dye even in the presence of a harsh acidic alcohol treatment: in summary they react positively with an acid-fast stain. These acid-fast bacteria have something else in common; they are all part of the synergistic, symbiotic relationship that humankind shares with their environment. Although some mycobacteria are free-living saprophytes, they are also animal and human pathogens. Changes in the way that our interactions with the environment have affected our relationship with these bacteria are illustrated beautifully by Richard Bentham and Harriet Whiley. They describe how recent health care advances have led to a human population increasingly susceptible to opportunist pathogens such as *Mycobacterium avium*, which has found a perfect niche for survival in biofilms found in hospitals.

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is one of the principal human pathogens on the planet. These bacteria were first isolated in the 19th century by Robert Koch who postulated that this was the 'evil' causing TB. Jaroslaw Dziadek and colleagues describe how this pathogen is not only insensitive to most known antibiotics but also able to evade the immune host responses. Learning more about the biology of these bacteria will hopefully lead to potential new antimicrobial chemotherapy approaches. Steven Smith, on the other hand, updates us on the progress vaccinologists are making towards designing and developing the next generation of TB vaccines to aid prevention of this terrible disease.

Mycobacteria that cause diseases currently failing to attract as much attention as TB include *Mycobacterium ulcerans*. This bacterium is responsible for Buruli ulcer, a neglected tropical disease (NTD) found mainly in poor, rural areas of West and Central Africa. Tim Steiner describes how Buruli ulcer is also endemic in temperate regions of Japan and Australia. With the environmental reservoir unclear, the need for a coordinated, well-funded and focused research effort to tackle this disease remains. Another NTD associated with poverty, leprosy, has a large number of new cases originating in South-east Asia, the Americas and Africa. Richard Truman and colleagues discuss the highly adapted niche pathogen *Mycobacterium leprae*. They explain that the USA population is also not immune, with reports indicating that zoonotic transmission of *M. leprae* from armadillos is responsible for up to 64% of all leprosy cases. Scientists are now investigating the role that armadillos may play in perpetuating leprosy in the Americas.

The Comment section is provided by Elizabeth Wellington and Orin Courtenay. They touch on the debate surrounding the transmission of bovine TB between wildlife (badgers) and cattle. Their current research detects the causal agent *Mycobacterium bovis* from environmental contamination of pasture and soil surrounding badger setts. They are keen to elucidate whether faecal shedding of the bacterium could be a reliable measure of transmission risk from badgers to cattle. It is hoped this may lead to suggestions to solve the current bovine TB crisis.

These articles show that we have a worldwide community of scientists engaged in trying to understand and ameliorate the consequences of infections caused by these bacteria. After reading this edition of *Microbiology Today*, I hope you agree that the articles reflect the wide range of positive contributions that microbiologists are making to improve human and animal health.

Laura Bowater
Editor
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Contents

Microbiology TODAY

Articles

41:3 Aug 2014

Features

Regulars

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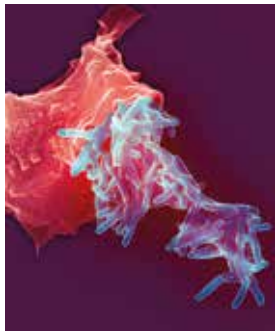

FSC Logo

Coloured scanning electron micrograph of a macrophage white blood cell (red) engulfing *Mycobacterium bovis* bacteria (blue). Science Photo Library

SOCIETY FOR GENERAL MICROBIOLOGY

Council 2013–14

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Professional Development Committee – Dr Sara Burton

Geoffrey Pope Building, University of Exeter, Stocker Road, Exeter EX4 4QD; **s.k.burton@exeter.ac.uk**

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Scientific Conferences Committee – Professor Mark Harris

School of Molecular and Cellular Biology, Faculty of Biological Sciences, University of Leeds, Leeds LS2 9JT; **m.harris@leeds.ac.uk**

From the President

Tuberculosis (TB) was once the scourge of the rich and poor alike. Tragic heroines in literature and music were often featured as suffering from consumption and succumbing to the disease. Thanks to the introduction of mass vaccination and improvements in simple hygiene measures, TB has been much less common in the developed world in recent years.

Photo Ian Atherton

However, TB remains a major health challenge. This edition of *Microbiology Today* focuses on some of the recent developments in combating diseases caused by mycobacteria and on the characteristics of these organisms.

It is appropriate that *Microbiology Today* focuses on these important pathogens. One of the delights of being a microbiologist is that the discipline is rarely far from the news. I am sure that many of us have been asked by friends, relatives and others what we think about bovine TB and the badger cull. Living in the South West, I am well aware of the strength of public opinion in both pro-cull and anti-cull camps. We are often approached to comment at short notice on items in the news – it is important that the Society gives expert opinion when asked about such issues. Recently we have been asked to comment on the increasing resistance to antibiotics, the death of babies from nutrient drips contaminated with *Bacillus cereus*, *Legionella* in a home-birthing pool and several other issues.

Of course, it is regrettable that many of the microbiological issues in the news are about tragedies. As well as the events above, the Ebola outbreak in West Africa and the May 2014 declaration of a polio public health emergency are two of the more wide-reaching microbiological events. Nevertheless, there are also positive stories about micro-organisms that we need to communicate – antibiotic producers, food producers and probiotics, for example. Two years ago we had an award-winning display at the Chelsea Flower Show showing how micro-organisms contribute to a healthy soil and to increased plant growth. The Society is keen that we present the profession effectively and well, with experts who are trained to talk to the media. As you will realise if you listen to an investigative journalist, talking to the media is not like talking to one's scientific colleagues or one's family. A radio journalist once told me that he disliked the 'two-handed scientist'. In other words he did not want to hear alternative views (i.e. 'on the other hand') but wanted a short, precise and catchy statement. My job was to present the facts; his job was to produce an entertaining programme. If you are interested in presenting a professional view of newsworthy issues in microbiology, then please let me know.

If your interests in representing the Society do not extend to talking to the media, have you considered becoming a Society Champion? We launched the Champions scheme in April 2014 and have had a good uptake, but there is still an opportunity to come forward and represent microbiology in your locality. The Society is working with its Champions to represent our discipline, to build our membership and to extend our reach. Further details are available by email.

I am writing this on the day that the Prime Minister has announced the creation of an internationally focused commission, led by the economist Jim O'Neill and partly funded by the Wellcome Trust, to examine the key issues of antimicrobial resistance. As I write, we do not know the composition of the commission, but I hope that Society members will be involved in its work. Through participating in important policy developments, as well as ensuring that our message gets across through the media, we can change public perceptions, affect policy decisions, and show that microbiology has an important contribution to make to modern society.

Nigel Brown
President
president@sgm.ac.uk

Q&A

Peter Cotgreave

Chief Executive

In June, Dr Peter Cotgreave joined the Society as Chief Executive. Peter joins us from the Royal Society, where he worked as Director of Fellowship and Scientific Affairs. We asked him about his background, his career and his thoughts on the future of the Society for General Microbiology.

Have you always been interested in science?

I was educated in Shropshire, where I grew up. I always knew that I was interested in science; I studied it for my A-Levels, at University and then did a PhD in Zoology. If you grow up in the middle of nowhere on the Shropshire–Wales border and are not interested in animals and plants you are going to be very bored!

Was there a particular moment that sparked your interest?

One that I do remember is this: my uncle was a farmer and he gave me a badger's skull when I was about eight years old. It absolutely fascinated me – the shape of the teeth, the fact that it had an articulated jaw (unlike any other mammal), for example. That was the moment for me, as I started to ask why these things were the way they were. I've still got the skull all these years later.

What was your research area?

I was a bird ecologist. I worked on community ecology – trying to understand why in any one place a particular bird species is more common than another. The work took me to Brazil, Tobago, Tanzania, Ethiopia – the great thing about doing bird ecology for a

living is that other people paid for me to go to amazing places where there were interesting species to see!

What made you step away from research?

I was cycling to work one morning – I was a lecturer at the University of Oxford at that point – and it occurred to me that while I'd done the textbook academic career, I'd never really stopped to think whether that's what I wanted to do. It just kind of happened because I was interested in the subject. I knew I didn't want to leave science, but I did want to leave research. I went to work for the Zoological Society of London – it was the best job in the world for someone in that position. I spent half of my time doing research and half bridging the gap between people in research labs and the public-facing parts of the society like the press office.

Tell us about your time at the Campaign for Science and Engineering?

For nine years, I was the Director of Save British Science, which became the Campaign for Science and Engineering (CaSE) on my watch. We were representing the grass-roots scientific community, trying to get messages across about the importance of funding for science and engineering.

What are you most proud of achieving during your time there?

I'd say two things. When Gordon Brown, then the Chancellor, announced his 10-year science strategy in 2004 and cast the plan as a response to what the science community had told him. The other is that my colleagues and I got to go to Number 10 several times, much to the jealousy of other, larger organisations. I asked them why we were invited and was told that: '*You filter out the cacophony of noise coming out of the Science Community. You're telling us the things that we really need to take seriously.*'

What did your role at the Royal Society entail?

My job was to interact with the Fellows and to make sure that the Royal Society was doing the things that its members wanted. I also oversaw the Society's scientific programmes and conferences, its diversity work and its work with industry.

How do you think this experience will fit with the Society for General Microbiology?

I think that many learned societies have for too long taken their members for granted. One of the things that I want to do is to get out to meet and get to know Society members: learn about what they're doing, what their concerns are, and how they think the Society can meet its goals, which are to advance the art and science of microbiology.

What are some of the challenges that the Society can, and should, be involved in?

One of the challenges we face is to get policy-makers, politicians and the public – anybody who's not in the world of microbiology – to get as interested in something that you can't see as you can about the panda. The medical aspects of microbiology are arguably more important now than they have been for the last 50 years, particularly with the increase in antimicrobial resistance. There are opportunities too, in the worlds of environmental and materials science, for example.

I think that microbiology is becoming less obvious as a distinct discipline within many university courses. I also think that many people who are microbiologists don't see themselves as such, and think of themselves as geneticists or ecologists. We need to work to change that.

What can the Society do to become involved in these discussions?

I've been hugely impressed with how clearly the Council knows what it wants and how the organisation has a clear strategy. This sounds so obvious, but you'd be surprised how many organisations struggle to encapsulate what they're trying to achieve. I wouldn't have taken the job if I didn't think the Society was very well placed to do lots of very interesting and exciting things in the areas I mentioned.

What are your plans for the Society?

We've got five strategic priorities (**microb.io/VhArMW**) and I think all of them are extremely important. I want to deliver on those in ways that support the members and the microbiological community as a whole.

There are a lot of learned societies in biology. We have to get better as a group at presenting a cohesive and united front, where it is appropriate to do so. The move to Charles Darwin House in London was a really important statement on that. As a Society, we have to leverage our influence by working with our partners, both here and abroad.

Benjamin Thompson
Public Relations Manager
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News

Coming soon – a new online platform and submissions system for Publishing

The Society's Publishing team is entering an exciting time of change. Over the next year, the Publishing team will be working hard with Publishing Technology to design, develop and launch a brand new platform to host the Society's publications. Journal content will be enriched to allow better searching and indexing, and the new platform will present an up-to-date and fresh look. The new sites will launch in summer 2015.

As well as this change, the Society will be transitioning its manuscript tracking system from Bench>Press to Editorial Manager (owned by Aries Systems) in autumn 2014. We have also selected Aries Systems to provide a new production tracking system (ProduXion Manager). Editorial Manager is a streamlined submission system that contains all of the modern features that authors expect. The ProduXion Manager tool means that authors will be able to log in to view the status of their article from submission through to publication, making the publishing process more transparent and simple to follow.

If you have any questions about the forthcoming changes please contact the Publishing team via email at **journals@sgm.ac.uk**

2015 SGM Journals pricing now available

The 2015 journal pricing is now available, for further information visit the journals website: **www.sgmjournals.org**

Upcoming grant deadlines

Grant deadline	Grant	Notes
01/09/2014	Travel Grants	For conferences and courses from 1 October onwards
22/09/2014	Society Conference Grants	For the Focused Meeting on Modelling Microbial Infection (17–18 November)
01/10/2014	Research Visit Grants	For visits from 1 December onwards
01/10/2014	International Development Fund	For visits from 1 December onwards
01/10/2014	Watanabe Book Fund	
01/10/2014	Education and Outreach Grants	
30/11/2014	Hayes-Burnet and Heatley-Payne Grants	

Rolling application: Microbiology in Schools Fund – School members can apply (at least three months in advance) for funds to support microbiology-related teaching projects.

Election results

The Society would like to congratulate the following members who will be joining Council Committees and Divisions in January 2015.

Council

Dr Mike Skinner Imperial College London

Professional Development Committee

Dr Douglas Browning University of Birmingham

Katherine Hargreaves University of Leicester

Divisions

Eukaryotic

Dr James Ajioka University of Cambridge

Dr Gareth Bloomfield MRC Laboratory of Molecular Biology

Dr Kevin Kavanagh National University of Ireland

Dr Jason King University of Sheffield

Professor Edward Louis University of Leicester

Dr Ian Roberts Institute of Food Research Norwich Research Park

Professor Colin Robinson University of Kent

Prokaryotic

Dr Stephen Michell University of Exeter

Dr Jennifer Mitchell University College Dublin

Dr Ryan Seipke University of Leeds

Professor Sheila Patrick Queen's University Belfast

Dr Lori Snyder Kingston University

Dr Sabine Tötemeyer University of Nottingham

Dr Martin Welch University of Cambridge

Virology – DNA

Dr Andrew Macdonald University of Leeds

Dr Jo Parish University of Birmingham

Virology – RNA

Dr Erica Bickerton The Pirbright Institute

Virology Translational

Dr Stephen Griffin Leeds Institute of Cancer & Pathology

Irish

Dr David Clarke University College Cork

Dr Marguerite Clyne University College Dublin

Annual General Meeting (AGM) and Celebration of the Society's Work

The AGM of the Society for General Microbiology and Celebration of the Society's Work will be held on **Thursday 11 September 2014** from 13.30 to 18.15. The AGM is at 15:45 in the Auditorium of Charles Darwin House, 12 Roger Street, London WC1N 2JU.

The celebration will begin with the presentation of the 2014 Outreach Prize (see below). This will be followed by the *Sir Howard Dalton Young Microbiologist of the Year* finalists giving 10-minute oral presentations. These presentations will be judged and the three best entries will be awarded prizes. Following the AGM there will be a Special Lecture and drinks reception. All members are invited to attend what promises to be both an informative and enjoyable afternoon with ample opportunity to network during the drinks reception. If you would like to attend, please email Rosie Waterton in advance at **r.waterton@sgm.ac.uk**

Programme

13.30–13:45 – Outreach Prize Award
13:45–15:45 – *Sir Howard Dalton Young Microbiologist of the Year* presentations
15:45 – AGM
16:30–17:15 – Special Lecture by **Professor Melanie Welham**, Director of Science at BBSRC
17:15–18:15 – Drinks reception with showcase of the Society's work and the 2014 Outreach Prize winner

AGM Agenda

1 Introduction by the Chair
2 Minutes of the 2013 Annual General Meeting
3 Matters arising from the Minutes
4 Financial Report
4.i Receiving of the Annual Accounts
4.ii Appointment of Auditor
4.iii Approval of membership subscription rates
5 New Members of Council, Committees and Divisions 2014
6 Special Resolution – amended Articles of Association
7 Any other business: Presidential election

Supporting papers can be downloaded from the SGM website: **microb.io/1aLpBSY**

Dr Peter Cotgreave, Company Secretary

Outreach Prize

Awarded annually to a microbiologist who has engaged in high-quality outreach activities during the last 2–5 years; the 2014 Prize has been awarded to **Dr Joana Alves Moscoso** from Imperial College London. She will receive her award and give a presentation on *Celebrating Diversity in Science* at the Society's AGM and Celebration of its Work (see above). She will be on hand during the drinks reception to talk further about her outreach work.

Dates for your diary

STI play, *If It's Not On, It's Not On* at the Arts Depot Theatre, London (8–11 September) – The Society, together with Théâtre Sans Frontières, would like to invite you to our play, *If It's Not On, It's Not On*. The play follows the story of Luke, from his first awkward sexual experience through to frank discussions with his friends and his Dad, in a humorous adventure through the history of sexually transmitted infections (STIs). Both Luke and the audience will discover the facts behind STIs, where to get help and advice, and much more. This play is aimed at anyone over the age of 14, carers, educators, and anyone who wants to know more about this subject. Tickets are available free of charge via Eventbrite (**microb.io/1pELVBI**).

UK Fungus Day (11–12 October) – The British Mycological Society with support from academics, field mycologists, educators and industry will be holding the UK Fungus Day event to raise awareness of fungi and fungal science. Events covering various regions across the UK and Ireland will take place. For further information visit their website: **www.ukfungusday.co.uk**

Biology Week (12–18 October) – Biology Week is a celebration of all aspects of the biosciences. It is organised by the Society of Biology. For further information visit their website: **www.societyofbiology.org/get-involved/biologyweek**

Behind-the-scenes guided tour of the Darwin Centre at the Natural History Museum (20 November) – Join us for an exclusive tour, designed specifically for Society members. The 60-minute tour will take members around many of the Museum's hidden treasures. The eight available places will be allocated by prize draw. To enter, simply tell us in no more than 50 words: what is your favourite microbe and why? Entries close on **Monday 1 September 2014**. Please email entries to our Grants & Membership Officer, Maria Fernandes (**m.fernandes@sgm.ac.uk**).

Guided tour of the Hunterian Museum, London (27 November) – The tour will feature John Hunter's collections and an insight into his contributions to modern surgery. Places are limited and on a first-come first-serve basis. Participation will cost £5 to cover the charges of the tour. Please email Maria Fernandes (**m.fernandes@sgm.ac.uk**) to attend.

News of members

Congratulations to the following Society members:

On the occasion of the Queen's 2014 Birthday Honours, **Professor Polly Roy** of the London School of Health & Tropical Medicine was awarded an OBE for services to virus research. Professor Roy has been a Society member since 1990.

Dr Julian Parkhill of the Wellcome Trust Sanger Institute, a Society member since 1990, was elected a Fellow of the Royal Society on 30 April 2014.

Dr Julian Davies, of the University of British Columbia and an Honorary member of the Society, was elected a Foreign Associate of the US National Academy of Sciences.

Sir John Skehel of the Medical Research Council National Institute for Medical Research was elected a foreign member of the US National Academy of Sciences. Sir John has been a Society member since 1973.

Society Council Member **Dr Paul Hoskisson** of the University of Strathclyde was appointed to The Royal Society of Edinburgh's Young Academy of Scotland (YAS). Dr Hoskisson has been a member since 1998.

The Society would like to extend warm congratulations to Professor Roy, Sir John, Dr Parkhill, Dr Davies and Dr Hoskisson.

Deaths

We regret to announce the death of **Dr Mick O'Connell** of Dublin City University who passed away on 30 May. He had previously been involved in the Society's Irish Branch and his research was in the area of siderophore-mediated iron transport.

In the May edition of *Microbiology Today* we notified members that **Professor Lorna Casselton** had passed away – her full obituary is in this publication on page 142.

Focused Meeting – Modelling Microbial Infection

An excellent opportunity to attend the Society's second Focused Meeting on *Modelling Microbial Infection* and network with key researchers working in this field. This meeting is also a great forum for early career researchers and students to present their work in a relaxed and supportive environment.

The meeting on *Modelling Microbial Infection* will take place from 17 to 18 November at Charles Darwin House in London. The closing date for abstract submissions is midday on **Monday 22 September**.

Online registration will close at midnight on **Thursday 13 November**, with early-bird fees available until midnight on **18 October**. To qualify for Society Member rates, membership subscriptions must be paid by **Friday 17 October**.

Dariel Burdass
Director of Strategy and Communications
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Champion Champions!

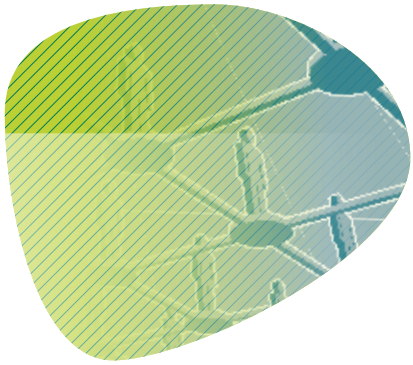
Since our call for Champions launched in April, we've had many enquiries and now have 12 members who have volunteered to help take the programme forward. We are working with them to put in place a number of local events that will help build the Society's profile and the organisation's support network.

Here are just some of the activities planned over the coming months:

- Microbiology talks to postgraduate students during fresher's week
- A local symposium for early-career microbiologists
- A TED-type talk to see how microbiology interacts with other disciplines
- A regular podcast/videocast to capture visiting expert speakers

Do keep an eye on the website for further details and future events.

If you have ideas of your own on how to engage with workmates, friends and colleagues in the name of microbiology, let us know. Or if you're already doing it but haven't told us yet, please get in touch!



There is still time to join the Champions programme. Drop an email to the Acting Head of Membership Services, Paul Easton, **p.easton@sgm.ac.uk**, with your name and contact details. He can tell you more about the programme and how to take part.

Paul Easton
Acting Head of Membership Services

SGM journals to launch Editorial Manager websites in autumn 2014

In autumn 2014 the Society for General Microbiology (SGM) will launch a new journal manuscript submission and tracking system, Editorial Manager. SGM will also begin using ProduXion Manager, a production tracking system. Both are provided by Aries Systems.

What are the benefits to authors?

Editorial Manager is a streamlined submission system which contains all of the modern features that authors expect. The user interface is clear and simple to navigate.

To simplify the review process, users will be asked to register keywords to indicate their areas of expertise. This will make finding suitable reviewers from the database quicker and easier for our Editors.

The ProduXion Manager tool means that authors will be able to login to view the status of their article from submission through to publication, making the publishing process more transparent and simple to follow.

After Aries was selected, Leighton Chipperfield, Head of Publishing at SGM, said: 'As a modern self-publishing society SGM is committed to providing its Editors, authors, reviewers and staff with the best tools for the job. We look forward to partnering with Aries to deliver an even better experience for all involved.'

If you have any questions about SGM's move to Editorial Manager then please contact our Editorial Office at journals@sgm.ac.uk. We welcome enquiries from new authors as well as our current authors wishing to know how the transition will affect their submissions.

For more information on the journals published by the Society for General Microbiology, go to sgmjournals.org.

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- Read the Publishing blog: sgmpublishingblog.com

SOCIETY FOR GENERAL MICROBIOLOGY

Heatley-Payne Award 2014

The Society for General Microbiology (SGM), together with the American Society for Microbiology (ASM), offers an annual award to recognise and reward the scientific excellence of a postdoctoral member's current programme of research and scholarly activity.

Dr Nicolas Eisele of Stanford University and Dr Faye Morris of the University of Birmingham.

The SGM Heatley-Payne Award recipient receives a contribution of up to £3,000 to cover costs to present their research at the ASM General Meeting or the ASM Conference for Undergraduate Educators (ASMCUE) and to make a short visit to an institute in the US. The visit can be used to learn a new technique or to carry out a defined piece of research. The award aims to help the recipient raise their international profile and experience the best of microbiology in the partner country.

This year's recipients were Dr Faye Morris of the University of Birmingham (for SGM) and Dr Nicholas Eisele of Stanford University (for ASM). Dr Eisele attended the SGM Annual Conference 2014 in Liverpool, where he met the SGM's reciprocal award recipient (pictured), and then visited the laboratory of Professor Gordon Dougan at the Wellcome Trust Sanger Institute.

Dr Morris delivered a poster at the ASM General Meeting in Boston, which she said was a fantastic experience from which she gained ideas for new directions to advance her research. This was Faye's first ASM General Meeting and she was impressed by both the range of cutting-edge science covered and the career development sessions. This was followed by a three-week visit to the laboratory of Professor Thomas J. Silhavy at Princeton University to receive training in the construction of depletion mutants in *Salmonella typhimurium*. Faye first met Professor Silhavy at an SGM Conference and says that the initial face-to-face meeting made it easier when it came to approaching him about a visit to his laboratory. In addition to the stimulating research discussions, a highlight of the visit was the friendships she has made with the lab members. She found the entire US experience invaluable for cementing her decisions on the next stage of her research career and is currently exploring postdoctoral opportunities overseas.

Think you could be an award winner in 2015?

Start planning your research visit now as the closing date for the 2015 awards is 30 November 2014. Details can be found at **www.sgm.ac.uk**

Karen McGregor
Grants and Careers Officer
k.mcgregor@sgm.ac.uk

Hayes-Burnet Award 2014

A similar award is made with the Australian Society for Microbiology.

The 2014 winner, Dr Erica Kintz of University of York, attended the Australian Society for Microbiology's Annual Scientific Meeting and visited the laboratory of Dr Richard Strugnell at the University of Melbourne to further her research of the host immune response to O antigens in *Salmonella typhi* infection.

Conferences

Focused Meetings

Not registered yet? There's still time. Simply visit the Society for General Microbiology's website (www.sgm.ac.uk) and complete the online registration form for the first of the Society's Focused Meetings.

Emerging Challenges and Opportunities in Soil Microbiology

Monday 1–Tuesday 2 September 2014 – Holywell Park Conference Centre, University of Loughborough, UK

Cracked soil. Franz Lanting, Minit Images/Science Photo Library

A fundamental knowledge of the functioning of healthy natural and agricultural soils and their resilience is a prerequisite to meeting the many natural and man-made challenges of the 21st century. These include climate change, food and (fresh) water security, nutrient cycling and availability, carbon capture, pollution and biodiversity. Microbial communities in soils can affect these processes and also have to be able to adapt to changes in the soil interface with, for example, water distribution, soil/nutrient particles, plants and other soil biota, and gas exchange with the atmosphere.

The last decade has seen tremendous advances in next-generation nucleic acid sequencing, mass spectrometry and high-resolution imaging technologies, such as atomic force and confocal microscopy, X-ray computed tomography and neutron radiography, which offer exciting opportunities for soil microbiologists to study the crucial ecological roles of soils. Soil microbial community composition, dynamics and functioning can now be probed to depths not possible before.

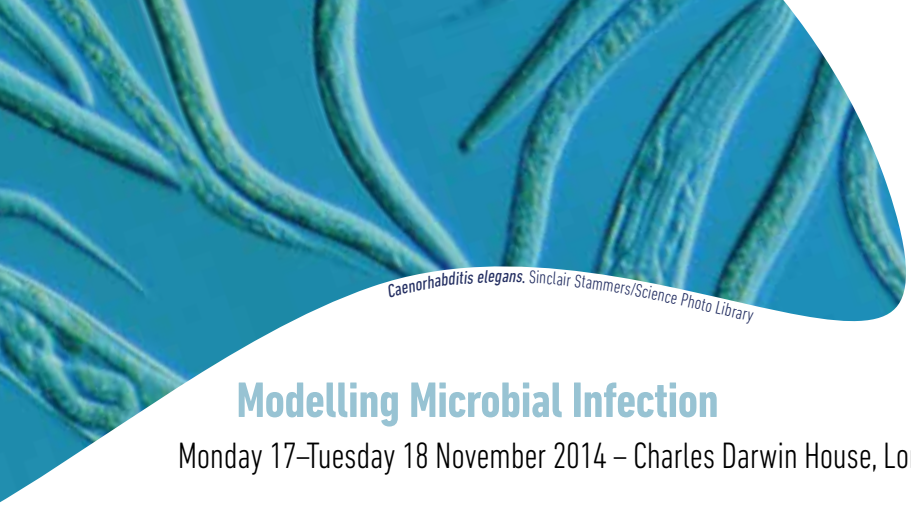
This Focused Meeting will bring together soil microbiologists, ecologists, soil scientists, geographers and technologists providing expertise in environmental 'omics', imaging and bioinformatics to present and discuss emerging challenges and opportunities in soil microbial ecology and to promote multidisciplinary collaborations. Early career scientists are especially encouraged to participate.

Topics will include:

- The impact of climate change, water scarcity, flooding and agriculture on soil microbial community functioning and vice versa
- Structural and functional soil microbial diversity
- Biophysical processes affecting the life of soil microbes
- Bioengineering soil sustainability
- Spatial ecology, biogeography and (changes in) land use
- (Re)cycling of nutrients, waste and pollution

Organisers: Geertje van Keulen (Swansea University), Alex Dumbrell (University of Essex) and Wilfred Otten (University of Abertay, Dundee)

On-site registration will be available at Loughborough University.



Caenorhabditis elegans. Sinclair Stammers/Science Photo Library

Modelling Microbial Infection

Monday 17–Tuesday 18 November 2014 – Charles Darwin House, London, UK

Infection models are essential for dissecting microbial–host interactions, unravelling disease processes and in the development of novel therapeutic agents. This Focused Meeting will discuss the range of models available to study microbial pathogenesis and will explore how technological advances, such as *in vivo* imaging, can increase the information obtained from these models. Bacterial, viral, fungal and parasitic infection models will be discussed and the use of alternative infection models debated. The use of models for drug discovery/development will also be discussed. This meeting is relevant to any researcher working in the area of microbial pathogenesis and offers the opportunity to learn about the range of models and resources available. The meeting will appeal to scientific researchers at all levels, and in particular PhD students, clinicians and those with an interest in translational and commercial research.

Organisers: Donna MacCallum and Carol Munro (University of Aberdeen)

Abstract submission deadline:
Monday 22 September 2014
Early-bird deadline:
Friday 17 October 2014

Irish Division Meeting 2015

17–19 June

University of Galway, Ireland

The Irish Division Meeting 2015 is titled *Microbial Interfaces* and will take place at the University of Galway, Ireland.

Topics will include:

- The host–microbe interface
- Health from the environment
- Microbiology for engineering and the bioeconomy
- The pathogen-device interface
- Ecosystems microbiology

Abstract submissions will open in **October 2014**.

Annual Conference 2015

International Conference Centre, Birmingham 30 March–2 April

Birmingham, UK. iStock

The Society's 2015 Annual Conference will feature a range of scientific sessions including:

- Natural and unnatural virus evolution
- Antimicrobial resistance
- Virus assembly
- Life at interfaces
- Rhizobiome
- Building blocks of microbial evolution
- Mitochondria
- Paleomicrobiology
- Microbes in space

A call for abstracts will be made in September.

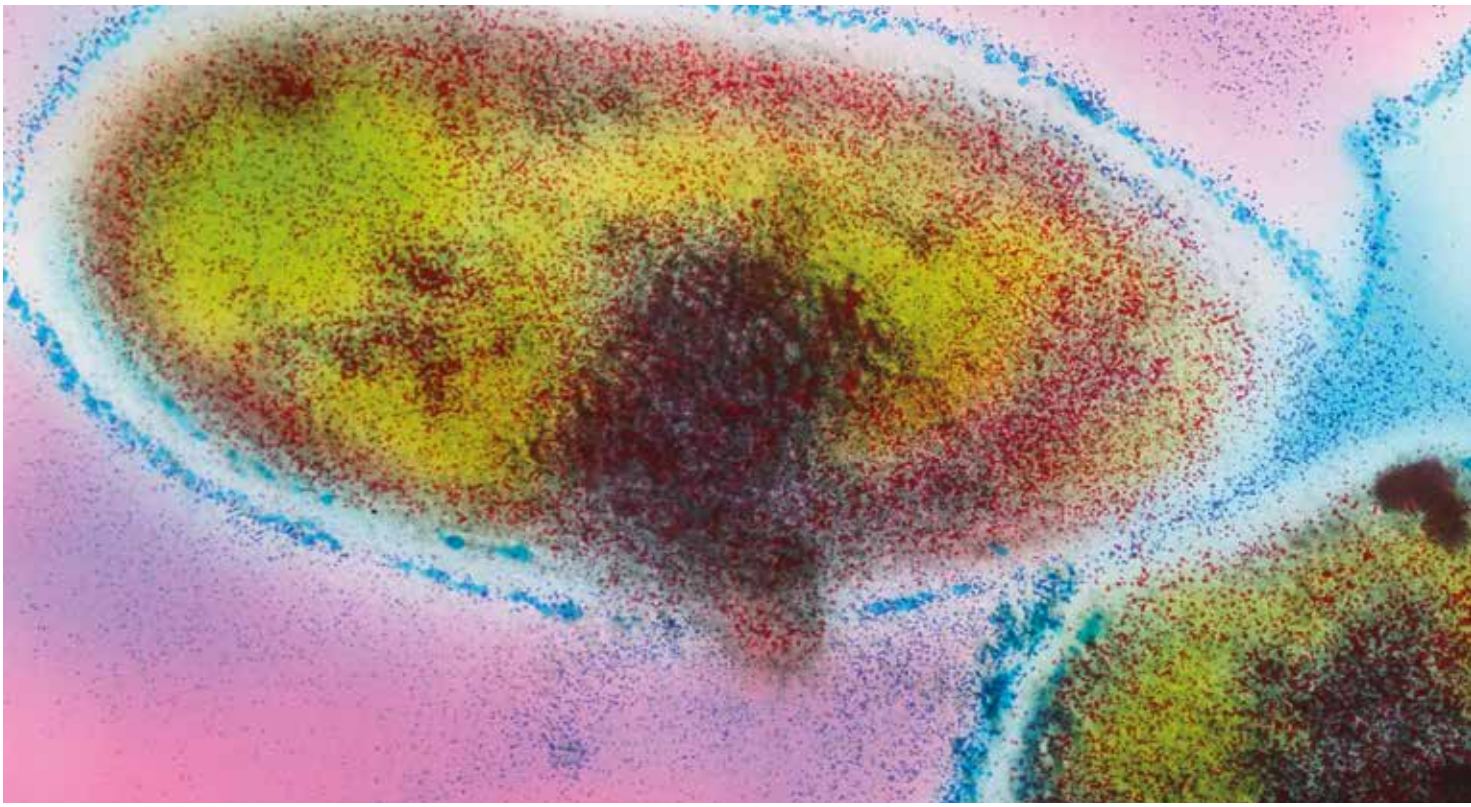
The closing date for abstract submissions will be **Monday 12 January 2015**. See the Society's website (**www.sgm.ac.uk**) for full conference details.

Grants

Grants are available to eligible Society for General Microbiology members. View the Society's website (**www.sgm.ac.uk**) for details.

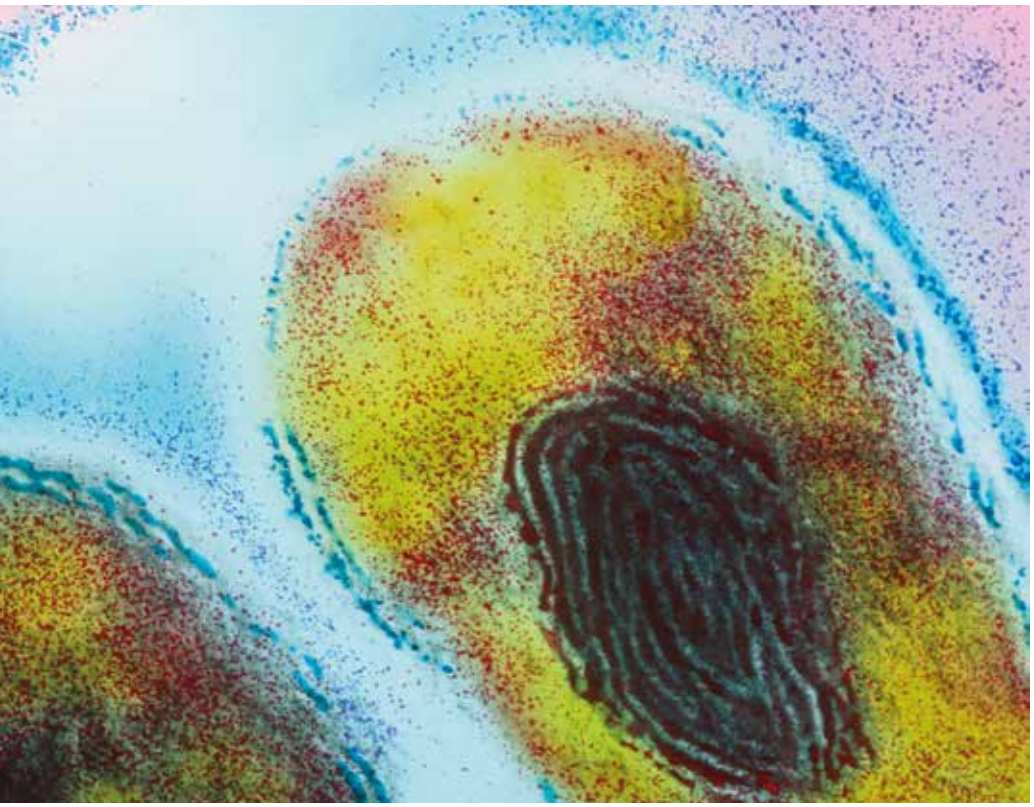
Mycobacterium avium Complex – making the worst of an opportunity!

Richard Bentham & Harriet Whiley



One of the downsides of recent advances in medicine and healthcare is that more people live longer! This in itself doesn't seem like a bad thing, and most of us would be quite happy to live longer. However, health advances have permitted a wide range of treatments that mean that an increasing number of us are continuing our lives with immune systems that are punching below their weight, the immune-compromised. This is where the downside occurs. A greater population of immune-compromised people has seen the emergence of a new set of diseases that affect them. These organisms are called 'opportunists'; they take advantage of a weakened immune system to cause infection.

Coloured transmission electron micrograph of a section through *M. avium* and *M. intracellulare* bacteria, causes of tuberculosis-type infection. Dr Kari Lounatmaa/Science Photo Library



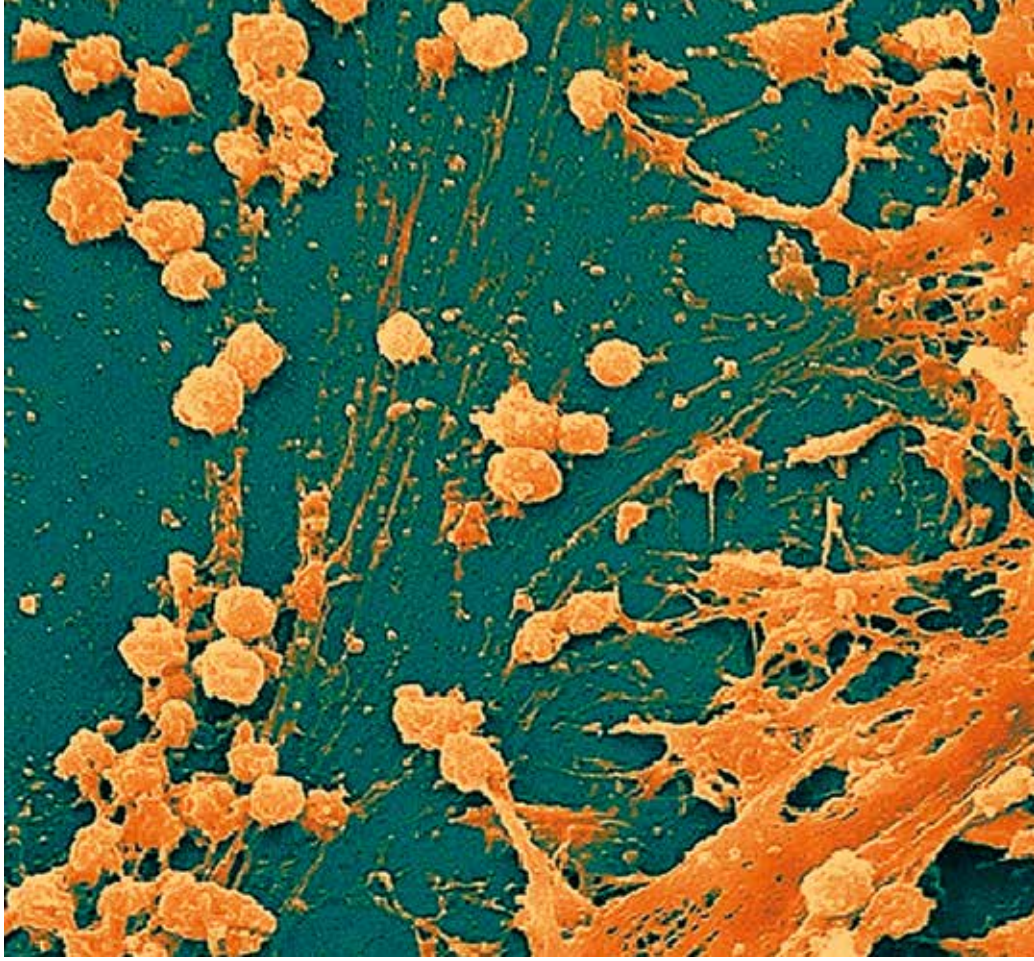
Opportunists

Mycobacterium avium is one of these opportunists. In fact a group of different and closely related species and strains of this bacterium form a group called the *Mycobacterium avium* Complex, MAC for short. MAC is a sub-group of the non-tuberculous mycobacteria. This means they do not cause tuberculosis, but can cause a range of other serious and life-threatening infections. In the majority of cases these infections are caused in people with poor immune systems such as the very young, the old, transplant recipients, cancer patients and those with AIDS. Disease caused by MAC was almost unheard of 30 years ago and has really only begun to be noticed as a serious problem in the last decade. It has now been listed as a 'notifiable disease' in many health jurisdictions. This means that physicians and pathologists must report cases of disease to their state or government health departments.

MAC-caused diseases

So what diseases does this group cause? MAC produces a range of infections. These can include infections in the respiratory tract, gastrointestinal infections as well as skin and soft tissue infections. In immune-compromised people MAC infections have the potential to spread throughout the body affecting multiple organs; when this occurs there are very high fatality rates.

MAC also causes infections of the lymph nodes; this is the most common presentation of MAC in children, primarily affecting those aged 6 months to 2 years old. Often lymph node infections need surgical removal of the infected tissue as antibiotic treatments may only subdue the infection and the disease may re-emerge years after treatment.



There is also increasing evidence linking MAC to Crohn's disease, which is a chronic inflammatory bowel disease. The link is unclear as ulcers in the intestinal tract may have MAC present within them. Whether the organisms are taking an opportunity to colonise the ulcer or actually cause the ulceration has not been determined. Some work has shown that antibiotic treatments that are effective against MAC may relieve symptoms of Crohn's disease sufferers.

MAC is an opportunist; unlike other mycobacteria it does not need a human or animal host to survive. This means that the organisms can survive and multiply in the natural environment. Furthermore, they survive and multiply in environments engineered by humans.

MAC characteristics

The bacteria are small and slow-growing with a waxy cell coating typical of other mycobacteria. MAC are also able to enter living cells and multiply inside them. These three factors assist them in successful infection and survival in the environment.

Although slow growth sounds like a disadvantage, MAC's slow growth and slow metabolic rate means that when exposed to disinfectants or antibiotics they take them up and metabolise them slowly. As a result, exposure to antimicrobial agents (antibiotics or disinfectants) in an infected person or a contaminated water supply will be ineffective against MAC at the same concentrations used to control other bacteria. Typically, treatment for a mycobacterial infection will take weeks rather than days.

The waxy coating on mycobacteria is a defining feature. All mycobacteria produce 'mycolic acids' that coat the cell surface in a layer of bacterial wax. The waxy layer slows down or prevents the entry of antimicrobial agents and enables the bacteria to survive long periods in harsh environments.

Intracellular growth is also a key feature of MAC infections. Once inside a host cell the bacteria can use it for a source of nutrients, protection from the immune system and from antibiotics. The mechanism of intracellular growth is complex and not fully understood but makes for a real challenge in combatting disease, especially if an infected person has a weakened immune system.
In the natural environment the bacteria are able to invade the cells of protozoa, and in particular amoebae. Amoebae are single-celled organisms similar in general structure to human white blood cells. They are the predators of the microbial community ingesting and digesting bacteria and other micro-organisms and are extremely abundant in both soil and water. They play an important role in normal healthy recycling of nutrients in the environment.

This intracellular multiplication is the same process that causes human infection. White blood cells (phagocytes) in humans also graze and digest bacteria as part of the normal immune defence process. When MAC is ingested by white blood cells from an immune-compromised individual it initiates the same infective process as that used for protozoa causing tissue damage.

Environment and disease

Soil and potting mix

A number of cases of MAC infection have been attributed to potting mixes and composts. Compost is organic material that has undergone an intense microbial

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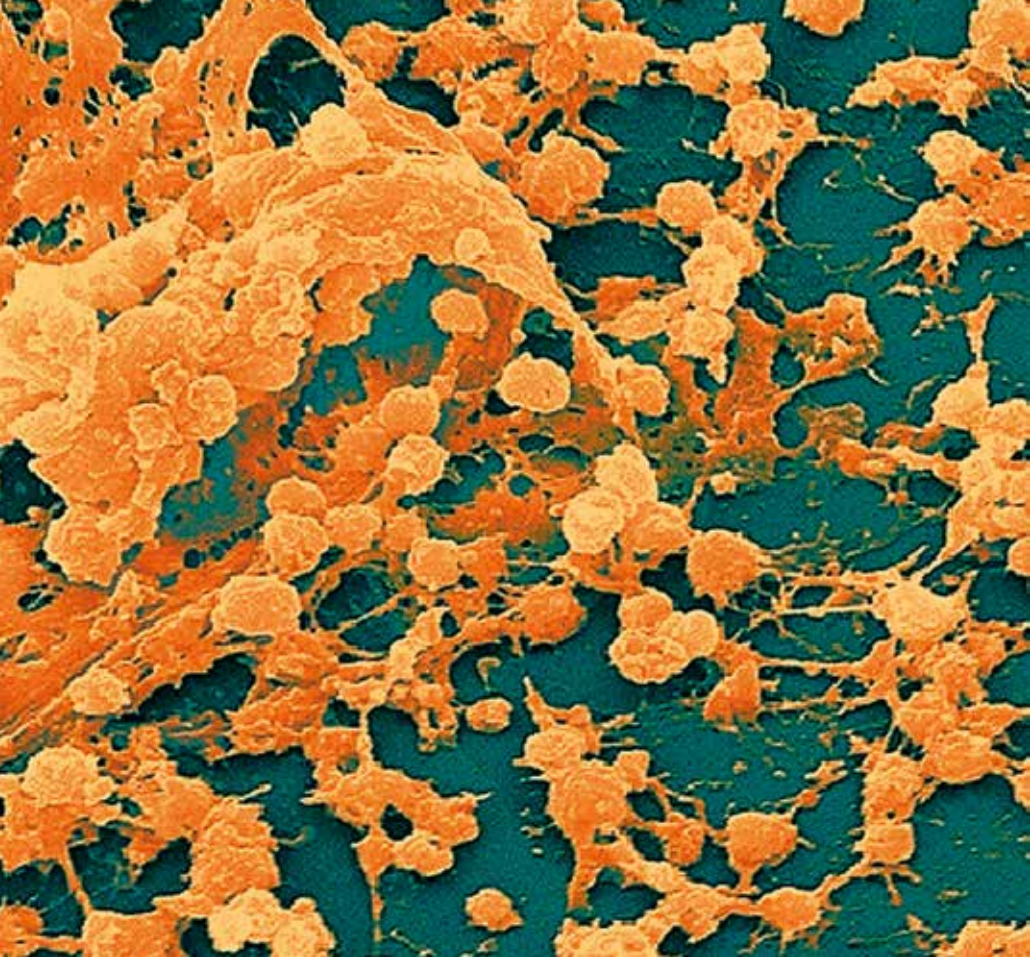

Colour-enhanced scanning electron micrograph of a *Staphylococcus* biofilm on the inner surface of a needleless connector. Science Source/Science Photo Library

degradation process. This creates an environment that is ideal for the growth of protozoa and amoebae that can graze the bacterial population. Obviously this creates the perfect environment for intracellular parasites of protozoa, like MAC to colonise. MAC infection has resulted from activities like gardening through contact of open wound sites, inhalation or ingestion of small amounts of compost material.

Aquatic environments

MAC infections have been linked to a range of natural and artificial aquatic environments. This includes, drinking water, warm water systems within buildings, showers, fountains, spas, hot tubs and swimming pools. MAC are able to survive within these environments due to their ability to survive disinfectants and their growth within biofilms.

Biofilms are complex communities of micro-organisms attached to surfaces and covered in their own slime (polysaccharide) coating. This coating will hold together a functional community of organisms including viruses, bacterial, fungi, protozoa, algae and more. Biofilms can be found in almost all wet environments on the planet. MAC have been shown to grow as part of biofilms in water systems. Protozoa graze biofilm surfaces and so provide the opportunity for MAC to parasitise them.

Biofilms are notoriously hard to disinfect, due to their polysaccharide coating and attachment to surfaces. They can be found in multiple environments in buildings, such as hot and cold water systems, showers, spa pools, swimming pools and cooling water systems. The complexity of these systems and their inaccessibility for cleaning means that biofilms provide huge surface areas for microbial activity. It is accepted that they are impossible to eradicate once established but may be controlled.

Warm water systems within buildings like hospitals and health care premises are a major source of MAC infections. This is a result of the unhealthy combination of a complex biofilm contaminated water system being distributed to a population who are in the building because they are sick. Water is an important resource in any healthcare premises and occupants are exposed to it through drinking, bathing or other activities like hydrotherapy pools. It has become essential to provide routine maintenance and disinfection in these facilities to reduce the risk of infections from MAC and other water-borne opportunists.

Summary

This brings us back to our first point. Due to advances in health care there is an increasing population with weakened immune systems. This has led to increasing numbers of immune compromised people, healthcare premises and aged-care facilities. This in turn means increased opportunities for the chance exposure, the case of mistaken identity, and MAC making the worst of an opportunity.

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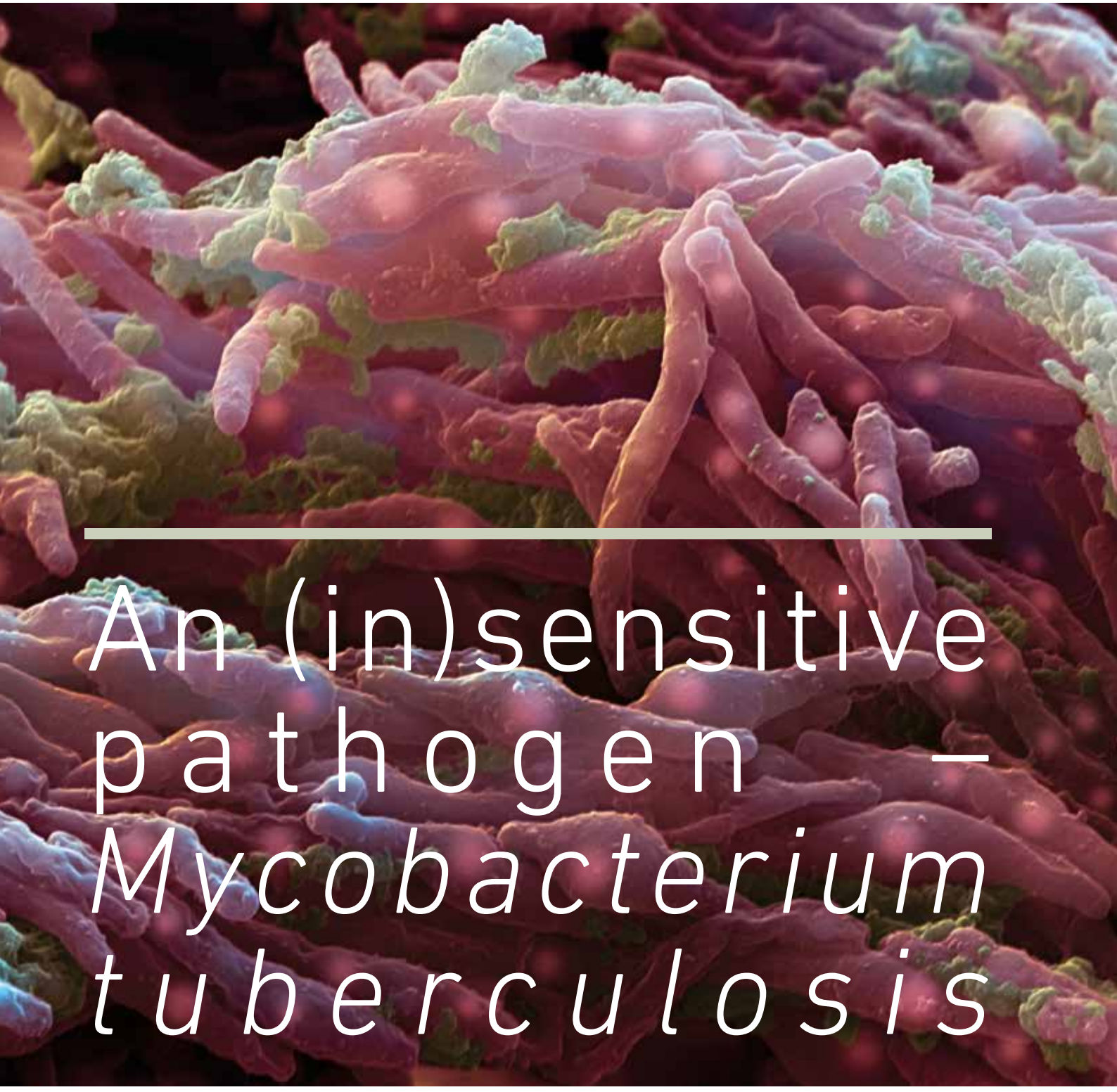
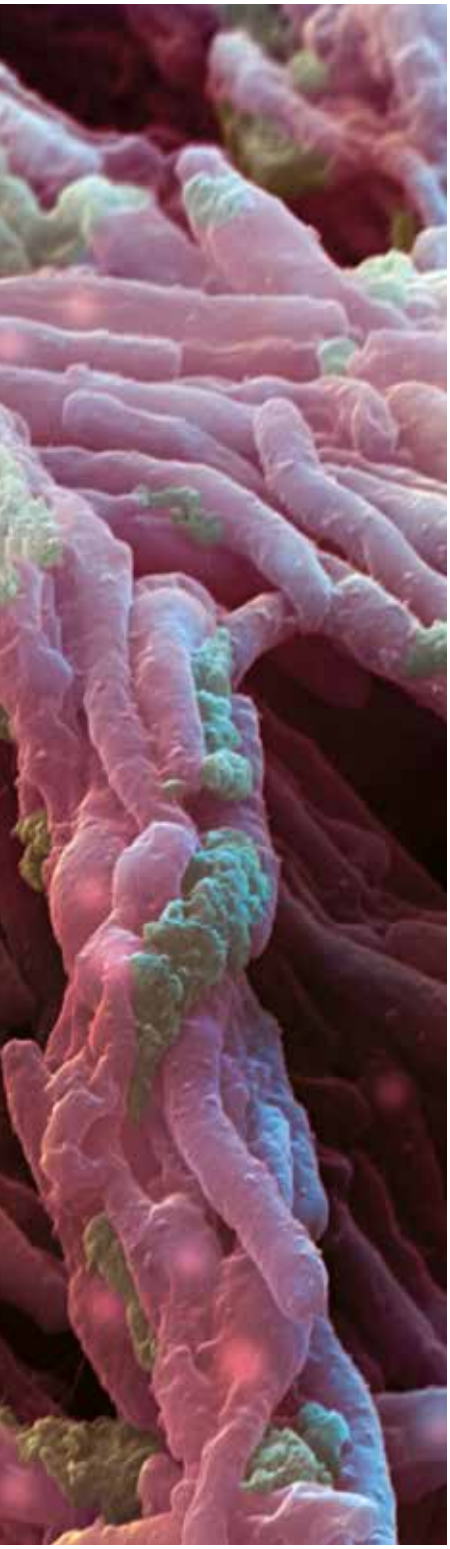


An (in)sensitive pathogen – *Mycobacterium tuberculosis*

Renata Plocinska, Jakub Pawelczyk & Jaroslaw Dziadek



Scanning electron micrograph of *M. tuberculosis*. Eye of Science/SPL

***Mycobacterium tuberculosis* is one of the principal human pathogens on the planet. It infects around 2 billion people worldwide annually, causing almost 1.3 million deaths in 2012.**

Most infected individuals do not go on to develop an active disease, but will remain latently infected throughout their lifetime. Nonetheless, 5–10% of infected individuals will develop the life-threatening form of tuberculosis, with symptoms such as fatigue, weight loss, enhanced sweating and coughing, and even coughing up blood. If it is untreated or undiagnosed until its late stages, tuberculosis may lead to severe lung damage and death.

What does *Mycobacterium tuberculosis* look like?

Not only is tuberculosis one of the most common bacterial infections that causes death to humans, but it is also one of the oldest known to humanity. Tuberculosis was recently found to be the most probable cause of death of several Egyptian mummies from thousands of years ago. However, it was only at the end of the 19th century when Robert Koch first isolated *M. tuberculosis* and postulated that this was the 'evil' causing tuberculosis. Microscopic observations revealed that the bacterium is rod-shaped, 2–4 μm in length and 0.2–0.5 μm in width.

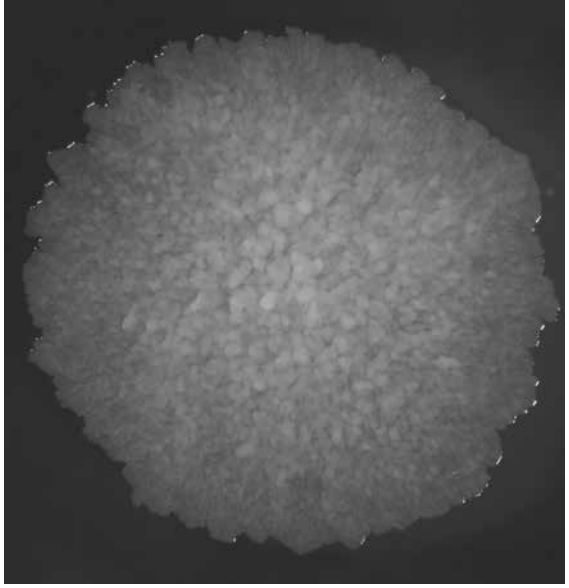
It only grows on rich media and divides every 16–20 hours, which is very slow compared to other bacteria, such as *Escherichia coli*, which can multiply every 20 minutes. *M. tuberculosis* requires oxygen to grow and forms rough, wrinkled colonies on solid culturing media.

Since the genome sequence of the *M. tuberculosis* H37Rv laboratory strain was determined in 1998, a new door for scientists has been opened and this has produced a better understanding of the biology of this pathogen. First of all it became apparent that the genome of *M. tuberculosis* is rich in G+C nucleotides (~70%) and it contains information for about 4,000 open reading frames, encoding many proteins involved in the cellular process of lipogenesis and lipolysis.

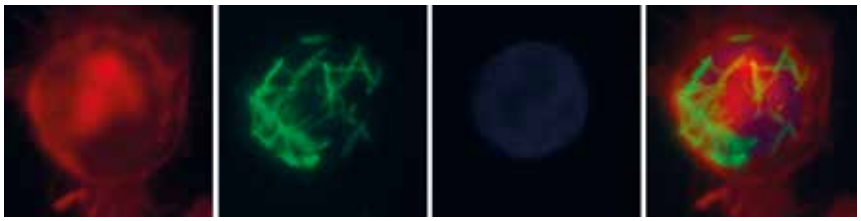
What makes *M. tuberculosis* a worldwide pathogen?

The success of *M. tuberculosis* as a pathogen is mainly due to its insensitivity to most known antibiotics and its ability to precisely sense the immune host responses and adequately adapt to their lifecycle.

Mycobacterial resistance to antibiotics is mostly due to the extraordinary composition of their cell wall. It is truly a bacterial fortress, with a thick and complex multilayer cell envelope that is impermeable to numerous compounds. The outmost layer of the mycobacterial coat is called the capsule, and is formed mostly of glycans that are directly exposed to cells of the human immune system, primarily macrophages, and they provide an antiphagocytic shield. Underneath the capsule there is a layer of lipids called mycolic acids, decorated with porins and attached to yet another layer of sugary arabinogalactan. Arabinogalactan is in turn attached to the peptidoglycan and both structures are intercalated with lipomannan and lipoarabinomannan.



The colony morphology of *M. tuberculosis* grown on solid media. Jakub Pawelczyk



Phagocytosis of GFP (green fluorescent protein)-tagged *M. tuberculosis* H37Rv bacteria by U937 cells, differentiated to macrophages with pokweed mitogen (PMA). Marcin Bartlomiejczyk

The complex cell-wall composition together with efflux mechanisms and a battery of antibiotic-degrading enzymes account for natural resistance of mycobacteria against β-lactams, tetracycline, fluoroquinolones, aminoglycosides and many other chemotherapeutics. Due to the low effectiveness of practically any single antibiotic therapy that would be safe for humans, the treatment of tuberculosis usually takes 6–12 months and combines four first-line anti-tuberculosis drugs: isoniazid, rifampin, pyrazinamide and ethambutol or streptomycin. This expensive therapy must be taken under a strict regime to avoid the development of bacterial resistance. If the first-line drugs turn out to be ineffective, a combined therapy of second-line drugs must be considered (amikacin, kanamycin, capreomycin). These drugs are generally more expensive and/or have more pronounced side effects and are, thus, less safe to use in humans.

M. tuberculosis is not only resistant to the bactericidal effects of many antibiotics, but it can cope well with the naturally occurring mechanisms of human immunity responses. It can shift between an actively replicating, highly infectious state and a physiologically muted – dormant – state, according to the host's immunity status. The phenomenon of dormancy is believed to be regulated via the two-component regulatory system DosR and DosS (or, alternatively, DosT), one of the sensing machineries of the bacterium. The tubercle bacilli contains several two-component regulatory systems, most of them paired, of a sensor histidine kinase and a response regulator. Sensor histidine kinases are usually membrane-bound proteins that, upon detecting an environmental signal, undergo autophosphorylation transferring the phosphoryl group onto the regulatory domain of the cytosolic response regulator. This in turn activates the output domain of the response regulator, which, in most cases, possesses DNA-binding properties and promotes or represses the transcription of selected genes. The canonical two-component systems in mycobacterial models were studied extensively in recent years. *M. tuberculosis* possesses 11 such two-component systems, e.g. SenX3/RegX3, PhoP/PhoR, DosR/DosS and MtrA/MtrB. Out of the known genetically linked regulatory systems, only PrrA/PrrB and MtrA/MtrB systems are believed to be essential for *in vitro* growth as well as for virulence of *M. tuberculosis*. Interestingly, the genome of *M. tuberculosis* possesses information for some orphaned two-component regulatory system elements, namely six response regulators and three sensor histidine kinases. The role of such orphaned elements in the bacterial response to environmental changes is fragmentary and remains to be determined. However, it is believed that such orphaned elements are involved in regulation of virulence and pathogenicity processes.

Development of drugs

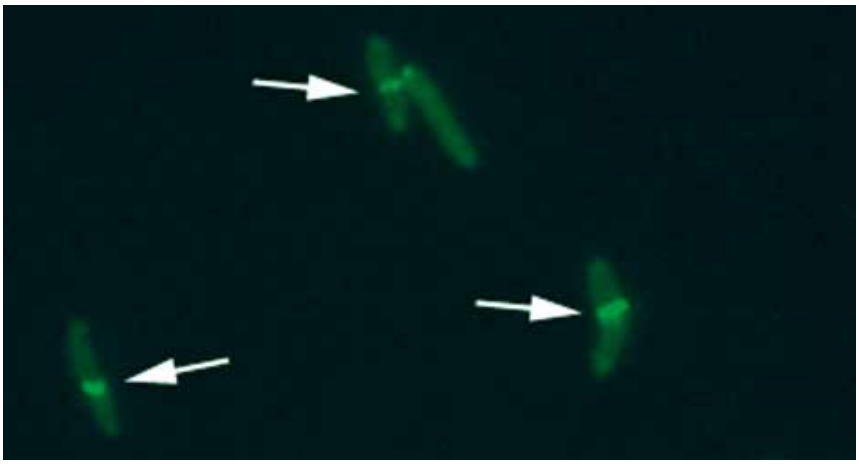
In recent years, observations of the increasing number of multidrug-resistant or even totally drug-resistant strains of *M. tuberculosis*, as well as co-pandemics with HIV-linked tuberculosis, has emphasised the need for the discovery of a new generation of antimicrobial agents. However, better understanding of the biology of the bacterium itself is fundamental for developing new and effective strategies to combat tuberculosis. Multiple studies are currently carried out worldwide, trying to identify new potential therapy targets. The characteristics of possible targets include protein elements that are involved in multiplication of the bacteria and other crucial processes like cell wall biosynthesis, DNA replication and repair, transcription, translation or virtually any protein that carries out an enzymatic reaction that is essential for bacterial survival. Inhibition of the activity of such protein candidates must not cause interference with human physiology.

Ideally, chemotherapy that would interfere with the bacterial cell division or cell cycle mechanisms could prevent the pathogen from proliferating and stop the infection. Unfortunately, mycobacteria differ significantly from other bacteria in some aspects of their biology. For instance, the cell division process in *M. tuberculosis* is poorly understood so far. However, as in other bacteria, FtsZ, the prokaryotic homologue of eukaryotic tubulin, appears to play a prominent role in the cytokinesis of this organism. FtsZ assembly into a circumferential ring at the mid-cell position initiates recruitment of several other proteins involved in this process and enables formation of the division septa. Some scientists consider FtsZ protein as a very promising target for antimicrobial drug discovery, primarily due to its leading and irreplaceable role in the bacterial cell division process, and, secondly, due to its well-studied structure and biochemical activity.

A list of other proteins being considered as potential candidates for new drug targets are NAD^+-dependent DNA ligase A and primase DnaG, both essential for growth and survival of *M. tuberculosis* cells and, importantly, present only in bacteria and not in humans. Another group of interesting targets include proteins involved in the biosynthesis of mycolic acids and arabinogalactan and the biosynthesis of isoprenoids; however, these are mostly exclusive to mycobacteria and are less likely to be active against any other bacteria.

Currently, there are numerous ongoing and developing studies trying to develop therapeutic agents that will help to efficiently eradicate *M. tuberculosis* from the systems of infected individuals. With continued financial support from various organisations and a joint effort from the scientific community to study tubercle bacilli, such developments will hopefully happen in the near future.

The success of *M. tuberculosis* as a pathogen is mainly due to its insensitivity to most known antibiotics and its ability to precisely sense the immune host responses and adequately adapt to their lifecycle.



Fusion of FtsZ with GFP in order to visualise Z-ring (indicated by arrows) formation in *M. tuberculosis* cells.
Renata Plocinska

Acknowledgments

Work was supported by grant: Iuventus Plus IP2011 042571.

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Further reading

Bretl, D. J. & others (2011). Adaptation to environmental stimuli within the host: two component signal transduction systems of *Mycobacterium tuberculosis*. *Microbiol Mol Biol Rev* **75**, 566–582.

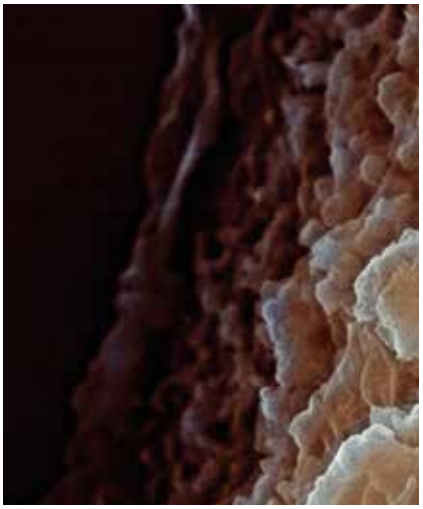
Centers for Disease Control and Prevention (2006). Emergence of *Mycobacterium tuberculosis* with extensive resistance to second-line drugs – worldwide, 2000–2004. *Morb Mortal Wkly Rep* **55**, 301–305.

Cole, S.T. & others (1998). Deciphering the biology of *Mycobacterium tuberculosis* from the complete genome sequence. *Nature* **393**, 537–544.

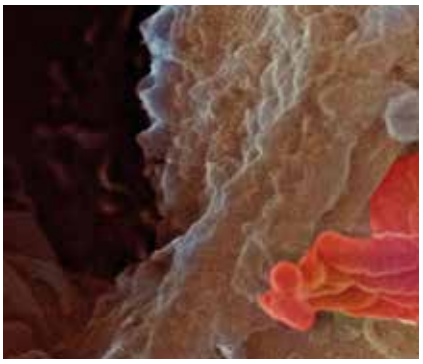
Dziadek, J. & others (2002). Physiological consequences associated with overproduction of *Mycobacterium tuberculosis* FtsZ in mycobacterial host. *Microbiology* **148**, 961–971.

Errington, J. & others (2003). Cytokinesis in Bacteria. *Microbiol Mol Biol Rev* **67**, 52–65.

Gorna, A. & others (2010). DNA repair systems and the pathogenesis of *Mycobacterium tuberculosis*: varying activities at different stages of infection. *Clin Sci (Lond)* **119**, 187–202.



A new vaccine against tuberculosis



Coloured scanning electron micrograph of a macrophage white blood cell engulfing BCG vaccine *M. bovis* bacteria (red). Science Photo Library

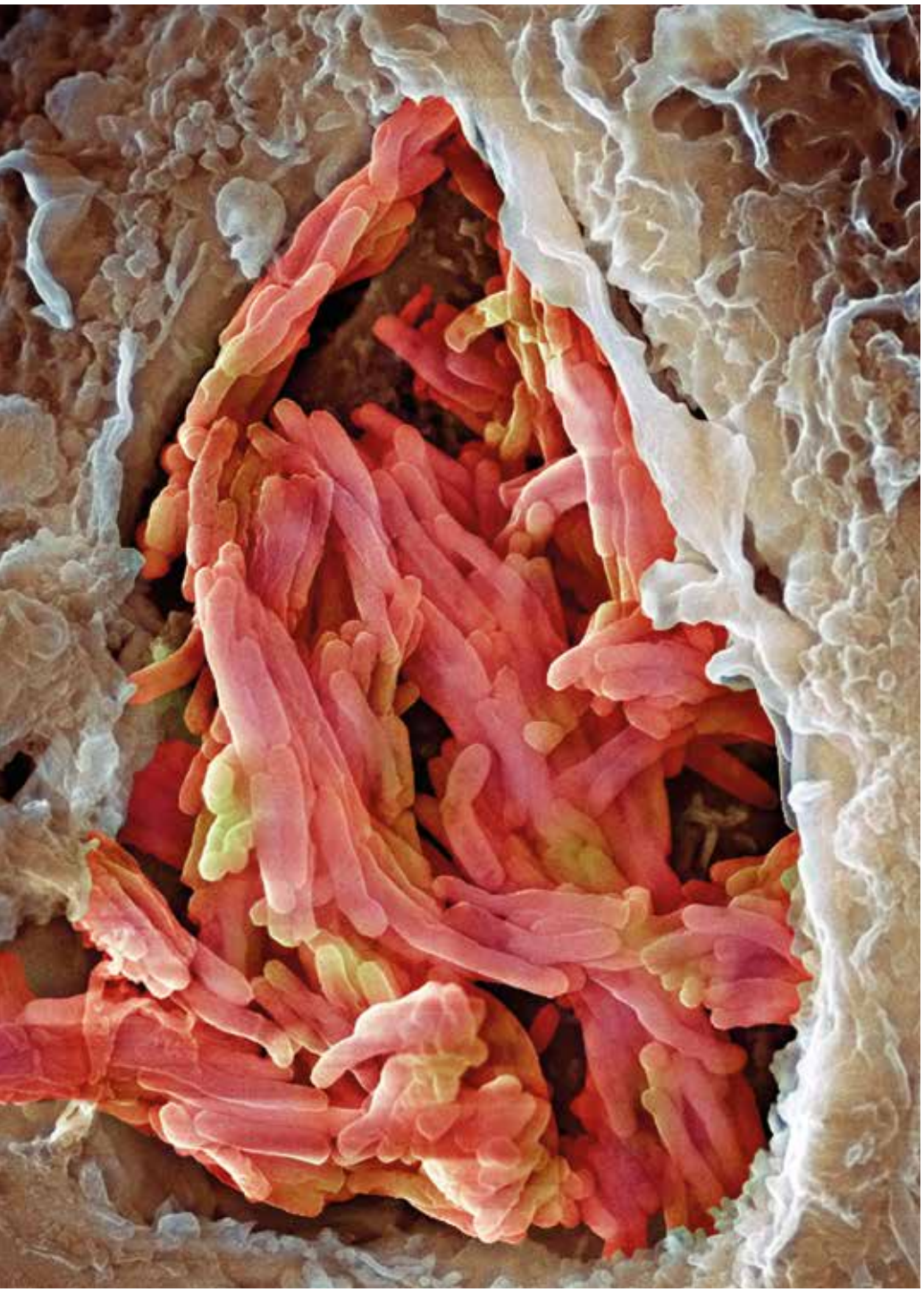
Steven Smith

Over a hundred years ago, two French scientists began to culture the species of mycobacterium that causes tuberculosis (TB) in cattle, named *Mycobacterium bovis*. About 13 years and 231 vaccine passages later they had attenuated its virulence to the extent that it could be injected into people as a vaccine for the prevention of TB.

In the same way as Edward Jenner before them, they had arrived at a 'live' vaccine that was related enough to a disease-causing pathogen to produce a cross-reactive immune response but that did not inflict disease upon the recipient. The vaccine was named bacillus Calmette–Guérin (or BCG) after its inventors and remains the only licensed vaccine for use against TB.

The problem with BCG

A vaccine does not remain in use a hundred years after its inception without proving its worth over that time. Accordingly, based on the results of a number of clinical trials, we know that BCG is capable of preventing up to 80% of adult TB cases as well as the various forms of TB disease that affect infants and children, usually at sites other than



the lung. And yet, in 1993, the World Health Organization declared a global TB emergency and prompted a new age of research effort towards better drugs and vaccines for TB. Why did BCG not herald the global eradication of TB in the same way that Jenner's vaccine eventually did for smallpox?

In scientific terms, the global efficacy of BCG is variable. In other words, although BCG vaccination of British schoolchildren can prevent nearly eight out of ten cases of TB over the subsequent 15 to 20 years, the same school vaccination programme in southern India would not prevent any TB. This startling contrast is apparent in many other settings. Depending upon where you stick your pin in the world map, BCG either protects against TB to some extent or it doesn't. Fascinatingly, the pattern is not a random one. For example, if your pin lands close to the equator, the chances are BCG will not prevent TB in that country. The further from the equator it lands, the better the chances that BCG will work. There are of course many possible factors that differ between a country such as Malawi in sub-Saharan Africa where BCG is known not to work well and one in northern Europe, such as the United Kingdom, where it does. The task of determining which are responsible for the effect on BCG's ability to prevent TB has proven substantial and is beyond the scope of this article.

The challenges of a new vaccine

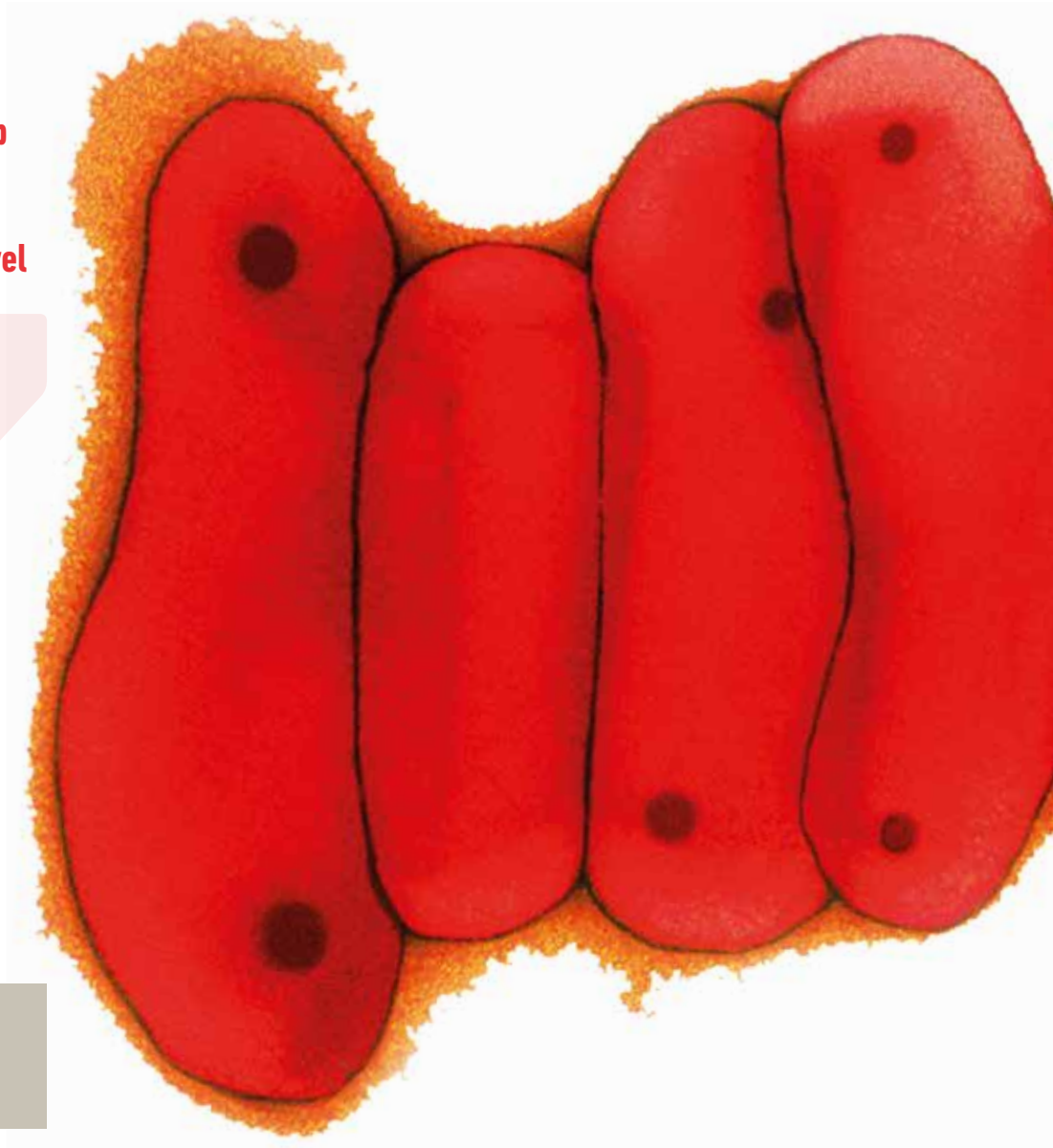
It is generally agreed that along with better TB diagnostics and drugs, a new vaccine that can succeed where BCG has not would represent a huge step towards the reduction and even eventual eradication of global TB. As such, the 21st century has so far seen many of the worlds leading vaccinologists and immunologists turn their attention to the challenge of producing such a vaccine. A disease that has been with us for millennia is not going to be beaten easily and TB provides a case in point. Despite our best efforts, we have yet to discover the most effective immunological weapons our bodies can deploy against the TB mycobacterium. Clearly they exist, as many people seem capable of resisting TB disease despite exposure to the pathogen. Certainly there are many clues and much scientific evidence that points to likely candidates. For example, people who are genetically unable to respond to the signaling protein interferon-gamma are susceptible to TB, as are patients infected with HIV whose T-lymphocyte

populations are depleted. Although these and other candidate weapons have not been ruled out, the usual outcome is that no one protein, signal or lymphocyte cell population appears to represent a magic bullet capable of stopping TB in its tracks. Promisingly, TB vaccinologists appear to have heeded this message and are developing vaccine candidates designed to utilise multiple immunological weapons simultaneously.

New vaccination strategies for TB

Aside from an incomplete knowledge as to the ideal immune responses a vaccine should activate, we have to realise that TB vaccinologists are not starting with a blank slate. Trying to supersede BCG is not easy as it works well in certain, important circumstances, not least its ability to protect infants and children from childhood forms of the disease. As such, new vaccine strategies fall into two broad camps. In one group are those that are intended to work as a follow up vaccination to improve the immunity imparted by a previously administered BCG jab. In the other group are those that are intended to replace BCG completely. In some cases, the latter group comprise candidates that have followed BCG's lead and take the form of a live mycobacterium, either BCG itself with some additional genetic modifications designed to improve its potency or, in the case of one promising candidate,

It is important that TB vaccinologists don't drop the ball in terms of attempting to devise novel concepts for the design of even newer vaccines.



Coloured transmission electron micrograph of a section through *M. tuberculosis* bacteria.
Dr Linda Stannard/Science Photo Library

Mycobacterium tuberculosis itself but, of course again, altered genetically to attenuate it and prevent it from causing the disease it is designed to prevent. Clearly, the hope is that these new mycobacterial vaccines will harness the best of BCG's abilities but with significant added capabilities that will hopefully allow them to succeed in settings where BCG has not.

Proponents of new vaccines that are intended as follow-ups to previous BCG adhere to an alternative philosophy. In their view, BCG does activate the type of immune response that is required to beat TB but not potently enough. Hence the type of vaccine that is required is one that can boost one or more of the responses initiated by BCG. Genetically modified viral vectors are particularly adept at this task and a number of these are in development. The key design feature is that these viruses are modified to encode key antigens found in TB with the hope that boosting the immune response to these antigens will result in better protection. The selected antigen approach is followed also by a third high profile category of new TB vaccine candidates; those that comprise purified recombinant proteins. These protein antigen vaccines are usually designed as fusions of two or three such antigens. As with the virally vectored vaccines, the recombinant protein vaccines may be deployed as a booster for a previous BCG vaccination. They may also be used as a replacement for BCG. One of the key features of this approach is the addition of an appropriate immune-boosting adjuvant to the protein itself. Purified recombinant proteins are relatively non-immunogenic themselves but can induce potent responses with the help of an appropriate additional immune stimulus. Consequently, adjuvant research has been an area of great innovation in recent times, as vaccinologists have begun to harness the latest knowledge of effective immune responses against TB to design more effective formulations.

A new era of TB vaccine design?

Clearly these are exciting times for TB vaccine research. However, despite the scientific knowhow and innovative design that have contributed to the approaches described here, it is important that TB vaccinologists don't drop the ball in terms of attempting to devise novel concepts for the design of even newer vaccines. Disappointingly, the first clinical efficacy trial of a new candidate TB vaccine did not improve upon BCG in South African infants. The vaccine, a viral vector encoding a known immunogenic TB antigen, was designed to boost lymphocyte responses initiated by BCG. Notably many of the new candidate vaccines are designed to do the same thing. If vaccinologists are to learn anything from the results of such trials as they emerge, maybe it should be to heed the requirement to explore the many new avenues of possibility that research into immune responses to TB is revealing and be even more creative when designing the next generation of TB vaccines.

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Further reading

Andersen, P. & Doherty, T. M. (2005). The success and failure of BCG – implications for a novel tuberculosis vaccine. *Nat Rev Microbiol* **3**, 656–662.

Andersen, P. & Kaufmann, S. H. (2014). Novel vaccination strategies against tuberculosis. *Cold Spring Harb Perspect Med* **2**, 4.

Dockrell, H. M., Smith, S. G. & Lalor, M. K. (2012). Variability between countries in cytokine responses to BCG vaccination: what impact might this have on protection? *Expert Rev Vaccines* **11**, 121–124.

Mycobacterium ulcerans, causative agent of Buruli ulcer

Tim Stinear

Buruli ulcer is a neglected disease found predominantly in tropical regions of the world, but the epidemiology of this disease is like the tip of the proverbial iceberg. Beneath the unusual name is a depth of mystery and intrigue that has simultaneously baffled and engaged researchers for the past 75 years.

What is Buruli ulcer?

Buruli ulcer (BU) is a bacterial infection of subcutaneous tissue in humans and other mammals. The bacterium gets into the fat layers below the skin and replicates, eventually causing great damage if left untreated but rarely killing the host. The disease initially presents as a painless nodule beneath the surface of the skin, often appearing on the extremities of the arms and legs. Over a period of weeks to months the disease slowly progresses with the skin around the nodule eventually breaking down to reveal an ulcer with a deep centre of necrotic tissue. Despite the extensive tissue damage the lesions are often painless and patients appear otherwise well.

BU likes it hot, but not always

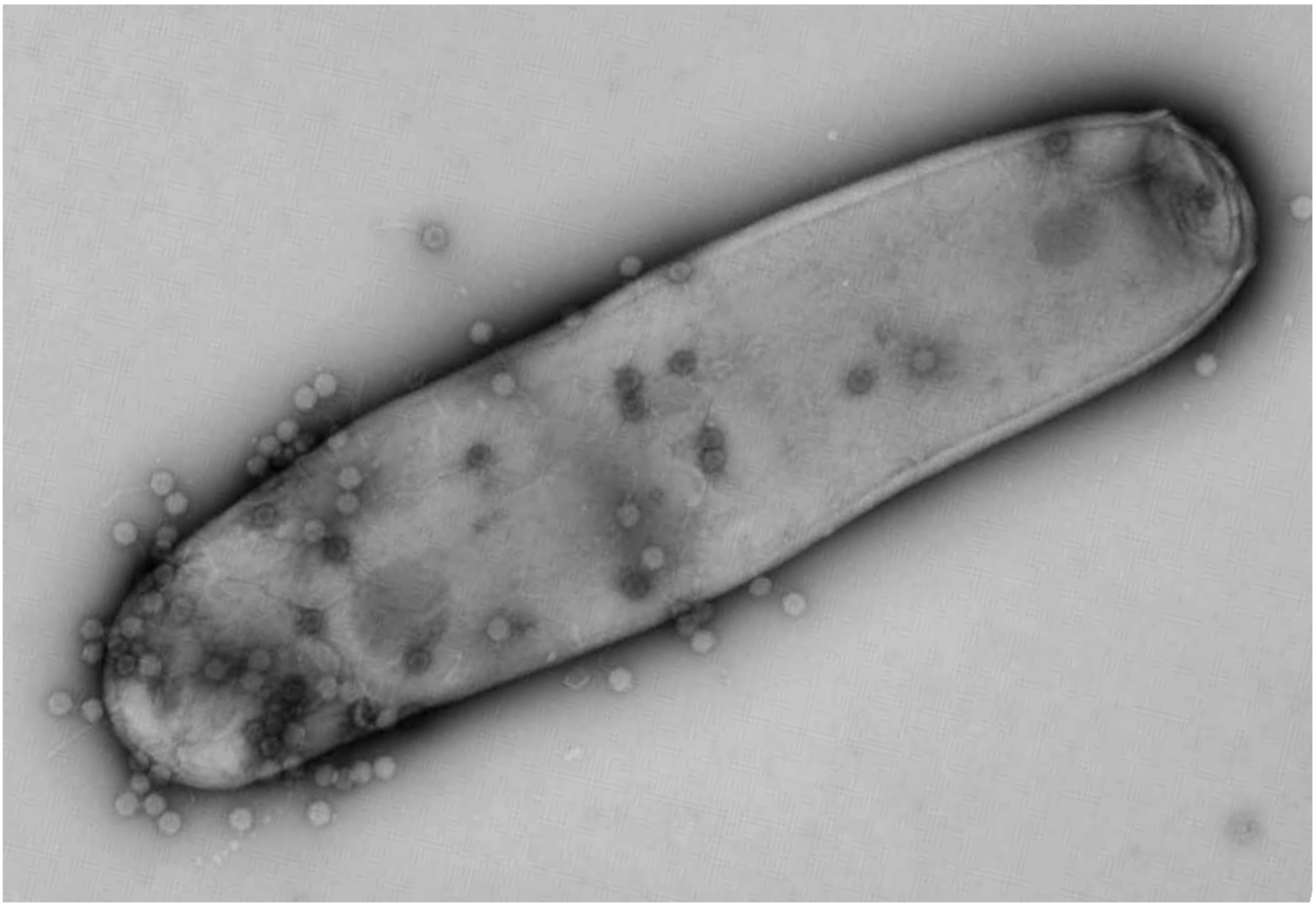
BU has been reported in more than 28 countries around the world, but is predominantly found in rural regions in West and Central Africa, although its distribution is not strictly tropical with endemic regions in temperate areas of Japan and Australia.

BU down under

The Australian connection with BU is long and auspicious. It was Australian researchers in the 1940s who – thanks in part to a malfunctioning incubator – discovered that this disease is caused by infection with a mycobacterium that grows preferentially at 32°C instead of 37°C. They called the organism *Mycobacterium ulcerans*. Although a close relative of *Mycobacterium tuberculosis*, the cause of tuberculosis in humans, *M. ulcerans* distinguishes itself from this and other mycobacterial pathogens by several important characteristics that are described below.

How do you get a Buruli ulcer?

The answer to this fundamental question has eluded researchers for more than 75 years, as they have tried to find the



Mycobacterium ulcerans. Reproduced from Rybniker, J. & others (2006). Host range of 14 mycobacteriophages in *Mycobacterium ulcerans* and seven other mycobacteria including *Mycobacterium tuberculosis* – application for identification and susceptibility testing. *J Med Microbiol* **55**, 37–42.

source of *M. ulcerans* in the environment and establish how the bacterium is transmitted to humans. Once you have been infected with *M. ulcerans* it takes a long time to develop a Buruli ulcer. Epidemiological studies have pinpointed an incubation period of around four months. Such studies have also uncovered a strong association between wetland areas and the occurrence of BU. Considerable effort has thus gone into testing all manner of possible reservoirs. Suspected sources include water, plants, aerosols, soils, bats, rats, lizards, fish, frogs, amoebae, biting flies and aquatic insects. In recent years much interest has centred on the last group with some field and laboratory evidence that certain carnivorous aquatic insects might be both reservoirs and vectors of *M. ulcerans*. In temperate south-eastern Australia it appears that the native possum is a reservoir of *M. ulcerans* and that biting insects such as mosquitoes may be transmitting the disease. However, there are no possums in Africa and a similar mammalian reservoir species has yet to be identified. In short, nothing is certain and focused research in the area of reservoirs and transmission remains a priority.

Who or what was Buruli?

Buruli was the name of a county in Uganda where many cases of *M. ulcerans* infection were reported during the 1960s. The distinctive focal epidemiology of this disease has led to a string of local names such as 'Bairnsdale ulcer' and 'Daintree ulcer' (Australia) or 'sik bilong wara Sepik' (Papua New Guinea) or 'Kasongo ulcer' (Democratic Republic of Congo) but the World Health Organization has adopted 'Buruli ulcer' as the official name for the disease caused by infection with *M. ulcerans*.

BU is not a human-specific infection

In Australia, BU has also been described in both native wildlife and domestic mammal species, and isolates of *M. ulcerans* from these animals are genotypically the same as strains causing human disease in the same geographic location. Affected wildlife species include koalas (*Phascolarctos cinereus*) common ringtail possums (*Pseudocheirus peregrinus*), a mountain brushtail possum (*Trichosurus cunninghami*) and a long-footed potoroo (*Potorous longipes*). Domestic animals with confirmed Buruli ulcers have so far included two horses, five dogs, two alpacas and a cat.

Treatment of BU

Antibiotics cure BU. The World Health Organization's recommendation for treatment of BU is an eight-week course of rifampicin and streptomycin. Trials are currently underway to explore the potential of replacing streptomycin with an alternative oral antibiotic; one that doesn't compromise efficacy and without the toxicity issues sometimes associated with taking streptomycin.

M. ulcerans makes an unusual toxin

Bacterial pathogens are renowned for producing toxins that damage host cells but these toxins are usually proteins; think cholera toxin or tetanus toxin. *M. ulcerans* is different. It makes an unusual lipid called mycolactone. Mycolactone belongs to a class of molecules that are called polyketides. Many polyketides have important pharmacological properties such as the antibiotic erythromycin and the immunosuppressor rapamycin. No one knows why *M. ulcerans* makes mycolactone but testing it in the laboratory has shown it too has potent biological activities. In trace amounts mycolactone can suppress human immune responses. As the concentration of mycolactone increases it causes cells to die, which explains the ulceration seen in patients with BU. Mycolactone has no antibiotic properties.

Something fishy going on

There is a close genetic relative of *M. ulcerans* called *Mycobacterium marinum*, and while they share much of the same DNA sequence they have very different phenotypes. *M. marinum* causes a disseminated disease in fish, occasionally causes relatively minor skin infections in humans and grows quickly in the laboratory. *M. ulcerans* causes necrotic ulcers in humans,

M. ulcerans and IS*2404*: tailor-made for molecular diagnostics

In 1995, Bruce Ross, an Australian researcher at the peak of his influence, together with his colleagues, discovered that *M. ulcerans* contains more than 200 copies of a very specific insertion sequence they called IS*2404*. The many repeats of this DNA sequence in the *M. ulcerans* genome and its absence in other organisms have made it an ideal molecular marker for rapid detection of this pathogen in both clinical and environmental samples.

Long-footed potoroo (*Potorous longipes*). G. Bayliss/Flickr

grows very slowly in the laboratory and makes mycolactone. Comparing these two mycobacterial species has helped us understand how *M. ulcerans* has evolved and causes disease.

Evolution has put the squeeze on *M. ulcerans*

Sequencing the genomes of *M. ulcerans* and *M. marinum* strains from around the world uncovered a very interesting evolutionary story. It showed how an ancestor of *M. marinum* probably acquired a plasmid that allowed it to make the toxin mycolactone. It seems that this new 'skill' led to a population of mycobacteria that could persist in a different environment. Further exploration of the *M. ulcerans* genome suggests that this environment was in some way protected or privileged as the genome is marked by many deleted or defunct genes and a preponderance of repeated DNA such as the insertion sequence IS*2404*. Expansion of insertion sequences and the accumulation of lesions in the DNA is a characteristic of bacterial populations that have been constricted and have passed through a metaphorical evolutionary bottleneck, on their way to becoming adapted to specialised and restricted environments. This makes *M. ulcerans* similar to the notorious human pathogens *Yersinia pestis* and *Bordetella pertussis* as they all have genomes with these signature features of adaptation and they do indeed persist in privileged niches; the mid-gut of the flea for *Y. pestis* and the upper respiratory tract of humans in the case of *B. pertussis*. So what or where is the *M. ulcerans* privileged niche? This puzzle remains to be solved.

The extraordinary genetics of mycolactone biosynthesis

M. ulcerans has an amazing arrangement of three very large genes that allow it to produce mycolactone. The genes are carried on a plasmid called pMUM and they are extraordinary because they are made up of unusual DNA sequence structure and are 50x larger than normal genes. These genes encode proteins called polyketide synthases. The whole system can be thought of as a molecular assembly line for churning out mycolactone. Some researchers are actually exploiting the intriguing structure of the mycolactone genes, where they are using genetic engineering to 'trick' the bacterium into making new polyketide-derived medicines (like rapamycin) rather than a potent toxin.

A solvable problem

BU is an emerging problem in many regions of the world. It is primarily a disease affecting the rural poor of West and Central Africa and as a consequence relatively little is being done to prevent its rise. There are a handful of dedicated research teams around the world attempting to address key BU research priorities but more resources are urgently required. Questions such as: 'How do people contract BU?' and 'What are the environmental reservoirs?' need to be answered so we can develop strategies to stop the spread of this disease. This is the 21st century and we have all the technology we need to better understand BU. BU is thus a solvable problem. The World Health Organization has helped the establishment of BU National Control Programmes in endemic countries around the world and there are some non-governmental organizations who have been working for many years to raise awareness and support BU initiatives. It's now time for a coordinated, well-funded and focused research effort to lift the lid on the mysteries of BU.

Questions such as: 'How do people contract BU?' and 'What are the environmental reservoirs?' need to be answered so we can develop strategies to stop the spread of this disease.

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Further reading

Chany, A. C. & others (2013). History, biology and chemistry of *Mycobacterium ulcerans* infections (Buruli ulcer disease). *Nat Prod Rep* **30**, 1527–1567.

Demangel, C. & others (2009). Buruli ulcer: reductive evolution enhances pathogenicity of *Mycobacterium ulcerans*. *Nat Rev Microbiol* **7**, 50–60.

Merritt, R. W. & others (2010). Ecology and transmission of Buruli ulcer disease: a systematic review. *PLoS Negl Trop Dis* **4**, e911.

Stop buruli. www.stopburuli.org *(last accessed 30 June 2014).*

World Health Organization. Buruli ulcer. **www.who.int/buruli/en** *(last accessed 30 June 2014).*

Mycobacterium the cause of

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. It damages peripheral nerves and can affect the skin, eyes, nose and muscles. Nerve injury in leprosy can cause severe disabling deformities.

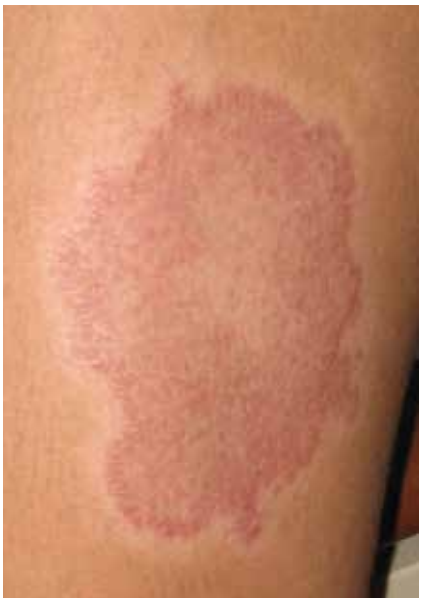

Fig. 1. Borderline tuberculoid leprosy lesion on lower extremity. The centre of this lesion was anaesthetic. Barbara Stryjewska

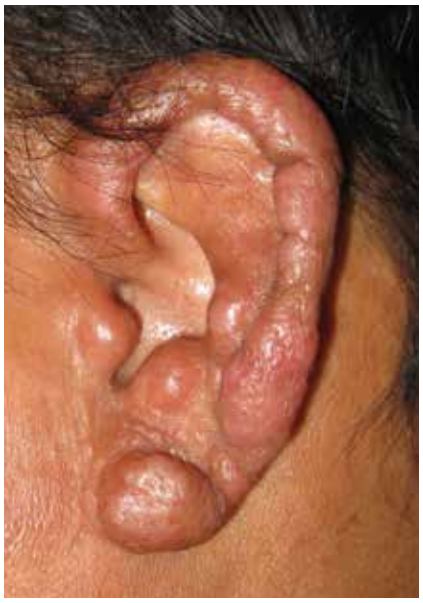

Fig. 2. Lepromatous leprosy lesion manifest on ear. Abundant intracellular acid-fast bacilli were present in this tissue, a cool site favourable for growth of *M. leprae*. Barbara Stryjewska

Although it is often thought of as a disease of ancient times, it still occurs today and the World Health Organization recorded 3.8 million new cases of leprosy from 105 different countries in the last decade. Leprosy is only rarely reported in Europe today, but it was once prevalent throughout the region and may still occur among people who live or work abroad in endemic countries. People with leprosy often suffer profound social stigma on account of their disease, and leprosy imposes tremendous economic and psychological burdens on individuals and healthcare systems.

Leprosy (also known as Hansen's Disease) is considered a Neglected Tropical Disease. It is a rare infection, usually found in fewer than 1:10,000 people in most populations, and often associated with poverty. The largest

leprae, leprosy

Richard Truman, Rahul Sharma, Maria Pena, Barbara Stryjewska, John Figarola & David Scollard

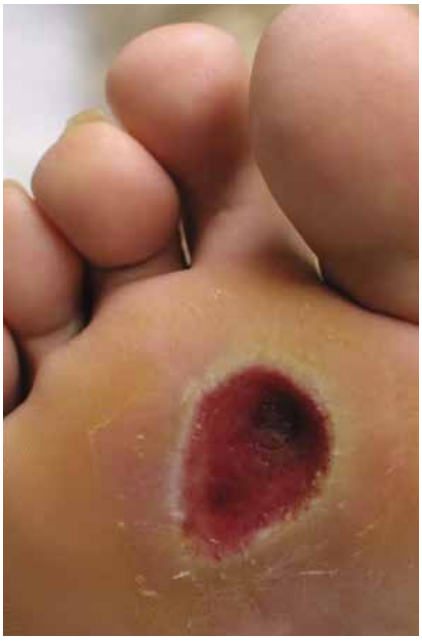

Fig. 3. **Plantar pressure ulceration due to anaesthesia is a common sequela of nerve injury in the lower extremity in leprosy.** Dane Hupp

numbers of new cases today originate in South-east Asia, the Americas and Africa. Leprosy is curable with multiple antibiotic therapy, usually consisting of rifampin, dapsone and clofazimine. Early detection and treatment can help avoid many of the disabling complications of leprosy. Although several prototype assays are in development, there are no current laboratory screening tests to aid early detection of leprosy, and the disease must be diagnosed clinically.

Clinical features

Leprosy is not highly contagious. Susceptibility to leprosy appears to be genetically based and 95% of all people appear to be naturally resistant to the disease. People who develop leprosy usually incubate the infection for 3–5 years before manifesting illness, and they exhibit a broad spectrum of clinical and histopathological responses to the infection determined by their immunological response to *Mycobacterium leprae*. In the tuberculoid portion of the spectrum, people have few discrete lesions consisting of well-organised granulomas with small numbers of bacilli (Fig. 1). While those in the lepromatous portion of the spectrum may have several nodular or diffuse lesions (Fig. 2) containing many bacilli in poorly organised granulomas. However, the most important pathological feature common to all forms of leprosy is involvement and damage of the peripheral nervous system (PNS).

Nerve injury

M. leprae has the remarkable capacity to invade Schwann cells of the peripheral nerve, which enclose and support the axons of sensory and motor neurons. Schwann cell infection causes many complex biological and pathological alterations including demyelination, de-differentiation and reprogramming of the cells. Axons unprotected by Schwann cells are vulnerable to injury and may be destroyed by the host's inflammatory response to *M. leprae*. Generally, small unmyelinated and myelinated sensory neurons are affected first, and as the disease progresses motor neurons and muscles may also be compromised. Patients lose sensation in areas affected by leprosy. They often cannot discern the difference between hot and cold, and anaesthesia in the hands and feet contribute significantly to pressure ulceration (Fig. 3) and traumatic injury and secondary infections, which may lead to the loss of digits and other serious consequences. If not interrupted by treatment, nerve injury may progress to motor weakness and paralysis of intrinsic muscles in fingers or toes, causing life-long disability (Fig. 4).

There are still large gaps in our understanding of neuropathogenesis of leprosy. Peripheral nerves not only serve as the principal target for *M. leprae* infection, but also serve as a safe haven for the bacillus since the blood–nerve barrier protects the organism from many host immune responses. *M. leprae* appears to take advantage of the remarkable regenerating capacity of the adult PNS in securing its preferred niche, and regeneration of damaged peripheral nerves even continues after treatment in patients with advanced leprosy. Nerve injury may progress gradually over the entire course of the disease and may be irreversible.

Intracellular parasite

M. leprae is a highly adapted niche pathogen. It is weakly acid-fast (Fig. 5). Its genome has undergone drastic reductive evolution. At only 3.3 Mbp it has the smallest genome among the mycobacteria, and non-functional pseudogenes also occupy nearly half the chromosome. This loss of functionality probably underlies our continuing inability to culture the organism on artificial laboratory media, and probably influences the organism's remarkably long generation time (12.5 days). *M. leprae* prefers cool temperatures. Lesions on patients are usually found in cooler areas of the skin. Viability of *M. leprae* decreases quickly at temperatures above 35°C. Most animals readily clear the bacilli and cannot be experimentally infected with *M. leprae*. Limited replication can be achieved after inoculation of *M. leprae* into the hind foot pads of conventional and athymic mice. However, the bacilli will not grow when inoculated systemically and exponential increases in growth require many months to attain.

Fig. 4. **Clawed hand resulting from advanced injury to the ulnar nerve due to leprosy.** Alicia Hoard

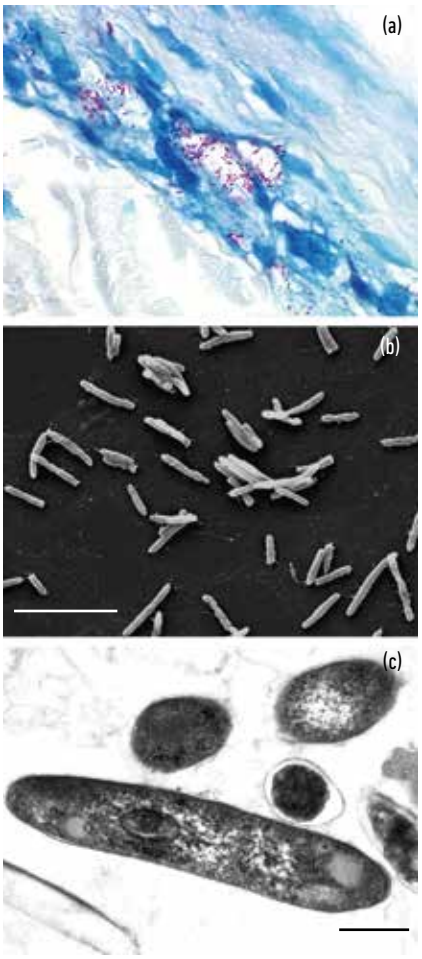

Fig. 5. **(a) Fite-stained section of skin showing *M. leprae* (red) in a cutaneous nerve, the pathognomonic feature of leprosy pathology. (b) Scanning electron micrograph of *M. leprae*. Bar, 5 µm. (c) Transmission electron micrograph of *M. leprae* in cross section. Bar, 250 nm.** Greg McCormick

Infection in mice does not involve the animal's nerves. The only animal that reliably recapitulates leprosy as seen in humans, and develops extensive neurological involvement with *M. leprae*, is the nine-banded armadillo (*Dasypus novemcinctus*). Other than humans, armadillos are also the only natural hosts of *M. leprae*.

Armadillos

Armadillos are exotic-looking animals about the size of house-cats (Fig. 6). With thick, tough skin and a hard, flexible carapace armouring most of their body, Rudyard Kipling suggested that armadillos were a blend of a tortoise and a porcupine. They are mammals of the order Xenarthra, and related to sloths and anteaters. Their normal body temperature ranges from 33 to 35°C, and it was this trait that first attracted the attention of leprosy researchers. Experimental infection of armadillos with *M. leprae* requires 18–24 months to manifest as a fully disseminated disease, but prolific quantities (10^{12}) of bacilli can be harvested from a single animal, and armadillos are the hosts-of-choice for propagation of leprosy bacilli. The remarkable quantities of *M. leprae* made available through armadillos have been a boon to leprosy research.

Shortly after initial discovery of the armadillo's unique susceptibility

to experimental infection, a naturally occurring, systemic mycobacteriosis was also found among free-ranging armadillos in the USA. Subsequent surveys confirmed that wild armadillos are a large reservoir for *M. leprae* and the animals had harboured a natural infection with *M. leprae* for many decades prior to their ever being used in leprosy research. Leprosy was not present in the New World during pre-Colombian times, and it is reasonable to assume that armadillos must have acquired the infection from humans sometime in the last few centuries. They are now recognised as the only non-human reservoir of *M. leprae*, and are part of the natural ecology of the disease in the USA. Recent reports indicate that zoonotic transmission of *M. leprae* from armadillos is responsible for up to 64% of all leprosy cases among persons born in the USA. Armadillos range from the southern USA through Latin America to Argentina, and biomarkers for *M. leprae* have been observed among some South American armadillos. The role that armadillos may play in perpetuating leprosy in the Americas is now being investigated.

Control of leprosy by vaccination or immunotherapy as an adjunct to drug therapy may have significant advantages over control by drug treatment alone.

Vaccine and diagnostics

M. leprae is usually thought to be transmitted from person-to-person by respiratory routes, and current global control strategies focus on antibiotic treatment of active cases to cure the infection and interrupt transmission. However, evidence is accumulating that an occult reservoir of pre-clinical asymptomatic cases, and perhaps armadillos or other environmental hosts, may play a more important role in the ecology of the disease, and leprosy probably cannot be eliminated through drug therapy alone. Control of leprosy by vaccination or immunotherapy as an adjunct to drug therapy may have significant advantages over control by drug treatment alone. A consortium of philanthropic foundations have promoted research on new diagnostic tests and a prototype vaccine since 2002. Scientists from all over the world are engaged in these efforts and their products are now beginning to move into trial. If technology triumphs, we may finally put an end to the suffering caused by one of the oldest known mycobacterial diseases.

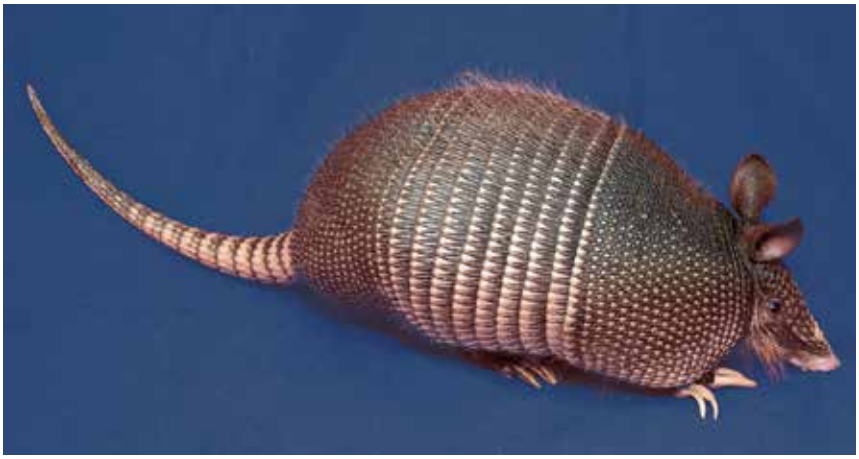

Fig. 6. **Nine-banded armadilllo (*Dasypus novemcinctus*).** Greg McCormick

Richard Truman, Rahul Sharma, Maria Pena, Barbara Stryjewska, John Figarola & David Scollard
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Further reading

Masaki, T. & others (2013). Reprogramming adult Schwann cells to stem cell-like cells by leprosy bacilli promotes dissemination of infection. *Cell* **152**, 51–67.

Monot, M. & others (2009). Comparative genomic and phylogeographic analysis of *Mycobacterium leprae*. *Nat Genet* **41**, 1282–1289.

Rodrigues, L. C. & Lockwood, D. (2011). Leprosy now: epidemiology, progress, challenges, and research gaps. *Lancet Infect Dis* **11**, 464–470.

Scollard, D. M. & others (2006). The continuing challenges of leprosy. *Clin Microbiol Rev* **19**, 338–381.

Truman, R. W. & others (2011). Probable zoonotic leprosy in the southern United States. *N Engl J Med* **364**, 1626–1633.

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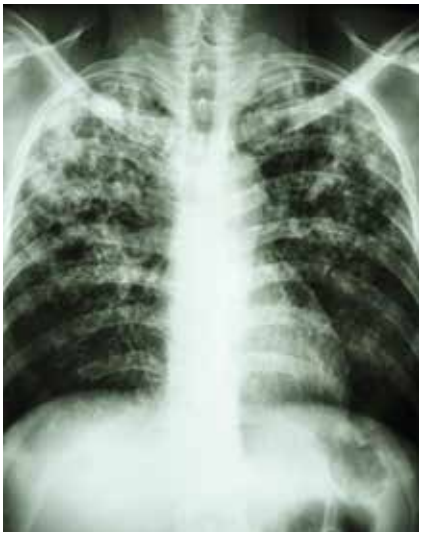


X-ray showing TB in the lung.
stockdevil/iStock/ThinkStock

Tuberculosis remains a global challenge – can its spread be halted?

Worldwide, infectious diseases are the leading cause of death of children and adolescents, and one of the leading causes in adults. Three of the top ten causes of death (2012 data) are from infectious diseases: lower respiratory infections (3.1 million), HIV/AIDS (1.5 million) and diarrhoeal diseases (1.5 million).

An infectious disease (communicable disease) can be defined as an illness caused by a specific infectious agent (pathogenic micro-organism) or its toxic products. The disease can be spread, directly or indirectly, from one person to another. Infectious diseases appear on the post-16 qualifications including Biology A-Level, for example cholera, HIV/AIDS. Tuberculosis (TB) is an excellent model to teach transmission, immune responses, prevention and treatment.

TB is caused by the bacterium *Mycobacterium tuberculosis*. It is primarily a disease of the lungs. TB is spread from person to person through the air. People with latent TB infection have no symptoms and are not infectious. People with TB disease have symptoms and may be infectious.

Background

TB remains a major health challenge with one-third of the world's population infected. In 2012, an estimated 8.6 million people developed TB and 1.3 million people died from the disease.

Although TB notifications and rates in the UK have remained relatively stable since 2005, the incidence of TB still remains high compared to most other Western European countries. In 2012, 8,751 cases were reported with the highest number of cases in London (39%).

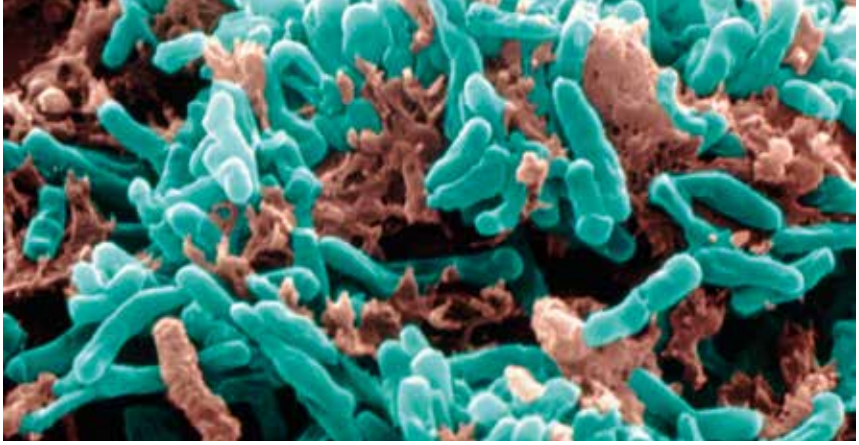
What causes TB?

TB is primarily a disease of the lungs caused by the bacterium *M. tuberculosis*. Most mycobacteria are non-pathogenic and are found in habitats such as soil or water. Some are opportunistic pathogens of humans; for example, *Mycobacterium avium* is a problem in people with compromised immune systems.

M. tuberculosis is an aerobe; consequently, the bacteria grow successfully in tissues with high oxygen concentrations such as the lungs. However, the infection can spread in the blood from the lungs to all organs in the body such as the kidneys and spine.

How is TB spread?

TB is spread from person to person through the air. When a person with active TB coughs, talks or sneezes, mucus and saliva loaded with the infectious organism are propelled into the air. The moisture quickly evaporates from these particles to leave droplet nuclei (dried microscopic pellets) that may remain airborne for hours or days and can spread over long distances.



Coloured scanning electron micrograph of *M. tuberculosis* bacteria. Eye of Science/Science Photo Library

Droplet nuclei are between 1 and 5 µm in size and contain 1–3 infectious organisms each. Infection occurs if the inhaled organism reaches the alveoli of the lungs. A single sneeze will release millions of mycobacteria into the air; one person with active TB can go on to infect 10–15 people throughout the year.

Only a small number of people newly infected with TB will develop immediate symptoms of the disease. The majority will not become ill and cannot transmit the bacteria. The mycobacteria remain inactive (latent infection) without causing the disease. They can become reactivated at any time, even years later, especially in people with a weakened immune system. Depressed immunity due to ageing, a poor diet, a low standard of living and over-crowding or infection with HIV, can lead to an increase in the likelihood of developing the disease.

Latent TB infection

People with a latent infection:

- Have no symptoms
- Don't feel unwell
- Can't spread it to others
- Usually have a positive skin test reaction

Active TB infection

People with the disease have the following symptoms that get more severe over time:

- Bad cough for longer than 2 weeks
- Pain in the chest
- Greenish or bloody sputum
- Weakness or fatigue
- Weight loss (the gradual wasting of the body gave the disease the name consumption)
- No appetite
- Chills
- Fever
- Night sweats

Diagnosis

Diagnosis of TB relies on X-rays of the chest, clinical examination of the patient and microscopic and microbiological examination of the sputum. Diagnosis can also be made by a positive tuberculin skin test. This test involves a small amount of an antigen (a protein that detects infectious agents) being applied to the skin.

Prevention and control

Drug therapy

Current treatment involves three to four different kinds of antibiotics given in combination over 6–9 months. Multi-antibiotics are necessary to prevent the emergence of drug resistance in the bacteria. Patients stop being infectious to others after 2 weeks. After 1 month patients should feel well and start to regain weight. A problem with treatment arises when patients stop taking the drugs as soon as they feel better, because of inconvenience or to save money, as this may lead to recurrence of illness in the individual and the emergence of drug-resistant strains of *M. tuberculosis*.

Vaccination

The BCG vaccine was developed in 1921 from a live attenuated strain of *M. bovis*, which is used today. However, the efficacy of BCG vaccine varies around the world and between populations, ranging from no protection to 70–80% protection. Genetic differences in populations and variations in exposure to environmental mycobacteria are thought to affect the efficacy of the BCG in different countries.

Latest research

New advances in basic sciences, such as molecular biology, immunology and genomics, are altering the way scientists design and make our vaccines. In 1998, scientists at the Wellcome Trust Sanger Institute and the Institut Pasteur sequenced the genome of *M. tuberculosis*. Researchers are now using this information to design novel vaccines and drugs and to identify parts of the organism most suitable for targeting with drugs and vaccines.

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Further reading

Health Protection Agency. Tuberculosis in the UK: 2013 report. **microb.io/1oBhuif** *(last accessed 30 June 2014).*

Smart Global Health. Infectious Diseases. **microb.io/1jZ6ln4** *(last accessed 30 June 2014).*

World Health Organization. Global tuberculosis report 2013. **microb.io/1qbGhc4** *(last accessed 30 June 2014).*

World Health Organization. The top ten causes of death. **microb.io/1n7PymC** *(last accessed 30 June 2014).*

For further information on TB download the free Fact file Tuberculosis: Can the spread of this killer disease be halted? **http://bit.ly/wDukhn**

Outreach

Team Microbes!

Bringing microbiology into primary schools

Are you Team Fungi? Or, Team Bacteria? How about Team Algae? Would you prefer to be a good bug or a bad bug? For three primary school classes in County Armagh, Northern Ireland, these questions were answered when Society staff members Dariel Burdass and Theresa Hudson went to two schools in May to deliver workshops on the wonderful world of microbes.

School children taking part in activities.

Learning about microbes

During the workshops, students learned about the different types of microbes: bacteria, protozoa, viruses, fungi and algae. They heard about 'good' examples from each group, such as the protozoa *Paramecium* that 'eats' sewage and the bacteria *Lactobacillus* that is used in the production of yoghurt and cheese; and 'bad' examples, such as the rhinoviruses that cause the common cold and the protozoan *Plasmodium*, which causes malaria. Students were assigned to a 'team' of microbes, with representative examples of GIANTmicrobes®, and wore t-shirts to show whether they were 'good bugs' or 'bad bugs'.

'Hands-on' science

The students also got to do some hands-on science experiments, blowing up balloons using the power of yeast, and testing the effectiveness of hand washing at reducing the spread of infection, with the help of a UV light and some Glo Germ™ powder. By the end of the half-day session, they could describe lots of different types of microbes and understand that the majority of microbes are very useful in our everyday lives. We also got some great feedback from the students:

Dariel Burdass demonstrating to one of the school classes.

The workshops give us a great opportunity to talk to Primary School children about the importance of microbes and highlight that they are not just agents of disease. As the workshops cater for Primary 7 pupils, we hope the sessions will have sparked an interest in science that they can take with them into Year 8 and beyond. We also get great feedback from the teachers who no longer have the opportunity to teach much science in the current curriculum; the resources supplied to them by the Society are very much appreciated. *Dr John McGrath, Queen's University, Belfast*

'The experiment was great!!! I learnt so much about microbes and I never knew that bacteria could be good for you!'

'It was the best science lesson I have ever had!'

'The experiment was amazing and interesting, I think learning about microbes was amazing. PS the t-shirts were cool.'

Member support

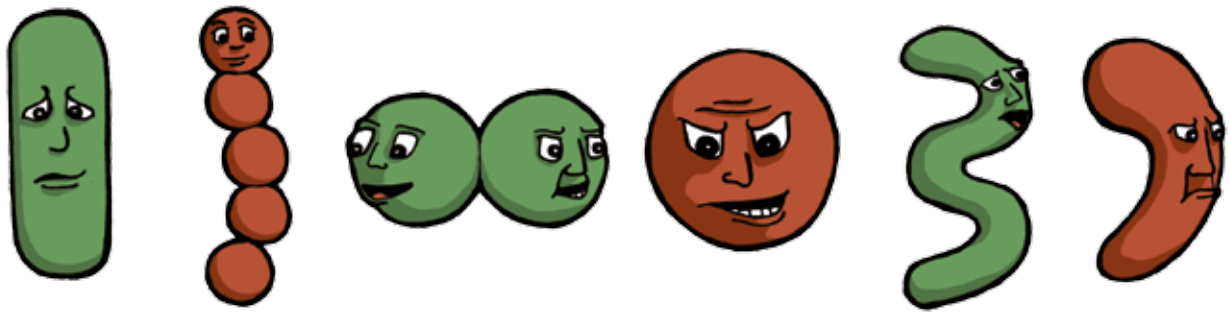
The workshops couldn't run without the help of Dr John McGrath, from Queen's University, Belfast, who helps coordinate the visits, liaises with the schools and provides expert answers on the day to the great questions asked by the students. The workshops happen alongside Continuing Professional Development training for teachers and technicians working in local high schools. This training is run by John Schollar from the National Centre for Biotechnology Education, as part of a decade-long investment by the Society to promote and encourage microbiology education in the area. Dr McGrath sees the benefits of this investment with a healthy number of local students going on to study microbiology at Queen's University.

We'd like to thank Dr John McGrath for his continued support with these workshops and the teachers at both schools for welcoming us into their classrooms to help share with the students just how amazing microbes are! We very much look forward to returning next year.

Theresa Hudson

Education and Outreach Officer

t.hudson@sgm.ac.uk



Bacteria are classified into five groups according to their basic shapes: spherical (cocci), rod (bacilli), spiral (spirilla), comma (vibrios) and corkscrew (spirochaetes). James B.W. Lewis

Membership Q&A

This is a regular column to introduce our members. This issue, we're pleased to introduce Geertje van Keulen.

Where are you currently based?

In 2010 I joined the Institute of Life Science in the College of Medicine at Swansea University where I was promoted to Associate Professor last year.

What is your area of specialism?

Microbial biochemistry would probably best fit my areas of research.

And more specifically?

My research group now focuses on natural antibiosis in pristine and polluted soil environments in order to find novel antibiotics, as well as gain knowledge on how the original producing micro-organisms use antibiotics and other bioactive compounds. This will also help to understand the processes of natural and harmful spreading of antibiotic resistance. We also study how microbes use functional amyloid proteins to selectively modulate the wettability of their own and environmental surfaces, a property which we are further exploiting by developing protein coatings for steel and other materials in collaboration with engineers. We also study how microbes adapt to drying, water-repellent, semi-natural soils and how they affect the hydrology, flooding potential and carbon sequestration in these soils from nano to larger field scales, using a range of metagenomic, metaproteomic, 'metametabolomic', high-resolution imaging and modelling techniques in collaboration with soil scientists, hydrologists and nanotechnologists.

Tell us about your education to date

I completed my education in The Netherlands. I was first inspired by science by my chemistry teacher in secondary school. I enjoyed chemistry and the molecular aspects of biology from the first day I was taught these disciplines, and luckily had a mind for it too! I then studied for an MSci in Chemistry at the University of Groningen, majoring in Biochemistry. I enjoyed my student research project on DNA-protein interactions and the effects on gene expression so much that I wanted to continue in this field. I applied for and was offered a research trainee ('AIO') job, which is typical for obtaining a Dutch-style higher degree. As a result I gained my PhD in Microbial Physiology by studying chemoautotrophic CO_2 fixation by linking signals from changes in physiological status to changes in gene expression.

Where did your interest in microbiology come from?

I have always followed my interests, which are wide-ranging and changing over time. With microbes being so versatile, omnipresent and affecting so many earthly and human processes, it was only logical that microbiology in the broadest way has become my livelihood.

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

I have encountered challenges in my education and at several stages in my career. I have dealt with these by developing stamina, self-belief, including sometimes going against advice if I felt it was not right for me, and confidence to be persistent in what I wanted to achieve. At times it felt impossible to overcome hurdles. By being creative, open to opportunities and having good mentoring I have usually found a way around hurdles, as you don't always have to go over them.

I have usually found a way around hurdles, as you don't always have to go over them.

Geertje van Keulen, with props demonstrating to the public her research on microbial environmental materials science on the beach at the first Soapbox Science event in Swansea Bay, www.soapboxscience.org.. G. van Keulen

I also find that gender equality is still a professional challenge at my current stage of career. Changing inappropriate, sometimes unconscious, behaviour is all about calling it out and putting it in the open, in the hope that in the near future opportunities will be equal for all at all stages in education and career progression. The Society is leading the way with their equality policy backed up with action by supporting initiatives aimed to promote equality in career and personal development. As co-organiser of the first Soapbox Science event in Wales, I am very grateful for the Society's support, allowing us to present the female face of science to the public on the street.

What is the best part about 'doing science'?

The never-ending cycle of hypothesis-experiments-results-new hypothesis. There is always something new and exciting emerging on the horizon to be studied.

Who is your role model?

I would say that both Professor Lubbert Dijkhuizen, one of my PhD supervisors/line-managers, and Professor Sir David Hopwood, eminent microbiologist pur sang, have been a major influence on me and my view of science, scientists and society. Lubbert has shown me how you can accomplish top-notch 'blue-skies' research effectively in combination with applied, industrial projects and sponsors, with entrepreneurial spirit and keeping society in mind. David has been truly fundamental in creating an inclusive and innovative research community, in which collaboration and sharing knowledge or materials is the gold standard between scientists and industrial groupings all over the world.

What do you do to relax?

I swim a lot with my local Masters swimming and triathlon clubs and I try to make it to water polo practice with the Welsh Wanderers as much as I can. Swimming can put me in a mode of trance, while water polo has been good for releasing built-up anger and irritation. When the weather is good, we try to enjoy the stunning Welsh outdoors as much as possible.

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

I like listening to talk radio so I would probably take a record of a lively philosophical discussion. I am going to steal the luxury item from someone who was on Desert Island Discs lately, which is a bath – as this sounded very practical and versatile: for use as a clean bed or shelter, for collecting water, to keep caught fish alive in, and for enjoying a bath of course! If I have to come up with something myself I would like to bring my e-reader with a photovoltaic battery charger and thousands of books uploaded to keep me busy.

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

My voice features on two tracks of an early album of the Norwich-based band 'Army of Mice', which was started up by two microbiologists from the Institute of Food Research Drs Chris Bond and Mark Reuter.

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

Long-distance trucker.

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

Submit your next case report to a new open access journal from the Society for General Microbiology

JMM Case Reports is a peer-reviewed, gold open access, online-only journal publishing original case reports on medical, dental and veterinary microbiology and infectious diseases, including parasitology.

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SOCIETY FOR GENERAL MICROBIOLOGY

Sneeze projected into the air.
CDC Public Health Library

Best of the blog

Earlier this year, the UK Government's Science and Technology Committee held an enquiry on Antimicrobial Resistance. We blogged about the event, which saw research funders highlight a lack of skilled microbiologists as a major factor holding back the UK's efforts to fight antibiotic resistance (**microb.io/1lasMXS**). The enquiry also saw Professor Dame Sally Davies – the Government's Chief Medical Officer – naming two new government programmes intended to coordinate antimicrobial research (**microb.io/1ekalta**).

One of our most popular posts from the past few months is quite the detective story. Microbiologists were asked to help solve a puzzle at a power plant in Hungary. What was causing the plant's ultrapure water system to malfunction? Given that you're reading a microbiology magazine, you'll be unsurprised to know that the culprit was a microbe. You can learn more about the newly discovered species, *Phreatobacter oligotrophus*, which is capable of growing in water containing almost no organic or inorganic matter here: **microb.io/1jJmfCJ.**

Speaking of newly discovered species, our regular *New to Science* column goes from strength to strength. Recently, we've learnt about microbes isolated from Belgian beer, pork tortellini and Japanese hot-spring baths. You can learn more about them here: **microb.io/1oThrxb**

In April, we spoke to Dr Heli Harvala, from the Royal Infirmary of Edinburgh, about her work looking at the co-circulation of viruses between humans and non-human primates in Africa, which represent a potential reservoir for enteroviruses (**microb.io/1eod3jC**).

In April, the Society held its Annual Conference in Liverpool. We spoke to a number of speakers, including Professor Joanne Webster from Imperial College London who told us all about the parasite *Toxoplasma gondii*, how it can affect rats' behaviour and how it might be involved in the development of schizophrenia in people (**microb.io/1ePvv53**). We also chatted with Professor Ron Eccles from Cardiff University's Common Cold Centre, who explained some of the strange things that happen to the body while you have a cold. Why do your nostrils block up alternately? Why do your limbs ache? You'll have to read to find out... (**microb.io/1jMC0Kf**).

Benjamin Thompson
Public Relations Manager
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Reviews

Clinical Laboratory Management, 2nd Edition

Edited by L. S. Garcia

Published by ASM Press (2014)

£128.00 ISBN 978-1555817275

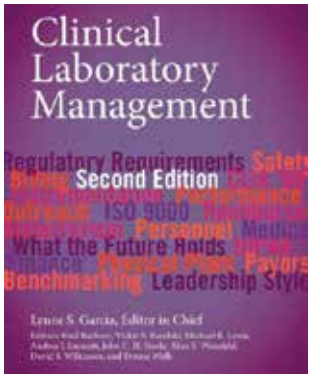
There are a lot of positive things about this book; it is comprehensive and well written, covering a wide range of topics with useful glossaries and extensive referencing.

However, you can never escape the fact that this is a book primarily published for an American audience; legislation, accreditation and regulation are critical to modern clinical laboratories but while ISO certification is briefly covered, the remainder often comes across as irrelevant to readers based in the UK and elsewhere.

Despite these flaws there remains much in this book that is extremely useful; many of the challenges and changes facing laboratories today can be found on both sides of the Atlantic, especially as laboratories in the UK gradually move towards a model that would be recognisable by many managers in the USA. Change management, recruitment and effective leadership are key issues for any manager and this book makes an ideal starting point for any scientist taking their first steps into a management role.

Simon Lewis

Royal Sussex County Hospital



GIDEON Guide to Antimicrobial Agents

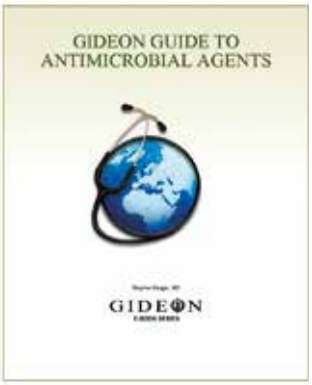
By S. Berger

Published by GIDEON Informatics Inc (2014)

GIDEON web monthly subscription $99.95

The Global Infectious Disease and Epidemiology Network (GIDEON) was created nearly 20 years ago to allow doctors and physicians access to a wealth of information to aid quick and easy diagnosis and treatment of infectious diseases. The system is available online, offering accessible information (from anywhere with internet access), as well as opportunities to update the information as new research becomes available. The *GIDEON Guide to Antimicrobial Agents* is an e-book that provides a comprehensive, detailed list of epidemiological diseases and pathogens found in every country in the world with corresponding information about available treatment options such as vaccines, antibiotics and other drugs.

The book is divided into three sections allowing easy access and



reference to facts and information. The first section has each pathogen and disease followed by the treatment option; the second section is a list of all diseases followed by GIDEON with generic treatment options; the third section is an alphabetic list of drugs with information about the mechanism of action, dosage, details about their metabolism and the associated contraindications. The three sections allow you to successfully retrieve the information you require from whatever your starting point.

I was able to find my way around the information quickly and easily. The e-book has a slight feel of the online British National Formulary (BNF): it is a comprehensive reference book that provides up-to-date accessible information. This format may particularly benefit those accessing it via a mobile phone. I can understand why it would work well in a clinical setting too, but it requires a subscription. In addition, it is worth noting that practise guidelines often differ from country to country, perhaps reflecting the different organisms and susceptibility patterns seen in different parts of the world or the availability of antimicrobial chemotherapy. Ensuring that these differences are not problematic and it offers something in addition to hospital guidelines, the BNF and Data Sheet Compendiums will be necessary before this book is likely to be widely adopted in a UK setting.

Laura Bowater

University of East Anglia

Medical Biotechnology

By B. R. Glick, C. L. Patten & T. L. Delovitch

Published by ASM Press (2014)

£85.00 ISBN 978-1555817053

Medical Biotechnology is a textbook aimed at students interested in the understanding of molecular biotechnology and its latest applications from a medical perspective. This book would suit undergraduate students encountering molecular techniques for the first time as well as individuals interested in learning about how biotechnology has had an enormous effect on recent medical advances.

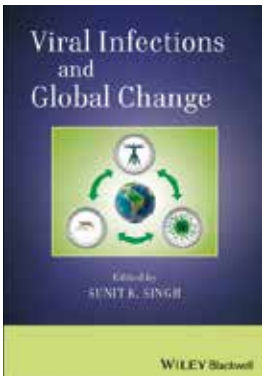
I find the book well written, it avoids the use of jargon and provides easy to follow explanations, which is very refreshing when reading a textbook. The 12 chapters are well structured and they cover different aspects of medical biotechnology, from fundamental concepts to practical applications, giving a current overview of the field and using up-to-date examples of how modern molecular techniques are being applied to medicine.

I particularly like the clear diagrams and the text boxes containing examples of relevant practical uses as well as explanations of the scientific papers that have significantly contributed to the development of breakthroughs in the field.

Because of the clarity of the text, its wide coverage and topical relevance, I would expect this book to be extensively used as a reference by anyone wanting to understand the basis of molecular biotechnology techniques in relation to their contributions to medical advances.

Lorena Fernández-Martínez

John Innes Centre, Norwich



Viral Infections and Global Change

Edited by S. K. Singh

Published by Wiley-Blackwell (2013)

£100.00 ISBN 978-1118297872

Several aspects of global environmental change, including international travel and trade, societal changes and climate change have been explicitly linked to emerging infectious diseases in humans and animals. This book has met the growing need for a single source of information, focusing on emerging and re-emerging viral infections in relation to global environmental change.

This book contains 32 chapters clearly written by many well-known scientists from across the world, with well-organised explanatory tables and figures included. It provides a good overview of the essential topics and allows easy retrieval of information on etiology, epidemiology and pathogenesis of important emerging and re-emerging viral diseases. Chapters are fully referenced and provide a useful update/review of a given area.

Part I of the book, General aspects, gives an overview of the impact of climate change on distribution and spread of the vector-borne and zoonotic viruses. Influence of climate change on the development and blood-feeding patterns of mosquitoes and arboviral host range, but also the role of human behaviour, land-use changes and agricultural practices, global travel, animal and meat trade and animal migration on the spread and (re) emergence of viral infections is also discussed. This section includes chapters describing the importance of surveillance systems, predictive modelling and development of novel detection and diagnostic methods.

Part II, Specific Infections, provides condensed information about emerging and re-emerging coronaviruses, orthopoxviruses, arenaviruses, bunyaviruses, flaviviruses and other important zoonotic and vector-borne viruses.

The main audience for this book includes research scientists, epidemiologists, and medical and veterinary students, working in ecology, environmental management, climatology, neurology, virology and infectious diseases. In my opinion, the book will be especially useful for postgraduate students and those who are looking for a comprehensive overview of the field. I learnt so much from the book and enjoyed reading it. It is definitely a welcome and timely addition to the biomedical literature.

Daniel Růžek

Czech Republic Veterinary Research Institute, Brno

Obituary

Professor Lorna Casselton 1938–2014

Lorna Ann Casselton, Professor Emeritus of Fungal Genetics at the University of Oxford, died on 14 February 2014: she was 75.

Lorna Casselton. Bruce Sampson/NTNU Vitenskapsmuseet

Lorna was born on 18 July 1938 in Rochford, Essex and attended Southend High School for Girls. She decided to study botany as an undergraduate; an interest she developed from her father William Smith, a keen amateur naturalist. She attended University College London and gained a BSc before receiving her PhD in 1964. She lectured for a year at Royal Holloway, University of London, before moving in 1967 to Queen Mary, where she was Professor of Genetics (1989–1991). She then moved to Oxford University as a senior research fellow, becoming Professor of Fungal Genetics in 1997. She was also a Fellow of St Cross College, Oxford and became one of the UK's most important female biologists of the past 30 years.

Throughout her career, Lorna used genetics to study mating in mushroom-forming fungi. Unlike animals and plants that have two sexes, many fungi have more: tens or even hundreds of different sexes in some species. As recognition of her outstanding and pioneering research, Casselton was elected a Fellow of the Royal Society in 1999, served on the governing council of the Royal Society in 2002–03, before being elected Vice-President and Foreign Secretary. In this influential role she acted as an ambassador for British science, visiting many countries during her time in office. She was made an honorary member of the British Mycological Society in 2002, and in 2012 she received a CBE for services to fungal genetics and international science.

After her first marriage to Peter Casselton and later divorce, she married William Joseph Dennis Tollett in 1981 who survives her.

Laura Bowater
University of East Anglia

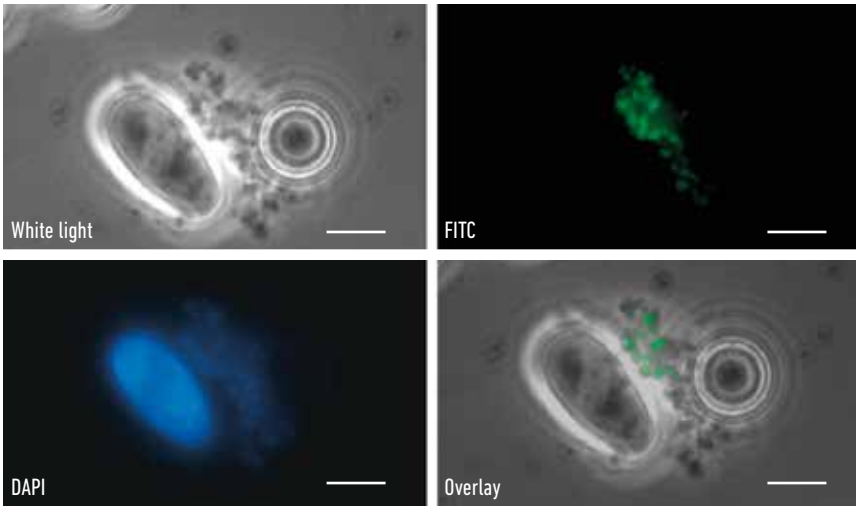
St Cross College, Oxford has established the Lorna Casselton Memorial Fund in Lorna's memory. The purpose of the Memorial will be to establish an annual lecture in her name and the Lorna Casselton Memorial Lecture will bring an eminent scientist to Oxford each year to give a keynote address and present groundbreaking research in a biological area.

If you would like to contribute in Lorna's memory, the details are available online: **microb.io/1qnm5UQ**

Comment

Badgers and bovine TB: how can environmental microbiology help?

Elizabeth M. H. Wellington & Orin Courtenay



It is well recognised that the incidence of bovine tuberculosis (bTB) in the UK has been growing alarmingly in recent decades. The problem of bTB in cattle has affected a number of countries worldwide – notably Ireland, USA, New Zealand and many countries in Africa.

Fig. 1. ***M. bovis*** **cells captured by magnetic beads with FITC** ***M. bovis*** **monoclonal antibody, with DAPI stain and image overlay white light and FITC. A large oval protozoan is visible in all images, except FITC. Bars, 3 µm.** E. M. H. Wellington

In all cases a reservoir of the disease has been identified in wildlife ranging from badgers in the UK and Ireland, to possums in New Zealand and white-tailed deer in the USA. However, the mode of transmission between wildlife and cattle is the subject of debate and once the disease becomes endemic the likelihood of cattle-to-cattle transmissions complicates the routes of transfer. Several years ago I became interested in the environmental aspect of this problem following discussions with a fellow microbiologist, Eamonn Gormley, who was working on bTB at the Veterinary Science Centre at University College Dublin (UCD). We developed an idea to investigate environmental contamination of pasture and soil surrounding setts where badgers lived, and determine if we could detect the causal agent *Mycobacterium bovis*. Working with Orin Courtenay, an epidemiologist at the University of Warwick, we considered whether faecal shedding of the bacterium could be a useful measure of transmission risk from badgers.

Previous studies have shown that cultivation of *M. bovis* from badger faeces lacked sensitivity due to contamination from the wide range of other bacteria in the samples and low numbers of cells (positive culture from 27/1064 samples of faeces). In addition, cultivation of a pathogen outside of its host is likely to reduce culturable status due to stress and the normal practice of decontamination with strong alkali proving too harsh when cells were recovered from soil. This led us to develop molecular assays for *M. bovis* in faeces and these proved useful to investigate shedding status of social groups. It should be noted that faecal shedding is an indication of infectiousness. Our studies with *M. bovis* also proved that polymerase chain reaction (PCR) detection in soil and faeces was a reliable indicator of intact cells as the turnover of cell-free DNA in soil and other substrates was rapid.

During the past decade, molecular detection of pathogens has become an accepted method of diagnosis, especially where antibiotic resistance was an important attribute as in the case of meticillin-resistant *Staphylococcus aureus* (MRSA) in blood and multidrug-resistant (MDR) *Mycobacterium tuberculosis* in sputum. Sampling wildlife is demanding and usually requires either live capture or

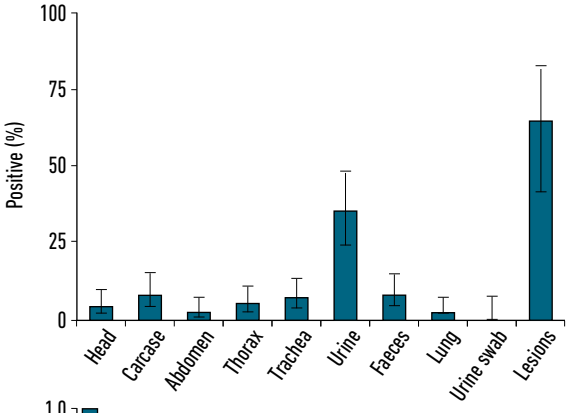


Fig. 2. The detection of *M. bovis* via qPCR RD4scar assay in badger tissues. E. M. H. Wellington

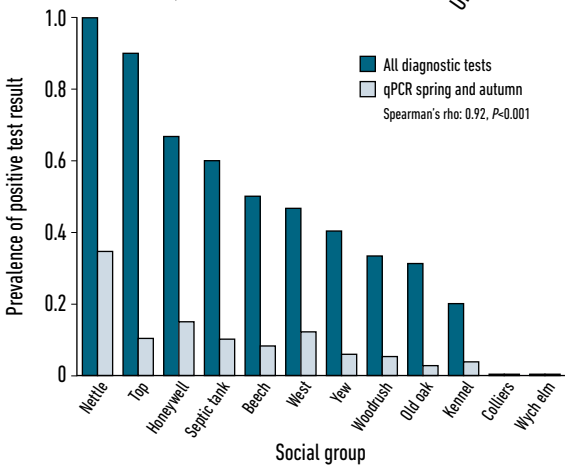


Fig. 3. Correlation between a suite of diagnostic test results carried out on trapped badgers shortly before faecal sampling in spring and autumn at badger social group latrines in Woodchester Park. E. M. H. Wellington

culling to determine disease status but the collection of badger faeces is non-invasive and does not involve any disturbance of the sett. So the possibility of using molecular detection of *M. bovis* in faeces was investigated. The badgers dig latrines near their setts facilitating the collection of faeces and samples to be examined by microscopy to identify the presence of *M. bovis* cells; these can be visualised using immunofluorescence staining (Fig. 1) and quantified in the lab by quantitative (q)PCR. In collaboration with Eamonn Gormley, we were able to compare PCR positives in tissue from diseased badgers and levels in tracheal swabs were comparable to rectal faeces across a range of sampled individuals (Fig. 2). Shedding (trachea, urine and faeces routes) correlated with animals exhibiting more severe disease status. In order to rigorously test and validate the qPCR assay (RD4scar) a number of studies were done in collaboration with the Animal Health and Veterinary Laboratories Agency (AHVLA) Weybridge and Woodchester Park providing opportunities for ring trials and comparison with results from long-term badger monitoring.

The latest study involved direct comparison of qPCR data with badger disease status obtained via trapping and the application of diagnostic tests. Trapping and testing of the badgers associated with the social groups under study was carried out by AHVLA Woodchester Park using IFN-gamma, Stat-Pak and culture of clinical samples to determine social group level disease prevalence. The faecal latrine sampling across the whole year was performed in close conjunction with the badger trapping and testing programme allowing comparison with the individual diagnostic tests as well as group bTB status. qPCR results varied by season, with spring and autumn exhibiting 100 and 80% sensitivity, respectively, against the combined trapped badger diagnostics for the same season. The degree of infection within a social group (trapped badger diagnostic test results) was strongly correlated with the degree of shedding as determined by faecal qPCR (Spearman's rho=0.92, $P<0.001$) (Fig. 3). Bacterial loads varied considerably between social groups. We suggest that a small number of high prevalence social groups may be responsible for the majority of *M. bovis* that is shed into the environment and therefore present the highest potential risk of onward transmission.

Any effective disease control strategy needs reliable monitoring of both infection status as well as individual or group transmission risk, to maximise cost-effective control measures such as vaccination and improved biosecurity. In our view, understanding transmission pathways by monitoring the pathogen non-invasively in environmentally shed samples is an important component of the solution to the current bTB crisis.

Acknowledgements

The authors are grateful for funding from the Department of Environment, Food and Rural Affairs (Defra) and the Biotechnology and Biological Sciences Research Council (BBSRC). We wish to thank AHVLA scientists Glyn Hewinson, Jason Sawyer, Dez Delahay, and UCD scientists Eamonn Gormley and Leigh Corner, and their respective research teams for collaboration. We thank our research team for their excellent field and lab work.

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Further reading

Courtenay, O. & others (2006). Is *Mycobacterium bovis* in the environment important for the persistence of bovine tuberculosis? *Biol Lett* **2**, 460.

Travis, E. R. & others (2011). An inter-laboratory validation of a real time PCR assay to measure host excretion of bacterial pathogens, particularly of *Mycobacterium bovis*. *PloS One* **6**, e27369.

Wilesmith, J. W. & others (1986). Tuberculosis in East Sussex. IV. A systematic examination of wild mammals other than badgers for tuberculosis. *J Hyg* **97**, 11.

Young, J. S., Gormley, E. & Wellington, E. M. (2005). Molecular detection of *Mycobacterium bovis* and *Mycobacterium bovis* BCG (Pasteur) in soil. *Appl Environ Microbiol* **71**,1946.

Watch Professor Wellington's Hot Topic lecture at the Society's 2014 Annual Conference on bovine TB: ***microb.io/UPKhEN***