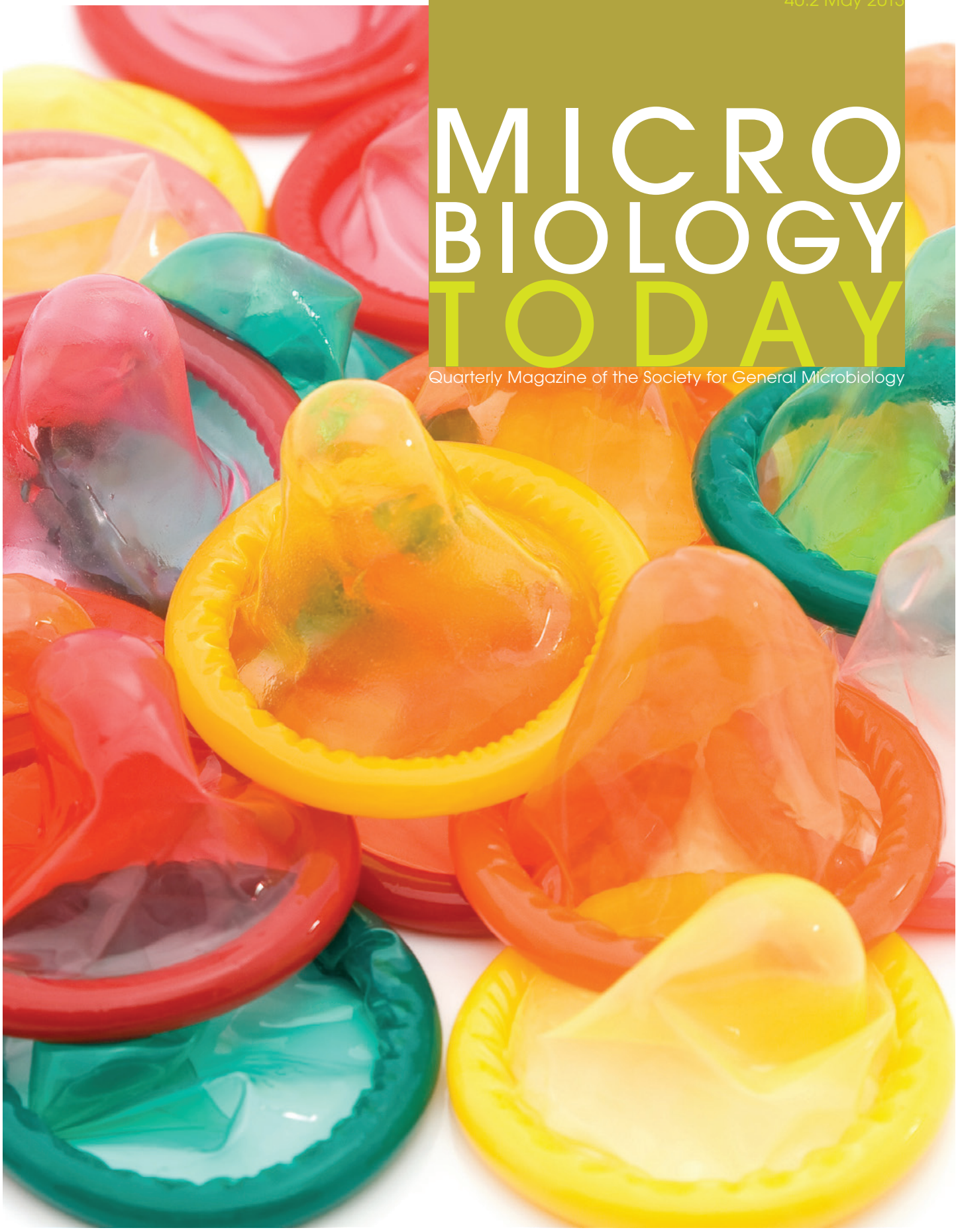
40:2 May 2013

MICRO BIOLOGY TODAY

Quarterly Magazine of the Society for General Microbiology



STIs • Syphilis – the great scourge
• Mysteries of *Chlamydia*
• The ongoing challenge of gonorrhoea
• HIV and the functional cure

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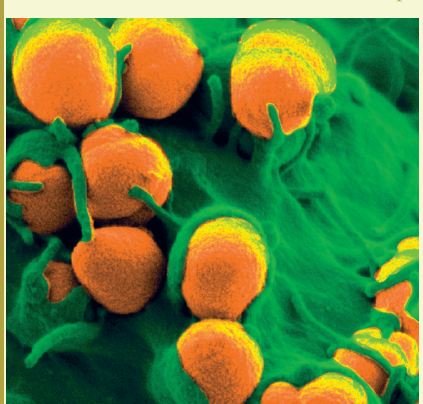

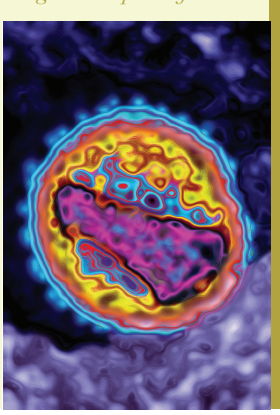

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society for general Microbiology

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FEATURES

REGULARS

EDITORIAL

Welcome to the May 2013 issue of *Microbiology Today*. This issue is primarily focussed on sexually transmitted infections (STIs).

Since the formation of the Royal Commission on Venereal Disease in 1913, the tackling of the '*hideous scourge*' has been at the forefront of successive generations and remains a significant health focus given that these infections have a cost to the NHS of approximately £165 million each year. As we approach the centenary of the Royal Commission, it is clear that STIs are still a priority, with increasing rates of infection, emerging drug resistance, changing demographics of infection and the need for better provision of specialist clinics and diagnostics. These issues have been identified by the Society for General Microbiology as a key policy priority and as such an Expert Panel has been established (www.sgm.ac.uk/en/policy/position-statements.cfm/publication/2013-sexually-transmitted-infections) and a position statement will be launched in the summer of this year. To mark this, the editorial board and I have put together an issue of *Microbiology Today* that tries to cover some of the important areas relating to STIs.

Professor Sir Richard Evans gives us a historical perspective on syphilis and how this disease has been a known scourge of mankind for over five centuries, followed by Dr Nicholas Thompson's article, which brings us up to the modern day, discussing how great advances have been made in *Chlamydia* biology through the use of high-throughput sequencing techniques. Dr Catherine Ison focuses on one of the priority areas of the SGM Expert Panel, looking at the rise of antimicrobial resistance in gonococci. Finally, Max Bachman discusses new public health regimes for treating HIV in South Africa. With this collection of articles, I think we have tried to give an overall flavour of the issues surrounding STIs and how these can be addressed. The work of the Expert Panel and the position statement from the Society will go a long way to mapping the key issues in sexual health, along with formulation of policy recommendations, and they will highlight the key role microbiology has to play in the prevention, surveillance and treatment of STIs.

The Comment in this issue is provided by Dr Ron Daniels, the chair of the UK Sepsis Trust and Chief Executive of the Global Sepsis Alliance, who provides us with an overview of the importance of sepsis and the barriers to treatment. He also offers us solutions to improve awareness and explains how we must change the systems and the issues surrounding antibiotics in a condition that causes the NHS an estimated £2.5 billion in expenditure.

I hope you enjoy reading this issue of *Microbiology Today* as much as we enjoyed putting it together.

PAUL A. HOSKISSON, Editor
Email paul.hoskisson@strath.ac.uk

FROM THE PRESIDENT

As flagged in the last issue of *Microbiology Today*, the Society for General Microbiology has been undergoing a number of significant changes.

Some of these will be highly visible to members, such as the new website launched just before our excellent Spring Conference in March, and others, such as the gradual relocation of the Society's offices to London, should be more transparent. By the end of 2013, we should be in a much better position to support members, engage with other learned societies and influence policy-makers.

The Society has already begun to have more influence in helping shape UK policy in areas of microbiological concern. When Professor Dame Sally Davies, the Chief Medical Officer for England, published her report on the threat of antimicrobial resistance in March, the Society was asked to comment by the Department of Health and we were quoted in their press release. This led to interviews on BBC News, BBC World and Sky News, as well as contributions to the Channel 4 website from the Society and from individual members. More information on this and our sponsorship of European Antibiotic Awareness Day are included in this issue.

It is crucial that microbiologists help avert the threat of antimicrobial resistance, which Professor Davies likened to terrorism in terms of its global impact. We can help directly by developing new antibiotics, identifying new targets in pathogenic micro-organisms and developing rapid diagnostic techniques that will allow GPs to prescribe the correct antibiotic during a consultation. We can also help indirectly through public engagement to reduce public expectation of antibiotic treatment for every minor infection and by influencing governments to incentivise companies to search for new antimicrobials and to reduce the prophylactic use of antibiotics in agriculture and aquaculture. Our reach must extend beyond the UK and Ireland if this global problem is to be effectively tackled.

We are about to launch our second Position Statement with the intention of making policy-makers and others aware of another major microbiological issue – sexually transmitted infections. This will be launched at the House of Commons in Summer 2013. As this issue of *Microbiology Today* indicates, the increasing incidence of STIs is a major public concern and our Expert Panel (see **www.sgm.ac.uk/en/policy/position-statements.cfm/publication/2013-sexually-transmitted-infections**) has drafted a report, which will be available to all members and to members of the UK and Irish parliaments.

The Society continues to contribute to national consultations which affect our members. During the first 3 months of 2013, we responded to consultations on Open Access publishing, on the Triennial Review of Research Councils and on BBSRC's review of its Strategic Plan. Our responses can be found on the website at **www.sgm.ac.uk/en/policy/consultation-responses.cfm**. If you wish SGM to contribute to a consultation in the UK or Ireland, or indeed at a European or wider international level, please let our Policy Officer, William Burns (**w.burns@sgm.ac.uk**), know.

The Society is a membership organisation. As always, if you have suggestions for how the Society could better serve you, I will be pleased to receive your emails, which should be sent to **president@sgm.ac.uk**

NIGEL L. BROWN
President

NEWS

PRIZE LECTURES – NOMINATIONS NEWS

A range of prestigious awards are made by the Society in recognition of distinguished contributions to microbiology.

Nominations are now sought for the 2014 prize lectures. The panel will take their recommendations to Council in September for approval.

Prize lecture rules and a nomination form are available on the Society for General Microbiology website: **www.sgm.ac.uk/en/grants-prizes/prize-lectures.cfm**

FLEMING PRIZE LECTURE

Awarded annually to recognise outstanding research in any branch of microbiology by a microbiologist in the early stages of his/her career.

MARJORY STEPHENSON PRIZE LECTURE

Awarded biennially for an outstanding contribution of current importance in microbiology.

PETER WILDY PRIZE LECTURE

This is awarded annually for an outstanding contribution to microbiology education.

The winners of the above prizes will each receive £1,000 and will give a lecture at the Society's annual conference, which will be held in Liverpool in 2014.

The closing date for nominations is **19 AUGUST 2013**.

MICROBIOLOGY TODAY ONLINE

Microbiology Today is now published online on a dedicated microsite (**www.sgm.ac.uk/en/all-microsite-sections/microbiology-today-latest-issue/index.cfm**). The articles are accessible to paid members and subscribers and will be published ahead of print. Even more reason to become a member! If you would like to subscribe, or require help with your sign-in details, contact our membership office: *Email* **members@sgm.ac. uk**; *Tel.* **01189 881803**)

NEWS OF MEMBERS

The Society notes with regret the passing of **MISS J. CRICK** (member since 1974); **DR R.M. JACKSON** (member since 1958) and **MRS J.P. ELEY** (member since 1962).

It is also with great sadness that we report the passing of **PROFESSOR SIR KENNETH MURRAY**, who developed the first vaccine against viral hepatitis B and thus saved countless lives worldwide.

HARRY SMITH VACATION STUDENTSHIPS 2013 – ANOTHER RECORD YEAR

The popularity of this scheme, which offers a great opportunity for undergraduate students to work on microbiological research projects, continues to grow! A record 129 applications were received this year. Following review of the applications (with thanks to the panel of referees for their efforts), 51 awards were made.

Applications are made by SGM members (the project supervisor) on behalf of undergraduates who wish to undertake a project in the summer vacation before their final year of study. The studentships provide support to the student at a rate of £185 per week for a period of up to 8 weeks, plus up to £400 for laboratory consumables. The student also receives free Undergraduate Membership of the Society for a year.

UNDERGRADUATE MICROBIOLOGY PRIZES – CALL FOR NOMINATIONS

The prizes aim to encourage excellence in the study of microbiology by undergraduate students and to promote scholarship in, and awareness of, microbiology in universities. The prizes are awarded annually to the undergraduate student in each qualifying institution who performs best in microbiology in their second year of full-time study (or part-time equivalent) for a Bachelor's degree. Each winning student will be awarded £200, a certificate and a free year's Undergraduate Membership of the Society.

One prize is available to each university in the UK and Republic of Ireland offering a degree course with significant microbiology content. The university chooses the assessed microbiological work for which the prize is awarded. The submission should be supported by formal marks. Winning students should have attained at least a 2(1) overall in their degree examinations at the stage at which the award is made.

Universities are now invited to nominate a student for a 2013 Undergraduate Microbiology Prize. The full rules and nomination form can be downloaded from the SGM website or obtained from the Grants Office. The closing date for nominations is **23 AUGUST 2013**.

A 2012 recipient of the prize, **ALEX BALDWIN**, now a third-year BSc Molecular Biology student at University of Exeter, is shown receiving his certificate from Dr Mark van der Giezen (right).

DANAE ROKANAS (left) received the University of Kent prize for her performance on the BSc Biology degree.

SCIENCE IS VITAL

The Society is now supporting the *Science is Vital* campaign – **http://scienceisvital.org.uk**

UK scientists and supporters of science who believe that a strong science base is vital to the UK's economy and reputation are asking the government to increase science funding in the budget for 2015–16 and beyond. Why not sign the public petition?

CONFERENCES

Brighton Royal Pavillion.
iStockphoto / Thinkstock

SGM Autumn Conference
2–4 Sept 2013 | University of Sussex

The packed Autumn Conference will feature seven parallel symposia over 3 days, covering subjects that will appeal to both prokaryotic and eukaryotic microbiologists at all career levels. The Society is delighted to be hosting a joint symposium, *Fungal diseases, diagnostics and drug discovery*, with the British Society for Medical Mycology on the first two days of the conference. The session will feature contributions from world-leading scientists on the major fungal pathogens such as *Aspergillus* spp., *Candida* spp., dermatophytes, *Cryptococcus* spp. and plant pathogens, as well the latest diagnostic techniques and advances in drug discovery. A companion symposium will focus on *Microbial survival in the host*, which will include both unicellular parasites as well as fungal pathogens.

Other sessions include *Impact of bacteriophage in the environment*, covering the increasing awareness and impact of bacteriophage on the ecology of the biosphere, and *Microbial modulation of cellular responses*, which will highlight the way different bacterial toxins and effectors subvert, inhibit or activate host cell pathways to the benefit of pathogens. *Pathogen genomics – current clinical applications* will show how clinical practice is changing based on the data generated by next-generation sequencing technology, and *Regulatory phosphate-based molecules* will outline progress made in understanding the actions of phosphate-based regulatory molecules, with a focus on (p)ppGpp, polyphosphates and cyclic dinucleotides.

Workshops and poster sessions will provide the chance for delegates to present both posters and offered oral papers. Registration and abstract submissions will open shortly. Keep an eye on the SGM website and newsletter for the latest details.

The Autumn Conference will take place at the University of Sussex, located to the north of the seaside town of Brighton.

SGM Conferences: Future Plans

Following on from a recent review of the Society's conferences, we are pleased to announce the trialling of a new conference programme.

From 2014 we will offer one annual conference, spread over 4 days, featuring a wide variety of symposia, workshops and poster sessions covering a range of microbiological areas.

In addition, a series of Focused Meetings held over 1 or 2 days will be organised, which will concentrate on more specific areas of microbiology. Details on the first Focused Meetings will follow later in 2013. Watch the conference pages of the website for more details.

SAVE THE DATES

Irish Division – Gut Pathogens and Gut Microbiome
University of Ulster, Coleraine | 29–30 August 2013

SGM Annual Conference 2014
Arena and Convention Centre Liverpool | 14–17 April 2014

Other Society-sponsored meetings

11th UK Meeting on the Biology & Pathology of Hepatitis C Virus
Rydal Hall, Ambleside, Cumbria | 17 May 2013

EMBO Workshop on Integrating Omic Approaches to Host Pathogen Interactions
Radisson Blu Hotel, Liverpool, UK | 25–27 June 2013

***Staphylococcus* Great Britain & Ireland [Staph-GBI] 2013**
Trinity College Dublin | 5–6 September 2013

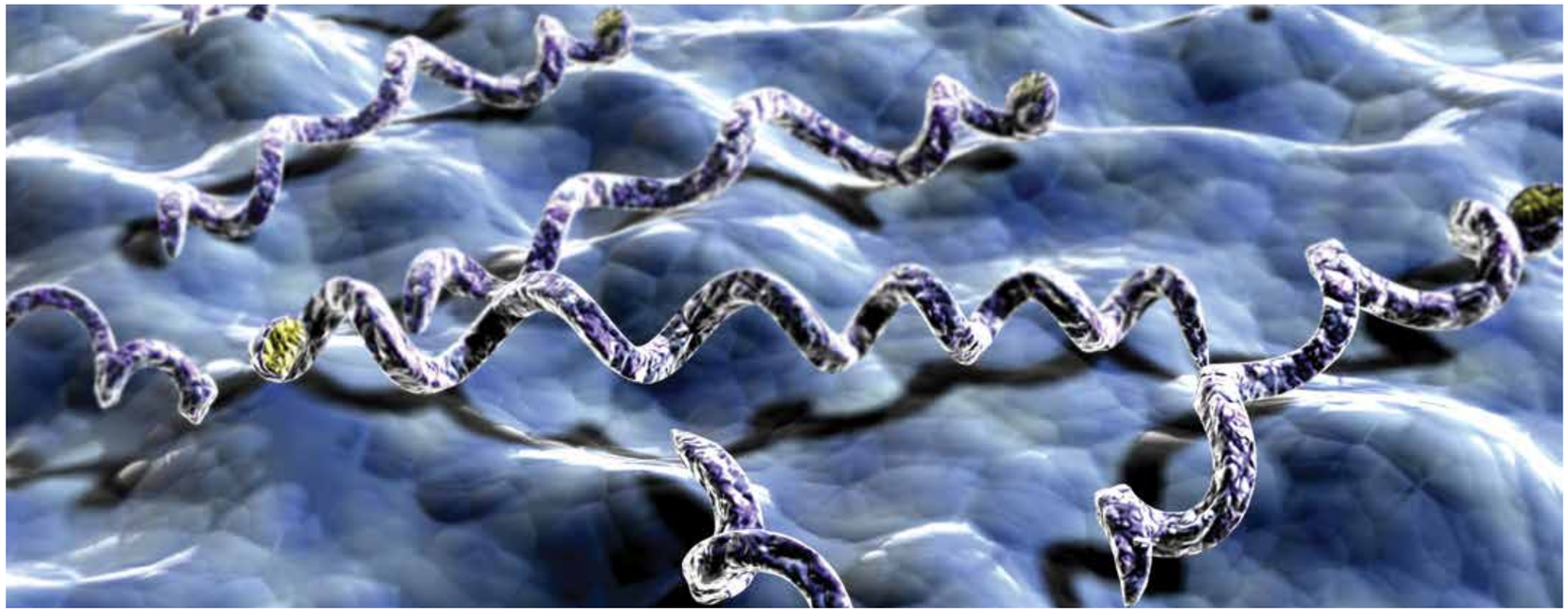
14th International Conference on *Pseudomonas* 2013
Lausanne, Switzerland | 7–11 September 2013

SIR RICHARD EVANS

Syphilis – the great scourge

The Turks called it '*the disease of the Christians*' while the Persians called it '*the disease of the Turks*'. It has variously been attributed to the French, the British, the Polish, the Germans and the Portuguese. But what cannot be denied is that syphilis has been a scourge of mankind for over 500 years at least – and unfortunately continues to be so …

The syphillis-causing bacterium, *Treponema pallidum*. *3D4medical.com / Science Photo Library*



ON 5 JULY 1495, a doctor accompanying Venetian troops as they pushed forward to expel an invading French army from Italy came across a new and disturbing sight among the captured soldiers of the French king. The doctor encountered '*several men-at-arms or foot soldiers who, owing to the ferment of the humours, had pustules on their faces and all over their bodies. These looked rather like grains of millet and often appeared on the outer surface of the foreskin. Some days later, the sufferers were driven to distraction by the pains they experienced in their arms, legs and feet, and by an eruption of large pustules, which could last for a year or more if left untreated*'.

Another Venetian doctor reported seeing sufferers who lost their eyes, hands, nose or feet, with sores penetrating to the bones. '*Through sexual contact*', he wrote, '*an ailment, which is new, or at least unknown to previous doctors, the French sickness, has worked its way to this spot as I write*'.

Most of King Charles's troops were mercenaries, not only from France but also from Flanders, Switzerland, Germany, Italy and Spain. As the defeated French troops were disbanded, they returned home, carrying the new disease with them. Within a couple of years, the '*French sickness*' had spread across Germany and by the early years of the new century the '*German sickness*' had broken out in Poland and then the '*Polish sickness*' in Russia. The Turks called it '*the disease of the Christians*' while the Persians called it '*the disease of the Turks*'. Before long, the disease was being spread by the crew of Vasco da Gama's ships to the people of India and Japan, where its origins were reflected in the name '*the Portuguese sickness*', while '*the British sickness*' eventually spread to Tahiti and the Pacific in the course of the 18th century. By 1553, the disease was widely known as syphilis, the root of the word coming from an epic Latin poem, *Syphilis sive morbus gallicus* – '*Syphilis or The French Disease*', published in 1550 by Girolamo Frascatoro, a medical student of Copernicus.

Where did this devastating new disease originally come from? Almost everyone who commented on the disease from 1494 onwards regarded it as something entirely new in Europe. This was the very year in which Christopher Columbus returned from his first expedition to America. The Portuguese doctor Rodrigo Diaz da Isla reported that he had treated a number of Columbus's crew for the disease when they landed in Barcelona. No doubt, patrons of the brothels of Barcelona were quickly infected with the disease brought by the returning sailors and from there, the disease spread to Italy with the troops.

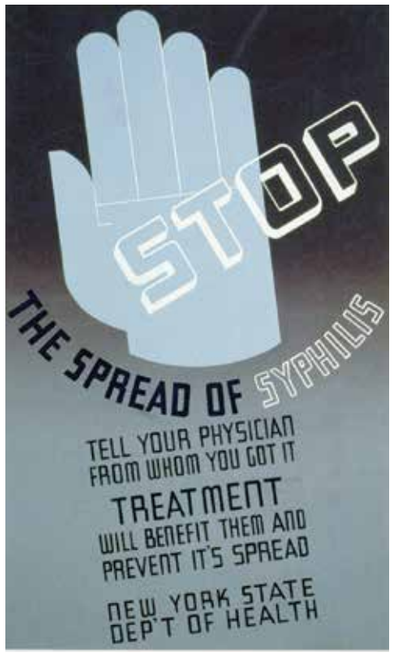
Some modern archaeologists have cast doubt on this view, suggesting that traces of the disease were found in the bones of Europeans buried long before Columbus's expedition. However, a systematic investigation of all 54 cases featured in published reports concluded, in December 2011, that none of this skeletal evidence was reliable in terms of diagnosis or dating when subjected to standardised analyses. The bacterium *Treponema pallidum*, which causes syphilis and, in various sub-forms, other related diseases, such as yaws, was genetically sequenced as long ago as 1998. This has helped further research into when exactly the disease arrived in Europe. As yet, no evidence has been found dating it to human remains before 1494.

By the mid-16th century, observers were beginning to note that the disease was declining sharply in virulence. Either people had developed some resistance to the most extreme symptoms or the disease itself had mutated. Whatever the reason, it settled into the form, or forms, it takes to the present day. Syphilis remained a common disease in the 17th and 18th centuries. Physicians did not

distinguish between syphilis and other sexually transmitted diseases so it is often difficult to decide what exactly someone like Dr Johnson's biographer James Boswell was suffering from when he reported in his diary that he had an attack of a '*disgusting disease*' after visiting a '*low house in one of the alleys in Edinburgh*', or Casanova when he reported that he had to undergo a 6-week course of treatment for '*the sickness we describe as French*'. The composer Robert Schumann's madness and premature death strongly suggest that he suffered from syphilis; with Franz Schubert the connection is less certain.

It was only in the later 19th century that progress was made in identifying the different types of sexually transmitted diseases. In 1838, Philippe Ricord, a French physician, established the existence of syphilis as a distinct form of infection. In 1905, two German scientists, Fritz Schaudin and Erich Hoffmann, identified the causative agent of syphilis. Shortly afterwards, Paul Ehrlich, a German physician and scientist, developed a chemical treatment for syphilis, which he called Salvarsan. It began being used in dispensaries set up in many countries during and after the First World War, although on the whole it was less than effective and had some dangerous side effects.

Infection rates soared as a result of the First World War. In the mid-1920s syphilis was killing 60,000 people a year in England and Wales, compared to



Above **Albrecht Durer's (1471–1528) woodcut of a syphilitic man covered in chancres. Note the astrological influence suggested by the Zodiac above him.** *NYPL / Science Source / Science Photo Library*

Left & right **Various 20th century propaganda posters.** *WPA Posters collection, Prints & Photographs Division, Library of Congress (LC-USZC2-838, -948 & -947)*

"While war and conflict continue to rage in various parts of the world, syphilis, which has been associated with unrest from the very beginning, will continue to wreak havoc on humankind, despite all the efforts to prevent and eradicate it."

tuberculosis, which was causing 41,000 deaths a year. An enormous propaganda effort unfolded, led by governments and a whole variety of voluntary associations, for the prevention of sexually transmitted diseases. In the USA, Roosevelt's New Deal pushed a major public health programme centred on the disease.

With the coming of the Second World War, the US government's efforts to protect the health of its troops were redoubled. The American obsession with finding a truly effective cure led to two clinical experiments that later became infamous examples of cavalier disregard for basic principles of medical ethics. In 1942, the US Public Health Service began trials with a carefully selected population of 399 poor black sharecroppers in Alabama who had already contracted syphilis. They were told that they were being treated for '*bad blood*' and were administered mercury, Salvarsan and bismuth in a variety of tests, all of which had unwelcome side effects. Some were given placebo treatments. The study was brought to an end in 1972 after concerned doctors alerted the press. By this time, 28 of the original 399 men had died of syphilis, 100 had died of related complications, 40 of their wives had been infected with the disease and 19 of their children had been born with the disease.

Even more shockingly, in 2010 it was revealed that the US Public Health Service, with the co-operation of the Guatemalan Government, had deliberately infected around 1,500 soldiers, prostitutes, prisoners and mental hospital inmates in Guatemala with syphilis and other diseases between 1946 and 1948 in an attempt to gauge the efficacy of treatment with antibiotics. The courses of treatment were broken off prematurely when the penicillin ran out, leaving many of the subjects to die a painful death. The US Government has since apologised to Guatemala.

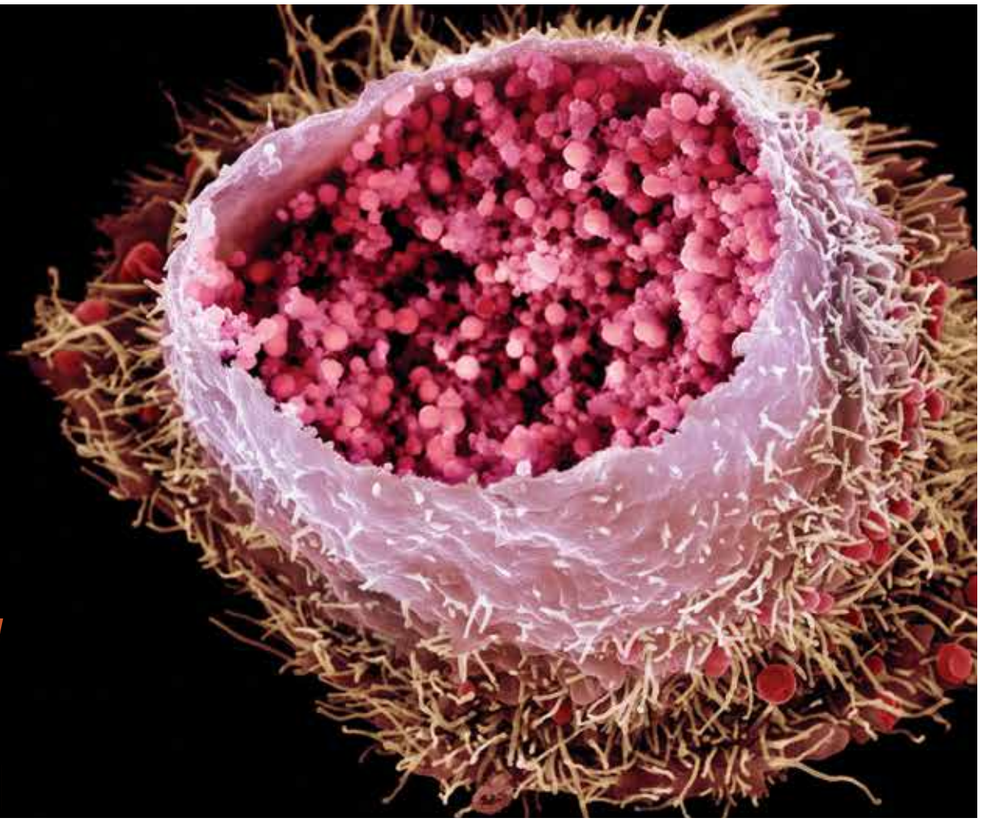
From the early 1950s, penicillin was used as a treatment and proved highly effective. Yet from the 1960s onwards, with the advent of the contraceptive pill, the incidence of the disease began to increase again. In 1999, there were 12 million cases reported worldwide. While war and conflict continue to rage in various parts of the world, syphilis, which has been associated with unrest from the very beginning, will continue to wreak havoc on humankind, despite all the efforts to prevent and eradicate it.

SIR RICHARD EVANS
Regius Professor of History and President of Wolfson College, Cambridge CB3 9BB; *Email* rje36@cam

Known-knowns, known-unknowns and unknown-unknowns: the mysteries of *Chlamydia*

NICHOLAS R. THOMSON

The difficulty in growing and handling *Chlamydia* in the laboratory has always hampered study of this important bacterium. However, recently genomics studies have allowed re-assessment and re-interpretation of what we thought we knew.



Coloured scanning electron micrograph of a cultured human cervix cancer cell infected by *C. trachomatis*. *Science Photo Library*

CHLAMYDIA TRACHOMATIS is an important and fascinating bacterium from many viewpoints. It is well known that chlamydia is the most prevalent bacterial sexually transmitted infection (STI) in the world, and in the UK costs the NHS up to £100 million every year (www.chlamydiascreening.nhs.uk). It also belongs to a bacterial order whose members exhibit some unique biology, which has been uncovered by exquisite experiments using cell culture, microscopy and immunohistochemistry. Despite its importance, until recently we have understood little about the natural history and evolution of this organism – a fact that is starting to be addressed through whole-genome sequence analysis. The application of new sequencing technologies has provided evidence that many of the established dogmas that have influenced a generation of researchers and epidemiologists alike, such as the notion that *C. trachomatis* does not recombine, turn out to have been based on unsafe assumptions or are simply wrong. This article will provide an introduction to the organism and the disease and will focus on recent insights into the biology of *C. trachomatis*, made possible by the falling costs of DNA sequencing.

WHAT WE NOW KNOW ABOUT THE BACTERIUM

C. trachomatis was first described in 1907 by Halberstaedter and von Prowazek who

presented beautiful hand-drawn figures showing infected stained conjunctival epithelial cells with '*intracytoplasmic vacuoles*' containing small and large particles. These sacks filled with *C. trachomatis* cells are now known as inclusions and the small and large particles are the two forms of *Chlamydia* cells, known as the elementary body (EB) and reticulate body (RB), respectively (Fig. 1). These cell types and structures are part of the distinct biphasic developmental cycle exhibited by all members of the order *Chlamydiales*. In brief, the infectious, but non-replicative, EBs bind to the host cell and are endocytosed. Once internalised, they are sequestered into specialised vesicles, the inclusions, where the EBs differentiate into larger, metabolically active and replicative RBs. After about 2 days, the RBs begin to revert back to EBs before being released into the milieu following host cell lysis where the infectious cycle continues. It is largely because of this complex developmental cycle that the true nature of *Chlamydia* has remained such a mystery for so long. From the early 1900s until as late as the 1960s, *Chlamydia* was thought to be a virus because it could not be grown in artificial medium and because the EBs are so small (0.3 μm) that they can pass through bacterial filters. The then known 'trachoma virus' was first isolated in 1957 having been grown in embryonated chicken eggs and Koch postulates were fulfilled by 1958, but only in the late 1960s was it clear that the causative agent was a bacterium (see www.chlamydiae.com for an outstanding account of chlamydial biology).

> " It is the obligate intracellular nature and difficulty in growing and isolating this organism that has presented one of the main challenges of working with *Chlamydia*. "

It is the obligate intracellular nature and difficulty in growing and isolating this organism that has presented one of the main challenges of working with *Chlamydia*. In equal measure, the lack of a system with which to transform this bacterium has considerably hampered research, meaning that there are no molecular tools with which to study gene function; however, this is beginning to change.

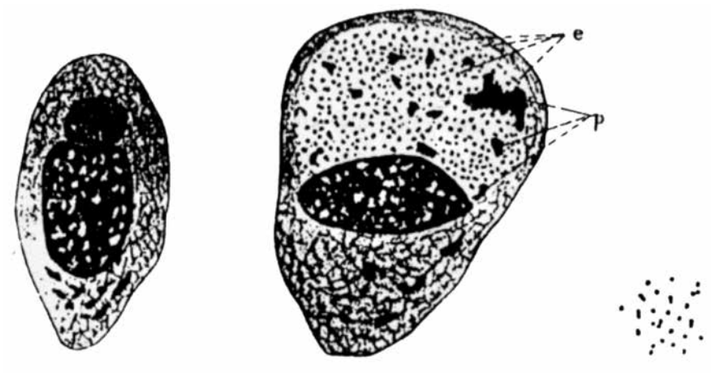


Fig 1. **Halberstaedter and von Prowazek's historic drawings from 1907 of a normal conjunctival epithelial cell (left), an infected cell (centre) and free chlamydial particles (right).** *Taken from www.chlamydiae.com*

HOW DOES C. TRACHOMATIS IMPACT ON HUMAN HEALTH?

There are two biovars of *C. trachomatis*. The first, the trachoma biovar, is characterised by causing localised infections of the epithelial surface. This biovar includes the urogenital strains that cause the majority of STIs (there were an estimated 101.5 million new cases among adults in 2005): clinical manifestations range from long-term asymptomatic infections to complications including pelvic inflammatory disease, epithelial scarring and infertility in women and epididymitis in men. Ocular strains also belong to the trachoma biovar and are the leading cause of infectious blindness world-wide with >40 million people thought to have active disease. The second biovar, Lymphogranuloma venereum (LGV), is distinguished by the ability to spread systemically and cause swelling of lymph glands, characteristic of a bubonic disease.

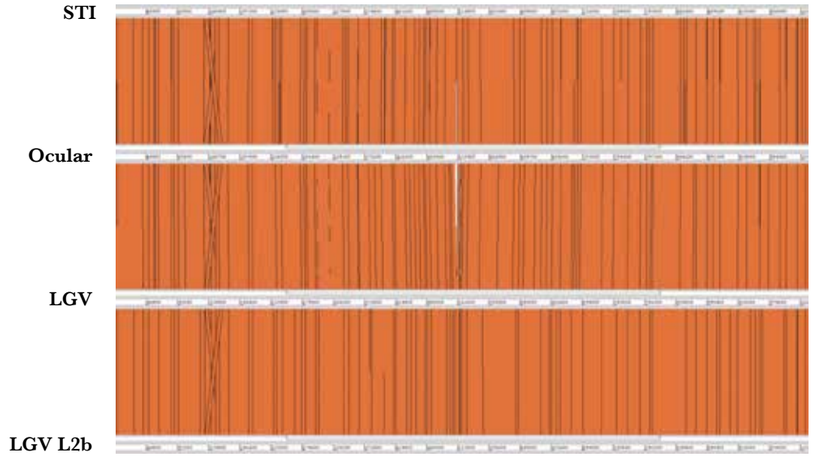


Fig 2. **ACT (Artemis Comparison Tool) comparison of the amino-acid matches between whole *C. trachomatis* genomes, representing ocular (Strain Har-13), urogenital (strain UW-3) and LGV strains (strains L2 and L2b; L2b was originally thought by some to be a new variant causing disease in men who have sex with men). The genome comparison shows few differences between the strains, except for a small region (white) in the middle of the genome. This is despite the clear differences in disease and site of infection between strains.** *Software is available free at www.sanger.ac.uk/Software/ACT*

Currently, these biovars are subtyped based on the sequence of the *ompA* gene, encoding the primary surface antigen. Based on *ompA*-typing, *C. trachomatis* can be subdivided into >15 genotypes: the ocular strains include genotypes A to C, the urogenital strains include genotypes D to K, and LGV includes genotypes L1, L2 and L3 and the new variants L2b and L2c.

WHAT HAVE WE FOUND THROUGH GENOMICS?

By comparing the genomes of single ocular, urogenital and LGV strains, it was apparent that *C. trachomatis* has a small conserved genome of around 1.1 Mb, containing approximately 900 genes, which shares a high level of synteny and sequence conservation between strains and has very few 'whole-gene' differences. It is clear from its genome that the species has followed a reductive evolutionary path, losing functions that are likely to have been important for growth outside of the host. There have been new discoveries, such as a Type III secretion system and the presence of the machinery necessary for recombination, which was surprising for a bacterium that was once thought not to recombine. More fine-scale differences between the urogenital and ocular strains include the possession of a functional cytotoxin remnant and an intact tryptophan synthetase gene, both of which have been used to explain differences in preferred infection site. Despite the clear differences in disease outcome, in general, the contents and architecture of the genome are highly conserved at this level between ocular, urogenital and LGV strains, leaving no obvious smoking gun but some subtle differences (Fig. 2).

WHAT WE KNOW ABOUT CHLAMYDIAL POPULATIONS

To provide the power to interpret the fine-scale differences between biovars, bacterial genomics has recently turned towards large-scale population-based sequencing projects. In the past 2 years, more than 58 genomes of all genotypes have been published by us and others. This number is small compared to sequencing studies of many other bacteria, reflecting the difficulty in growing and handling this organism. Despite this, these new data rephrased what we thought we knew about *C. trachomatis*.

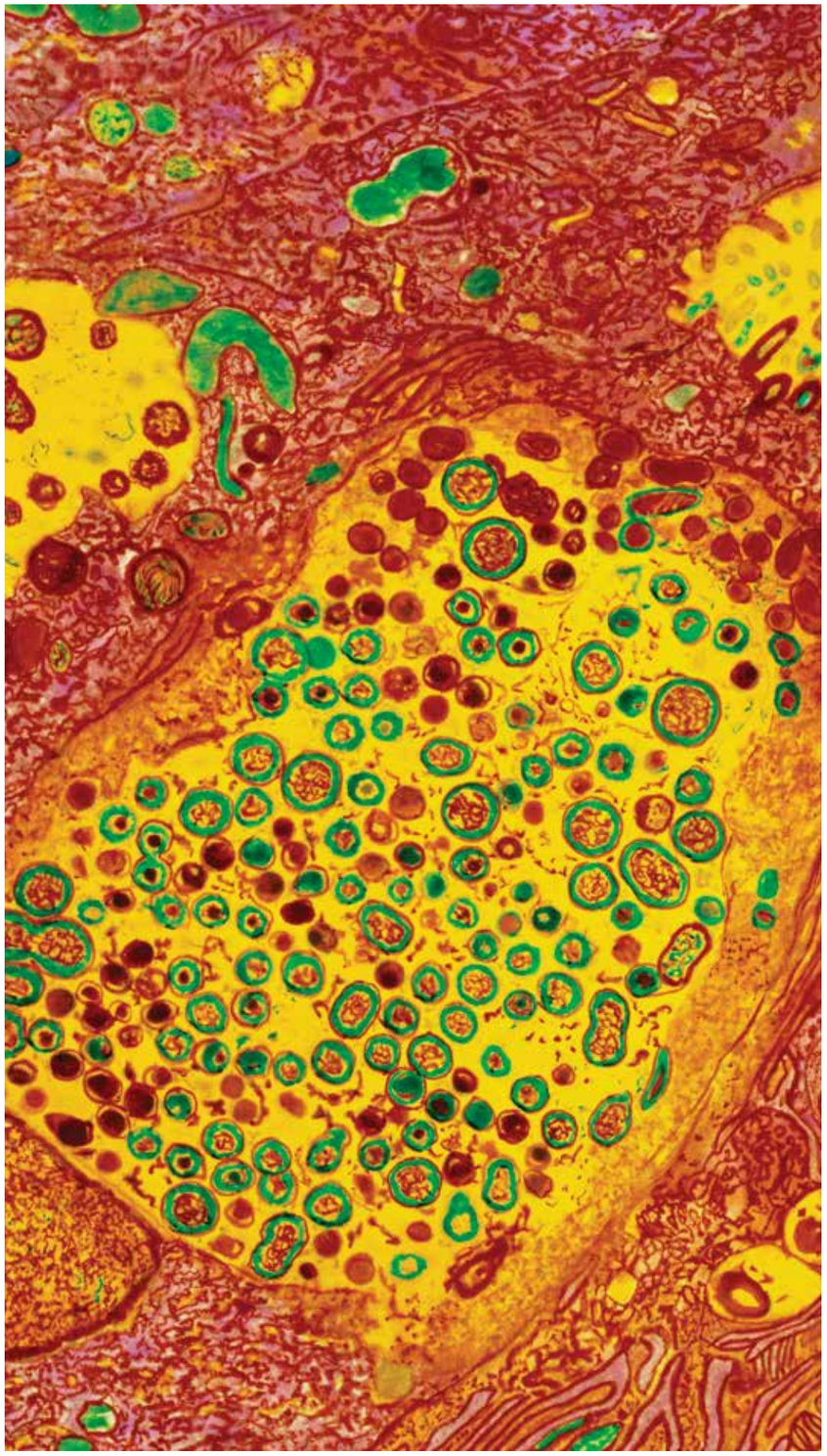
In our work, we looked at a global panel of strains representing all disease-causing *C. trachomatis* variants. We showed that LGV strains form a separate clade exhibiting low diversity, with the urogenital strains split into two distinct clades, T1 and T2 (T stands for trachoma), with T1 also including the ocular strains. Over the last few years, it had become clear that the dogma relating to *Chlamydia* not recombining may have been an unsafe assumption. From our analysis, there was clear evidence of widespread DNA exchange between clinical isolates affecting different body sites and causing both sexually transmitted and ocular infections. This is exemplified by the *ompA* gene itself, which we showed was a chimera formed by a 'mix and match' process of recombination and exchange, whole or in part, between strains.

Why is this important? The whole-genome phylogeny now provides a robust scaffold upon which to frame *C. trachomatis* biology. It now is clear that we knew little about the true diversity of the circulating *Chlamydia*, as it was effectively being masked by the standard typing methodology. From this phylogenetic framework it is now relatively straightforward to spot genetic regions that have been exchanged and so it's clear that co-infection with two

different types of *C. trachomatis* may not be as rare as previously thought. Following on from this, the barriers that we assumed would prevent recombination, such as *Chlamydia*'s closeted intracellular lifestyle, and a strong association between genotype and site of infection, appear not to exist, at least in the way we previously thought. Together, these data have major implications for our understanding of *Chlamydia* epidemiology.

WHAT WE KNOW, DON'T KNOW AND THOUGHT WE KNEW ABOUT *CHLAMYDIA* EPIDEMIOLOGY

Based on traditional assumptions that the *ompA* genotype was a reliable predictor of relatedness, studies looking at urogenital strains have shown that the most common genotypes world-wide are E, F and D. This has led to a pervasive notion that the overall distribution of genotypes is stable, i.e. chlamydia lacks the dynamism displayed by most infectious diseases; this makes little sense. Moreover, using *ompA*-typing there is almost an equal number of studies that have shown an association when looking for links between genotype and the hosts' age, gender, number of sexual partners or clinical symptoms, compared to those that have not. If *ompA*-genotypes occupy unrelated positions on the phylogenetic tree due to recombination, this could explain the disparity between studies. The good news is that by having a detailed population framework for *C. trachomatis*, we now have the tools with which to carry out this sort of analysis and make these associations, should they exist.



Coloured transmission electron micrograph (TEM) of cells sectioned in a woman's fallopian tube, infected with *C. trachomatis*. Spherical Gram-negative Chlamydia bacteria (green/brown) are seen at centre and upper left inside cell inclusions (yellow). *Credit: Dr R. Dourmashkin / Science Photo Library*

One salient tale about the dynamism of *C. trachomatis* comes from Sweden, where, in 2006, some counties noticed a drop in chlamydia cases. A new variant of *C. trachomatis* (nvCT) had emerged that was evading several commercial molecular diagnostic tests based on the presence of specific plasmid sequences. A 377 bp deletion in the plasmid removed the test target, meaning nvCT strains returned a negative diagnosis when a single target test was applied. Despite the apparent drop in incidence, the truth was that failure to detect, and hence to treat those infected with the new variant, had led to a significant increase in cases. In some Swedish counties 20–64% of current infections are now caused by nvCT. A case of Darwinian diagnostic-driven evolution provides the opportunity for the nvCT to evade the test and be promoted to dominance in a short period of time.

> "The whole-genome phylogeny now provides a robust scaffold upon which to frame *C. trachomatis* biology."

WHAT'S NEW? LOTS!

Technologically there have been two recent breakthroughs. The first was by a group in Southampton lead by Yibing Wang and Ian Clarke who have shown for the first time that *Chlamydia* is transformable. Using a simple calcium-chloride-based approach, they successfully introduced a GFP-tagged plasmid into a plasmid-free *C. trachomatis* strain, opening up one of the most significant barriers for chlamydial genetic research. Second, the UK and many other European countries have recently moved away from culture-based diagnosis for *C. trachomatis*, potentially threatening the major source of purified DNA for genomic research. To alleviate this potential problem, we have been successful in developing an approach to sequence directly from clinical samples without the need for culture. In the absence of live isolates and with no routine test-of-cure this is essential if we are to have a possibility of detecting drug resistance if or when it emerges.

In the UK we have been through a period in which chlamydiologist numbers have dwindled; however, there are signs that this is changing. Considering the recent scientific gains and the threat to public health posed by this bacterium, this bodes well.

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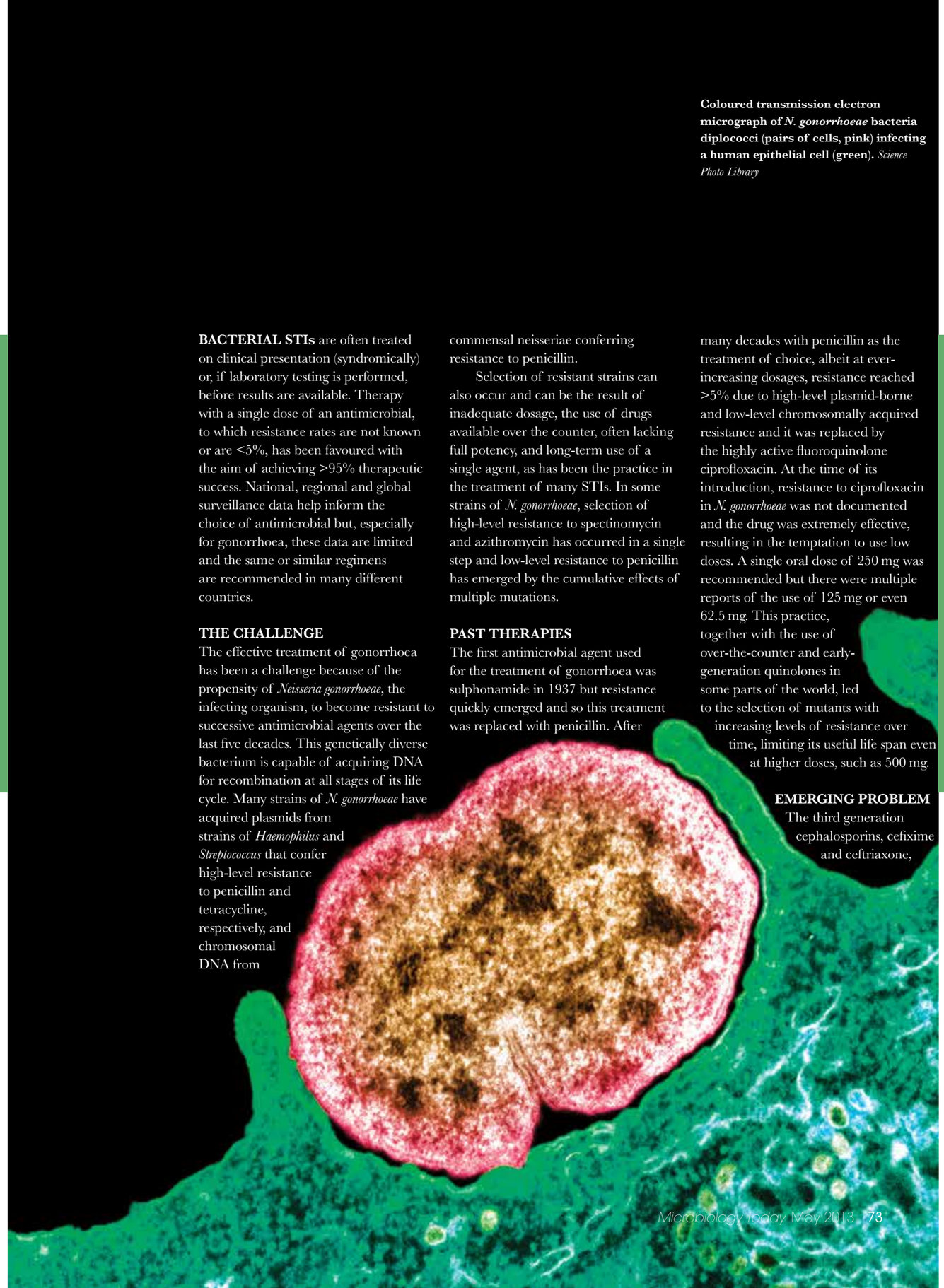
CATHERINE ISON

Antimicrobial-resistant gonorrhoea

the ongoing challenge to ensure gonorrhoea remains a treatable infection

The control of bacterial STIs for public health is dependent on delivery of prevention messages to raise awareness, use of appropriate diagnostic tests to reduce the burden of infection and provision of effective antimicrobial therapy to break transmission. In the absence of an apparent protective immune response, and hence no effective vaccine, antimicrobial therapy is an essential component of control but is often compromised by resistance resulting in therapeutic failure.



Coloured transmission electron micrograph of *N. gonorrhoeae* bacteria diplococci (pairs of cells, pink) infecting a human epithelial cell (green). *Science Photo Library*

BACTERIAL STIs are often treated on clinical presentation (syndromically) or, if laboratory testing is performed, before results are available. Therapy with a single dose of an antimicrobial, to which resistance rates are not known or are <5%, has been favoured with the aim of achieving >95% therapeutic success. National, regional and global surveillance data help inform the choice of antimicrobial but, especially for gonorrhoea, these data are limited and the same or similar regimens are recommended in many different countries.

THE CHALLENGE

The effective treatment of gonorrhoea has been a challenge because of the propensity of *Neisseria gonorrhoeae*, the infecting organism, to become resistant to successive antimicrobial agents over the last five decades. This genetically diverse bacterium is capable of acquiring DNA for recombination at all stages of its life cycle. Many strains of *N. gonorrhoeae* have acquired plasmids from strains of *Haemophilus* and *Streptococcus* that confer high-level resistance to penicillin and tetracycline, respectively, and chromosomal DNA from commensal neisseriae conferring resistance to penicillin.

Selection of resistant strains can also occur and can be the result of inadequate dosage, the use of drugs available over the counter, often lacking full potency, and long-term use of a single agent, as has been the practice in the treatment of many STIs. In some strains of *N. gonorrhoeae*, selection of high-level resistance to spectinomycin and azithromycin has occurred in a single step and low-level resistance to penicillin has emerged by the cumulative effects of multiple mutations.

PAST THERAPIES

The first antimicrobial agent used for the treatment of gonorrhoea was sulphonamide in 1937 but resistance quickly emerged and so this treatment was replaced with penicillin. After many decades with penicillin as the treatment of choice, albeit at ever-increasing dosages, resistance reached >5% due to high-level plasmid-borne and low-level chromosomally acquired resistance and it was replaced by the highly active fluoroquinolone ciprofloxacin. At the time of its introduction, resistance to ciprofloxacin in *N. gonorrhoeae* was not documented and the drug was extremely effective, resulting in the temptation to use low doses. A single oral dose of 250 mg was recommended but there were multiple reports of the use of 125 mg or even 62.5 mg. This practice, together with the use of over-the-counter and early-generation quinolones in some parts of the world, led to the selection of mutants with increasing levels of resistance over time, limiting its useful life span even at higher doses, such as 500 mg.

EMERGING PROBLEM

The third generation cephalosporins, cefixime and ceftriaxone,

> Strengthening our prevention measures, particularly for at-risk groups, is essential to reduce the burden of gonorrhoea. It is paramount that the versatility of *N. gonorrhoeae* is never underestimated.

eventually replaced ciprofloxacin as resistance levels soared; in the UK, this occurred in 2004. Cefixime, an oral agent, was preferred due to its ease of administration, whereas ceftriaxone, an injectable, was used for pharyngeal infections because it was known to penetrate this site more effectively than cefixime. Resistance and treatment failure were not documented in *N. gonorrhoeae* at that time, although past events should have been a warning to the scientific and medical community that it was only a matter of time before this would occur again. The first report of treatment failure to cefixime was in Japan in 2001, probably resulting from the use of a number of other oral cephalosporins, some at suboptimal doses. Further reports of treatment failure were slow to appear but this may have been an artefact, in part, due to the widespread use of molecular testing for diagnosis and the challenge of verifying treatment failure without identifying the infecting organism. Subsequently, treatment failure to cefixime was documented in a number of countries with the first reports in the UK in 2011, although the true prevalence is unknown and was almost certainly greater than is evident.

Surveillance programmes began to describe decreased susceptibility to cefixime but in the absence of sufficient data from treatment failures, the definition of resistance was unclear. This is of concern, particularly in the case of the emergence of a bimodal population, suggesting the establishment of a 'resistant' population. Decreased susceptibility to cefixime has been found to be associated with the acquisition of mosaic *penA* genes, which alter the target site for penicillin and cephalosporins in penicillin binding protein 2 (PBP2). It is thought that these genes may have been acquired from commensal neisseriae present in the throat during pharyngeal gonococcal infection. Mutations in other genes affecting penicillin resistance, such as *mtr* (efflux) and *penB* (porin), have also been implicated but appear to play only a minor role, although full levels have not been replicated in the laboratory, suggesting the presence of an, as yet, unknown factor X. Molecular typing studies indicate that this drift towards decreased susceptibility is clonal and likely to have originated in Japan but is now the predominant strain in many countries and found widely in Europe. In some countries, such as the UK, infection has been found predominantly among men who have sex with men (MSM) but heterosexual infection has also been detected in some countries and may just reflect circulation in different sexual networks rather than a preference of this strain for any particular anatomical site.

INNOVATIVE RESPONSE

Concern began to mount in 2011 that this was the beginning of the end of the useful life of third-generation cephalosporins for treatment of gonorrhoea and consideration was given as to whether a change in therapeutic agent was necessary. There was no precedent for changing therapy before it became <95% effective, as recommended by the World Health Organization, but the potential for gonorrhoea to be difficult or impossible to treat appeared to be becoming a reality. The lack of suitable alternative agents to which *N. gonorrhoeae* was susceptible was limited and left few options for treatment, including use of combinations of drugs, a return to agents used previously such as gentamicin or longer courses of treatment. In the first instance, ceftriaxone, believed to be the more active drug, was the obvious choice as emergence of decreased susceptibility had been slower than for cefixime and only occasional reports of treatment failure had occurred. Also, serious concerns were raised about the logistical problems associated with widespread use of an injectable and the effect this had on compliance, but choices were limited. The recommended dose of ceftriaxone was also controversial as pharmacokinetic data suggested that if a 250 mg dose were to be used, this would likely be useful for only a short time. Higher doses of 500 mg or 1 g are licensed for use and give a greater concentration of the drug and persist for a longer time in the bloodstream, giving the bacterium a greater challenge to overcome before this treatment too would become insufficient.

These concerns resulted in timely changes to guidelines, most recommending ceftriaxone at an increased dose of 500 mg in combination with azithromycin at 1 or 2 g, intended to treat any concomitant *Chlamydia* infection, but also to give additional cover for gonorrhoea if, or when, decreased susceptibility emerged. In 2012/2013, plans were published at a global, national and regional level to raise awareness and give advice on combating the threat of antimicrobial-resistant gonorrhoea and, most importantly, giving guidance on the definition of a probable or confirmed treatment failure.

THE FUTURE

The response to the threat of antimicrobial-resistant gonorrhoea has been prompt, despite some criticism of scaremongering. The emergence of decreased susceptibility appears to have been arrested in many countries, although this is balanced by recent reports of therapeutic failure due to multi-drug-resistant strains, often reported as 'superbugs'. It is impossible to attribute the decline in resistance entirely to the innovative approach taken; it is highly probable that this has delayed rather than reversed the problem but this has bought time for new drugs to be developed and different approaches to treatment to be put through clinical trials. The future strategy needs to be multifaceted and should include the appropriate use of new diagnostic tests and retention of expertise in the isolation of viable organisms to enable both the detection of emerging resistance and the provision of timely surveillance data. Strengthening our prevention measures, particularly for at risk groups, is essential to reduce the burden of gonorrhoea. It is paramount that the versatility of *N. gonorrhoeae* is never underestimated. The challenge is to ensure that gonorrhoea remains a treatable infection.

Use of Etest strips to measure the resistance of bacterial cultures to different antibiotics. *C. Ison*

Albert Neisser (1855–1916), the German physician who discovered and gave his name to *N. gonorrhoeae*. *National Library of Medicine / Science Photo Library*

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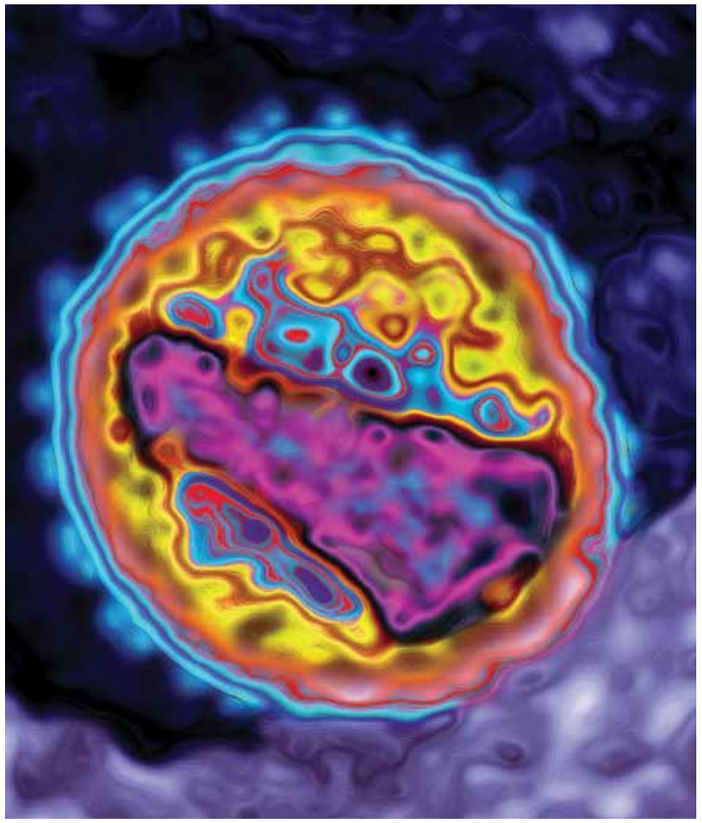
HIV and the 'functional' cure

BEN THOMPSON

Earlier this year there was much media coverage surrounding news that doctors in the US had 'functionally cured' a baby born with HIV, who now no longer needs medication for the disease. Here's a short background explaining the case.

THE RESULTS of this case were presented by researchers at the *20th Conference on Retroviruses and Opportunistic Infections* in March 2013. They described the case of an unnamed child born in Mississippi State to a mother who was unaware of her HIV status until she was tested during labour and found to be positive. Doctors began treating the baby 30 hours after the birth with a cocktail of three antiretroviral drugs, a different treatment regime from the one or two drugs usually given to prevent mother-to-child transmission after birth.

While initial tests showed the child to be HIV-positive, 1 month on the three-drug therapy caused the virus levels in the blood to drop to undetectable levels.



False-coloured transmission electron micrograph of ahuman immunodeficiency virus (HIV) particle, the retrovirus that causes acquired immune deficiency syndrome (AIDS). *James Cavallini / Science Photo Library*

The baby remained on the therapy for 18 months before treatment ceased for approximately 5 months. Normally, a break in treatment causes levels of HIV to bounce back to detectable levels. In this case, much to the surprise of the clinicians, the child's virus levels remained undetectable, although traces of viral genes were detectable.

This is where the word 'functional' in functional cure becomes important; while viral genes were detected, it appears that the child need never take antiretroviral drugs again and is unlikely to be infectious to others. This is clearly a remarkable discovery but currently no one knows how, or why, it occurred. The science is yet to be published in a peer-reviewed journal and it is important to note that n=1.

The circumstances surrounding this case are unusual too. Had the mother known she was HIV- positive, an appropriate treatment regime would have lessened the chances of her having an infected child. The UK Health Protection Agency reported that routine antenatal screening meant that 99% of the babies born to women diagnosed as HIV-positive in the UK between 2006 and 2010 were not infected with HIV (**www.hpa.org.uk/webc/hpawebfile/hpaweb_c/1317131685847**).

Around the same time, in a study published in *PLOS Pathogens*, French researchers demonstrated another functional cure, this time in a group of patients who were part of a 'Viro-Immunological Sustained CONtrol after Treatment Interruption' (VISCONTI) study. Fourteen members of the study (out of a total of 70) who received a standard HIV antiretroviral combination within the first two months of being infected maintained low or undetectable virus levels several years after this long-term drug therapy (**ww.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1003211**).

s before, this is clearly an important result and shows that prolonged, timely therapy can lead to a functional cure; however, it clearly doesn't work for everyone. The science that underpins why certain patients maintain these low or undetectable levels of virus after therapeutic treatment remains unreported. It is potentially of use in sub-Saharan Africa, which saw approximately 1.8 million new infections in 2009, but is a tantalising possibility that remains some way off. This treatment regime (**www.unaids.org/globalreport/documents/20101123_GlobalReport_full_en.pdf**) requires rapid diagnosis and treatment, which is unavailable to many in this region.

Until these findings produce meaningful clinical applications – and this could take years, if not decades – ensuring that people have access to education, condoms, screening and affordable, effective treatment remains the best way of tackling this disease.

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Update on the Society's work on sexually transmitted infections

Sexual health – long-described as '*The Cinderella of Medicine*' – risks missing out on the dramatic advances in basic scientific research that are now shaping other medical fields. This is the argument we plan to make in a forthcoming policy statement on sexually-transmitted infections (STIs), due for release on 3 July 2013.

THE STATEMENT is about research on STIs but it also applies to microbiological research on infectious diseases in general. Microbiologists should, rightly, have a leadership role in the infectious disease field. The statement seeks to reassert that leading role.

WHY STIs ARE A POLICY PRIORITY

Following an extensive scoping exercise based around our policy priorities, the Society for General Microbiology Policy Committee, led by Professor Nigel Brown, decided that microbiological research on STIs needed the boost only a formal policy statement can give.

We are still working on the content and welcome members' views. The statement will likely focus on four major STIs: HIV/AIDS, chlamydia, gonorrhoea, and syphilis. HIV is a virus that destroys the immune system; the others are bacteria that can cause infertility, miscarriage, stillbirth and ectopic pregnancy.

Despite our best efforts to combat these infections by existing methods, new diagnoses have risen in the UK and internationally over the last decade. In the UK, we estimate that the numbers of people afflicted with these four infections are similar to those affected by cancer (around 300,000 people per annum). At the same time, antimicrobial resistance threatens to undermine treatments for gonorrhoea.

As we will point out to readers of the policy statement, microbiological research has been crucial in defining sexual health as a fixable scientific problem, rather than a moral failing. Pioneering bacteriologists discovered the infectious causes of gonorrhoea, syphilis and chlamydia and, as the historian John Lesch has eloquently shown, intensive chemotherapy research in the first half of the last century massively improved the treatment of bacterial STIs and infections in general.

In the 1980s, studies conducted by microbiologists like Professor Robin Weiss, a former SGM President, helped demystify the HIV/AIDS epidemic in Britain at a time when this deadly disease caused understandable fear.

As microbiologists, we know that microbiology matters. It is a vibrant scientific discipline that plays a major role in solving practical problems in healthcare, the environment and industry, as well as responsibly pushing the frontier in areas such as synthetic biology.

Unfortunately, not everyone knows this. This is why the Society, and many of our members, is making the case for microbiology among the broader academic community, policy-makers and politicians through initiatives such as the STI statement.

THE WORK OF THE EXPERT PANEL

To write the statement, we brought together an Expert Panel. The chair was Professor Peter Borriello, member, Editor-in-Chief of the *Journal of Medical Microbiology*, advocate for sexual health and a leading figure in the UK's infectious disease policy, who has briefed government ministers.

Professor Borriello recruited panellists from the key microbiological disciplines (virology and bacteriology), public health doctors, civil servants in relevant departments, representatives from funding agencies and the sexual health charities, a sociologist and a historian of medicine.

As the panellists pointed out, microbiology is inherently interdisciplinary, spanning from the very small (a viral particle or single bacterial cell) to the very large (epidemiology). It transcends short-, medium- and long-term agendas, from immediate practical uses to blue-skies research.

Over two fascinating day-long meetings held in rooms at Portland Place, London, the panel discussed the problems and challenges of sexual health policy and sought to identify key problems that could be solved through research. They then discussed how we could work together to bolster these priority areas.

Microbiology was seen throughout to have a unique and important role as a bridge between the many disciplines contributing to future improvements in sexual health.

THE STATEMENT

Reflecting discussion in the meetings, the statement will identify STI research priorities in four areas:

- Rapid diagnostics for antibiotic resistance
- New therapeutics, vaccines and microbicides
- Emerging threats
- Animal and *ex vivo* models for STIs

The Expert Panel, chaired by Professor Peter Borriello (above), meeting at Portland Place, London. *Ian Atherton, Corbicula Design*

As we prepare the STI statement, we really welcome comments and advice from members as to focus, content and headline topics. Please get any contributions to us soon by emailing our Policy Officer: **w.burns@sgm.ac.uk**

HOW WE ARE LAUNCHING IT

We will launch the statement on 3 July in the Houses of Parliament with the help of Dr Julian Huppert, a research scientist by profession who is also the MP for Cambridge. The launch event aims to draw together influential figures from the academic, policy, funder, health and charity sectors to ask them to back STI research.

The Society for General Microbiology walks the walk and talks the talk. The launch event will kick off our own programme backing STI research, with the Society aiming to support members working in the field through various initiatives, such as a themed session at forthcoming scientific meetings.

The critical role of members in steering this work, through the Policy Committee and the Expert Panel, draws attention to the importance of engaging with the Society and getting your voice heard. Members at all career stages are encouraged to apply to join the Policy Committee and engage with policy work in other ways.

As a first step, why not find out what policy work could mean for you and how you can contribute? There isn't a more important time to help strengthen our subject.

WILLIAM BURNS, SGM

Getting the message out …

The Society for General Microbiology (SGM) leads the way on antimicrobial resistance

Antimicrobial resistance … a catastrophic threat

On 11 March 2013, Dame Sally Davies, the Chief Medical Officer (CMO) for England, published Volume 2 of her Annual Report *Infections and the rise of antimicrobial resistance*.

In this report she makes 17 recommendations. These include better surveillance, the need for rapid diagnostics, better training, the role of vaccination and better management of antibiotic use. The CMO likened the threat of antibiotic resistance to that of terrorism, in that both are threatening global phenomena that require governments to act.

Nigel Brown, President of the SGM, was asked to comment on the report and backed Dame Sally's comments stating that '*Professor Dame Sally Davies rightly flags the issue of antimicrobial resistance to be of national and international concern. Urgent action is required by microbiologists and other scientists to identify and produce new antibiotics, and to tackle the problem of antibiotic resistance and its transmission*'.

'*The SGM brought these issues to the attention of its members in the November 2012 issue of* Microbiology Today. *Our members will be working on understanding infectious disease processes, reducing transmission of antibiotic resistance, helping develop new antibiotics and educating the users of antibiotics about these issues. The techniques of microbiology and new developments such as synthetic biology will be crucial in achieving this.*'

In addition to a quote in the Department of Health Press Release, Nigel was interviewed by BBC TV, BBC World and Sky News; his comments also received extensive media coverage, appearing in 32 online editions of national and international news media from the *Mirror* to the *Independent*.

Nigel also responded, along with other experts, to questions received from Channel 4 viewers after news bulletins. The answers were posted on their website **www.channel4.com/news/superbugs-antibiotics-and-me-the-key-questions.**

The theme of antibiotic resistance was highlighted further at the SGM Spring Conference where the theme of next-generation approaches to antimicrobial therapy was discussed by a panel of experts who took part in TWiM, which was live-streamed. The episode can be viewed at **http://bit.ly/ZBUqQG**

Other SGM members who also commented on the report were Christopher Thomas, Professor of Molecular Genetics, University of Birmingham, and Laura Piddock, Professor of Microbiology and Deputy Director of The Institute of Microbiology and Infection at the University of Birmingham, and Director of *Antibiotic Action*.

If you are interested in the issues surrounding antibiotic resistance, become an *Antibiotic Action* Champion. Champions are needed to get the message out and promote the importance of antibiotics, why they need to be used appropriately and why it is important for new agents to be developed. No experience is needed to become a Champion. Further information can be found at **http://antibiotic-action.com/champions/**

The *Antibiotic resistance; are we getting the message right?* session at the SGM Spring Conference in Manchester. *Ian Atherton*

Are we getting the message right?

The focus on antimicrobials and antimicrobial resistance at the Society's Spring Conference 2013 could not have been more timely …

The *Antibiotic resistance; are we getting the message right?* session at the Spring Conference took place 2 weeks after CMO Dame Sally Davies described the growing concerns of antimicrobial resistance and the lack of new drugs as '*a ticking time-bomb not only for the UK but also for the world*'. Choosing to highlight this issue in her first annual report ensured that the attention of the public, the media, policy-makers, healthcare professionals and pharmaceutical companies remains focused on these concerns and the challenges they raise. Her report highlighted the role of education in combating antibiotic resistance in key user groups, a theme that emerged during the session.

Although scientists, clinicians and researchers continue to play a crucial role in the continuing battle against antibiotic resistance (also see the *Next-generation antimicrobials* and *New approaches to exploit Streptomyces* sessions at the Society's Spring Conference 2013), delegates learned that more work still needs to be done to address the current issues in antibiotic resistance and the continual need for the development of new drugs. Drawing attention to this cause resulted in the launch of *Antibiotic Action*, a campaign that seeks to educate, inform and raise awareness about these pressing concerns. This campaign asks scientists to take an active role in raising awareness by signing a petition, seeking opportunities to highlight the issues of antibiotic resistance and becoming *Antibiotic Action* champions. The campaign has already resulted in more than 10,000 petition signatures and an Early Day Motion in the House of Commons.

Delegates who took part in this session also agreed that scientists should be doing more to raise awareness. Further suggestions included encouraging more scientists to move into government and lobbying for increased funding for research into next-generation antimicrobials. It was also highlighted that improved guidelines may be required for the controlled use and disposal of antibiotics in laboratory environments, including school laboratories that use them.

Talks in this session also focused on educational measures that are already in place in the UK, including the work of the Health Protection Agency, which has long understood the need for antimicrobial stewardship in primary care, including safe and effective antimicrobial prescribing. The session also considered whether enough is being done to educate the next generation of scientists and microbiologists about the issues of antimicrobial resistance and the dearth of new drugs on the horizon. Delegates mapped where biology students, including microbiology students, encounter antibiotics throughout their degree programmes in a workshop at the end of the session. Interestingly, Fresher's Week and visits to campus GPs were picked up as an initial encounter experienced by a significant swathe of the undergraduate student population. The taught curricula, in general, cover antibiotics in lectures and tutorials that outline the mechanisms of natural selection in the environment, antibiotic biosynthesis and antibiotic resistance mechanisms and their use in combating bacterial infections. In addition, a significant amount of teaching involves the use of antibiotics in practical classes and research projects.

Although the message about the issues of increasing antibiotic resistance and decreasing antibacterial drug discovery already exist, the consensus was that there is room for improvement in this respect. Teaching should also cover the history of antibiotic discovery, the present day concerns and the future impacts in society associated with antibiotic resistance. In addition, teaching about antibiotics could be more cohesive throughout undergraduate curricula. Suggestions to facilitate this included improving teaching materials, including textbooks, and providing clearer safety guidelines on the use of antibiotics in practical classes and research projects. Finally, it was felt that guidelines for lecturers to teach about antibiotic resistance in a variety of curricula should be a necessary part of accreditation of biological sciences degree programmes by learned societies.

LAURA BOWATER, University of East Anglia; *Email* laura.bowater@uea.ac.uk

Learn about the TARGET toolkit, a web-based educational resource housed on the General Practitioners website: **www.rcgporg.org.uk/targetantibiotics**

Sign the petition and find out more at the *Antibiotic Action* website: **www.antibioticaction.com**

Read abstracts from the talks at the SGM Spring Conference 2013 at **www.sgm.ac.uk/en/events/conferences/index.cfm/spring-2013-conference**

Blast a Biofilm – a hands-on activity

Blast a Biofilm is an activity developed by Society for General Microbiology members Victoria Marlow and 2011 Microbiology Outreach Prize Winner Nicola Stanley-Wall (based on an idea by Taryn Kiley) as part of *Magnificent Microbes*, an event held at Dundee Science Centre in 2010. This hands-on activity was adopted and adapted by the Society's Education and Outreach Officer for this year's *Big Bang Fair*. Here, we explain how it's done and invite you to have a go!

Model biofilm using lemon jelly and bacteria made from modelling clay. *Vicki Symington, SGM*

Students at the *Big Bang Fair* blasting biofilms. *Vicki Symington, SGM*

AIMED AT CHILDREN and adults with little or no knowledge of microbiology, this activity introduces the concept of biofilms by inviting participants to build biofilms and then attempt to 'blast' them away. Focussing on the topic of antibiotics, it helps highlight the healthcare-associated problems posed by biofilms. This activity works well in the classroom and at public science events.

GETTING STARTED

First, establish prior knowledge of microbes or biofilms by discussing common biofilms and any familiar features, such as their sticky appearance for example, leading on to an understanding that the sticky matrix that holds biofilms together protects them from antibiotics and, in the case of biofilms on or in the body, the host's immune system.

BIOFILM BLASTING WITH MAGNIFICENT MICROBES

In their natural environments, bacteria do not often exist as the single isolated bacterial cells that are observed in laboratory cultures. In nature, they live in highly organised communities called biofilms.

A biofilm is an encased community of microbial cells that are attached to a surface by a gelatinous adhesive, which the microbial cells excrete. The adhesive consists of extracellular polymeric substances (EPS) that provide a matrix for the microbes, holding them together as well as anchoring them to surfaces.

Micro-organisms in biofilms are protected from many forms of chemical treatment (antibiotics, biocides and disinfectants), grazing organisms and – where relevant – the host's immune system. The biofilm provides microbes with nutrition, gas exchange and a system for removal of waste products.

To build your biofilm you will need:

- Model microbes of different colours, shapes and sizes (these models can be made from modelling clay - we used STAEDTLER® FIMO® modelling clay) (*see image on left*)
- Hair gel labelled 'matrix'
- A high-sided tray to contain the activity
- 1–2 plastic containers

To blast your biofilm you will need:

- A water pistol (what else!) labelled 'Antibiotics'

To set up the activity:

- place the containers upside-down inside the tray (these will be the surfaces to which the biofilms will attach). Have your 'microbes', 'antibiotics' and 'matrix' close to hand.

GET BLASTING!

Make and blast biofilms by:

- Placing microbes onto the plastic containers
- Covering one set of the microbes with matrix
- Blasting the microbes using the 'antibiotics', taking care to observe and explain the difference between the presence and absence of matrix

During or following the blasting, you may like to discuss the positive and negative implications of biofilm production, along with where you may find biofilms.

The resistance of biofilms to antibiotics can be directly compared to planktonic microbes in this hands-on activity and can contribute to knowledge and an understanding of microbes to support curriculum-related topics and enhance understanding of this important area of microbiology.

Blast a Biofilm is currently being developed into an educational resource by Nicola and Victoria.

BLASTING BIOFILMS AT *BIG BANG*

This activity, developed by Nicola, Victoria and Taryn, can be used to effectively communicate messages such as the importance of good oral hygiene. We took the opportunity to partner this activity with our comic – ***Marvellous Microbes: A trip to the dentist*** – for our activity at the *Big Bang Fair* this year.

We adapted the activity by using strips of ice-cube trays to represent teeth and, when blasting with water pistols, discussed the action of saliva in the mouth. We also used some giant toothbrushes to brush the bacteria away!

PLAQUE ATTACK!

In addition to *Blast a Biofilm*, we offered *Plaque attack: giving bacteria the brush off*, an activity to demonstrate removal of plaque (simulated by using a thick cornflour and water paste) from giant teeth models and from the teeth of phantom heads (kindly supplied by A-dec) using manual, electric and giant toothbrushes. In this activity, we talked about the different environments in the mouth where plaque may 'hide'. We also showed the effect of toothpaste (and plaque acid) on teeth using eggs as models (see the 'Egg-speriment' which accompanies the *Marvellous Microbes* comic strip, available to download from our education website).

Ice-cube trays represented 'teeth' and hair gel (or 'matrix') was used to hold the 'biofilm' together before being blasted away using water pistols of 'saliva'. *David Bradley, SGM*

When talking about biofilms, you could even make a model biofilm using lemon jelly and some of the model bacteria as shown in the figure (centre). (*Immunology News*, August 2012).

These activities require no specialised equipment and provide simple, fun ways to introduce this familiar area of microbiology, clearly developing an understanding of the importance of microbes and biofilms in our everyday lives. If you are interested in having a go with any of these activities yourself, get in touch with our Education Office for advice (**education@sgm.ac.uk**).

VICKI SYMINGTON, SGM

Advice for Job Seekers – managing your online presence

The professional image you present to potential employers is no longer measured solely by your CV, covering letter and what your referees say about you, it is also based on how you present yourself online. In this article, Karen McGregor, SGM's Membership Services and Grants Officer, gives some tips on how to make your online image enhance, rather than detract from, the image presented in your CV. And to ensure that you, and your potential future employers, like what you see.

THERE ARE MANY REASONS why you might have an online presence:
Professional – for example, to publicise your research to the general public or others in your field, to network and instigate collaborations for use in your current role, to engage with key groups or to use it as a career tool to help you find potential jobs.
Social – for example, to engage with family and friends or to promote an activity or hobby you are involved with outside of work.

If you are about to start looking for a new job, now is the time to review your online presence and check it is communicating the message you want it to. Left on its own, your online profile will be hugely incomplete or obsolete.

Google yourself. After all, how can you manage your online persona without knowing what is out there in the first place? Remember that most people (including a busy potential employer) will likely only look through the top ten search results to make decisions about you. Try different search terms, for example, googling 'Karen McGregor' might make you think I'm a Canadian who writes books on inner wisdom – I'm not – whereas googling 'Karen McGregor microbiology' brings up links to my current role, my *Twitter* and *LinkedIn* pages.

What if you don't find 'you' in a Google search? If your name is John Smith or Britney Spears there is little you can do to get 'you' appearing in the top results of a search solely based on your name. You need to look for ways to distinguish yourself from others with similar names or roles. Using your full first name and/or middle initial (e.g. Jonathon P. Smith) in your online profiles and on your CV would lead a potential employer to use this as their search term and more likely bring up the results you want.

PhD students and postdocs may have an online presence courtesy of their University or employer – use this. However, the page may be standardised. Having your own online profile means you are in control of it and you can use it to show more of your personality than you would do in a CV. Where possible, link one type of presence to others; for example, include links to your official employer's website and *Twitter* on your *LinkedIn* page. There is an increasing number of choices of digital profile sites, including some specifically for researchers. Look at what tools colleagues and peers in your area are using to see what works well or poorly in their online presence but don't get too carried away with setting up multiple sites. Unless you are certain you have the time to maintain them, it is better to have one complete, up-to-date site than 10 half-baked ones.

What if you do find 'you', but not one that you want potential employers to see? You shouldn't rely on privacy settings in social media to protect your personal data or to segregate your professional and personal profiles. Likewise, even if you have asked a friend to un-tag you from an embarrassing photo, remember it is still online. Basically, never put online anything you would not want a supervisor or future employer to see. It is unfortunate that a stray or intentional remark about you from a friend, former colleague, former spouse or even just someone who shares your name could dominate your online presence and there may be little you can do about it. Hopefully, setting up 'good' sites and linking them will move these to the top of Google search results and move any 'bad' content down to a page that may not be looked at. There are various free tools for the purpose of linking your profile sites. One is **about.me** (see http://about.me/karen.mcgregor for an example page). You could include a link to such a page on your CV to allow employers to readily find 'you' and your complete professional online presence.

Finally, remember that managing your online presence and building your professional profile is a continual process. Now you've got your online presence communicating what you want it to, keep it up and build on it.

KAREN McGREGOR, SGM

DIGITAL PROFILE SITES FOR RESEARCHERS

Googlescholar – you can set up a profile so it generates search results for your name.

Academia.edu – for sharing research papers.

figshare – for sharing research (what worked and what didn't).

Mendeley – a reference manager and academic social network.

ResearchGate – a kind of *Facebook* for scientists.

FURTHER READING

Social media: A guide for researchers **www.rin.ac.uk/our-work/communicating-and-disseminating-research/social-media-guide-researchers**

LinkedIn for Beginners. M.-K. Looi & B. Carter. March 2013. **http://wellc.me/linkedincrib**

LSE impact 'how to' guides. **http://blogs.lse.ac.uk/impactofsocialsciences/category/how-to**

You've been Googled: what employers don't want to see in your online profile. *Guardian* 12 April 2011. **http://careers.guardian.co.uk/careers-blog/google-online-searches**

Nitrozac & Snaggy – Geek Culture (www.geekculture.com/joyoftech/joyarchives/1041.html)

Voice of the Future

Four outstanding young Society for General Microbiology members met MPs and government scientific advisers at the annual *Voice of the Future* event in Parliament this March. They heard first-hand – and minus the usual journalistic spin – what our political leaders think about science. Here they record their experiences.

RECENT EVENTS, such as the H5N1 influenza censorship dispute, drew my attention to the challenging and often abrasive interface between politics and science. Compared to other sectors of the UK economy, these two share a particularly unusual relationship with scientists both advising on policy decision-making, whilst simultaneously having their own working environment affected by such decisions.

Considering this, it was a fantastic opportunity to be able to attend the *Voice of the Future* event courtesy of the Society for General Microbiology. Bringing together a range of political figures, from the Government Chief Scientific Advisor to Select Committee members and David Willetts MP, gave insight into the whole spectrum of scientific influences within government.

Putting young scientists centre-stage meant that a huge breadth of questions were thrown into the debate, ranging from gender inequality issues to the technicalities of a manned mission to Mars. The responses revealed some of the compromises required to balance UK scientific strategy, as well as the power that scientific advice wields over political decision-making.

Within the group of delegates, there was a wide range of backgrounds and it was encouraging to see that the experience gained from the event would be taken back to a range of workplaces and locations across the UK. Personally, I found it very rewarding to hear issues debated in an open and candid atmosphere, especially those affecting my own career. It was a pleasure to meet the other participants and reassuring to find that many of the challenges facing working scientists are shared, giving hope that, through consensus, we can bring about change. I appreciate the Society's support for young scientists such as myself in attending events like this, providing an invaluable opportunity for us to broaden our horizons.

BEN BLEASDALE

Ben Bleasdale.
William Burns, SGM

Leena Nieminen.
William Burns, SGM

IT WAS REALLY ENJOYABLE to be able to take part in the recent *Voice of the Future* event at the House of Commons. Sitting on the chairs normally reserved for MPs and questioning those with responsibility for Government research budgets gave me, and others in the science community, a real sense of power. The speaker of the House of Commons, the Rt Hon John Bercow MP, whose warm words of welcome made one feel respected and privileged to be sitting within a great institution, opened the event. The live broadcasting by BBC Parliament added its own excitement to the day and the fact that the session was also broadcast via the internet meant that my parents at home in Finland could tune in without leaving their living room. I was positively impressed by the interest the attending MPs showed towards science and technology. For me, the highlights of the 2.5 h question time included discussions about landing on Mars and around cloning human beings. The scope of questions also allowed me to enjoy a debate on a subject that is close to my heart, namely antimicrobial resistance, which was jokingly referred to by a speaker as '*the problem with bugs*'. One notable aspect, which was highlighted throughout all the sessions of the day, related to issues around gender equality within science. It was clear from discussions at the event that our field faces an array of issues, both scientific and social. From what I saw, I can rest assured that our politicians and their advisors are aware of these issues and are keen to engage. All that is left now is for us scientists to get out and engage with policy-makers, who decide ultimately what the nation's scientific funding priorities are.

LEENA NIEMINEN

Scott Nicholson.
William Burns, SGM

Alison Graham (*2nd from left*).
William Burns, SGM

I WOULD LIKE TO THANK the Minister for Universities and Science, the Shadow Minister for Universities and Science, the Government's Chief Scientific Adviser, Sir John Beddington, and the honourable members of the Select Committee on Science and Technology for attending the *Voice of the Future* 2013 event.

I spoke on the rise of antimicrobial resistance and the urgent need to discover new drugs to prevent humankind entering a 'post-antibiotic-era'. I was reassured to hear Sir John Beddington's concern at the event and glad that he had already mentioned antibiotic resistance when answering a previous question regarding scientific challenges.

I personally have a large involvement in local politics and stood for the first time as a candidate for city council last year. Within my political party, there is a great amount of work being put in to field candidates that have had a job outside of politics. One thing that the event did highlight for me is that as successful as people like Sir John Beddington have been, scientists are only advisors to government and do not make the decisions themselves. The event has really inspired me to continue in my pursuit of elected office and perhaps, one day, use my knowledge of microbiology to help make informed scientific policy decisions.

In addition to this, it was good that the event took place during National Science and Engineering week as I think it is fantastic that such a constructive dialogue is looking to be built between Parliament and our nation's young scientists and engineers. I hope that in the future, the outcome of Sir Andrew Witty's review exploring how universities can support growth in their regions by working with organisations such as Local Enterprise Partnerships, will recommend investment to allow young scientists like those at the event to link research with our nation's decaying productive capabilities in order to kick-start much needed regional economic recovery.

SCOTT NICHOLSON

I AM VERY GRATEFUL to the Society for General Microbiology for giving me the opportunity to attend this event. One of the highlights was being able to interact with policy and decision-makers first hand. It was very interesting to see how the witnesses responded to the questions and the themes of the questions as they reflected the current concerns of the scientific community. Issues that were raised repeatedly included antimicrobial resistance, the career development of young scientists, women in science, the impact of fees on the next generation of graduates and priority areas for science funding. It was great to be able to interact with the witnesses on Twitter beforehand and several seemed to be looking forward to being questioned by scientists!

Members of the Science and Technology Select Committee highlighted the value of good quality work experience to the future employability of science graduates. Stephen Mosley, MP for Chester, described a science degree as a '*fantastic building block*' that allows you '*to do whatever you want to in your future career*' – both are messages that I will certainly be passing on to the students I teach. Meeting the other scientists at the event was also a bonus. By speaking to people who work in policy, including the Society's Policy Officer William Burns, I discovered possible ways to influence science policy and parliamentary discussion that I had not really thought about before. The only downside to the whole event was the lack of time. There were so many questions and so many worthy of follow-up discussion that it could have lasted all day; however, it was Budget Day and most of the witnesses had a busy afternoon planned! I hope the Society of Biology organises a similar event next year.

ALISON GRAHAM

REVIEWS

Intracellular Pathogens 1: *Chlamydiales*

Edited by M. Tan & P. Bavoil

Published by American Society for Microbiology (2012)

US$189.95 pp. 406 ISBN 978-1-55581-674-2

This excellent book offers an in-depth look at the world of the *Chlamydiales* from a basic science perspective. It will be of particular interest to those who have a fascination with these highly successful obligate intracellular pathogens, which cause infections affecting the respiratory tract, eyes and genital tract. Molecular diagnostic techniques revolutionised the detection of *C. trachomatis* in the latter part of the 20th century and this book illustrates how evolving technologies continue to enable a greater understanding of the biology and pathogenesis of these organisms, often challenging our previous concepts.

Chapters from many well-known scientists are clearly written, fully referenced and cover topics including bacterial cell biology, infection and invasion processes from the initial interactions with host cells to gene regulation, protein secretion and the host immune response to the infection. Bacterial persistence is also explored and the authors draw on comparisons with infectious organisms known to persist and cause chronic disease to attempt to explain this as yet unconfirmed (in humans) anomaly. Progress towards a vaccine and ground-breaking developments in the genetic manipulation of this notoriously difficult genus are also discussed and open up exciting new prospects for future research.

This reference book would be extremely useful to any researcher wishing to have a well-rounded understanding of the *Chlamydiales*.

CATHERINE ISON & RACHEL PITT, Health Protection Agency

Neurospora: Genomics and Molecular Biology

Edited by D.P. Kasbekar & K. McCluskey

Published by Caister Academic Press (2013)

£159.00 pp. 294 ISBN 978-1-90823-012-6

A book with this title is bound to attract a biologist's attention. *Neurospora* is one of the great model systems for classical and molecular genetic approaches to many research areas, now supported with post-genomic technologies. It is the ideal book for someone who does not yet work with *Neurospora*, but needs a rapid overview of its 21st century state. This could be either to compare it with one's current organism of choice, or for advanced teaching. Each chapter starts with background then moves swiftly into its topic, taking every advantage of a decade of genome sequence perusal. There are a wealth of diagrams, photographs, genetic maps and tables. A sense of the *Neurospora* research community comes through, including the vital role of the Fungal Genetics Stock Center.

MERIEL JONES, University of Liverpool

Malaria: Methods and Protocols, 2nd edn

Edited by R. Menard

Published by Humana Press (2013)

£112.50 pp. 626 ISBN 978-1-62703-025-0

As anybody who has worked with them will attest, malaria parasites are amongst the more difficult experimental subjects and a methods book such as this is a welcome tool in the quest to better understand and control these key pathogens. The senior authors of each chapter, for the most part, are recognised experts in the malaria field with long track records of successful, and in some cases, pioneering experimental approaches, especially in the notoriously challenging area of parasite transfection and gene manipulation. Very detailed protocols are clearly laid out but the book is not ring-bound to facilitate use at the bench, as is often preferred for this type of volume. A wide diversity of experimental techniques is documented with 41 chapters arranged in 7 sections, ranging from parasite culturing and the biology of different life-cycle stages, through immunology and drug screening, to transfection and latest 'omics' technologies. Particularly in the latter areas, great progress has been made since the first edition of this book appeared in 2002 and all malaria labs would benefit from having this new and updated work on their shelves.

JOHN HYDE, University of Manchester

Practical Bioinformatics

By M. Agostino

Published by Taylor & Francis/CRC Press (2012)

£25.00 pp. 300 ISBN 978-0-81534-456-8

This new text from Garland Science aims to provide a clear practical introduction to modern bioinformatics. This is exactly the kind of text that I have been looking for to support my bioinformatics teaching on the York MRes in Functional Genomics, and it should provide good practical guides for using multiple methods to analyse the properties of DNA and proteins, without in-depth descriptions of how the algorithms/software works. Agostino stresses the importance of and need for biological interpretation of the data and critical assessment of the outputs, as one would for any laboratory experiment, which is something I constantly strive to get through to my students. To minimise the entry barrier for using bioinformatics, the author uses only free Web-based tools and even gives nice examples of how to use the Find & Replace command in Word to solve simple data formatting problems. There is really good coverage of the many flavours of BLAST, multiple sequence alignments and common tools for DNA and protein sequence analysis, with clear and interesting worked examples and critical analysis of outputs.

My only gripe with the text is that it is highly human-focused, especially the later stages, and prokaryotes and other microbes get rather forgotten. The chapter on 'Browsing the Genome', for example, does not mention a prokaryote nor does it mention Artemis, the workhouse platform for annotation and analysis of bacterial genomes, even though this can be run via the Web. My ideal text would have a good balance of both prokaryotic- and eukaryotic-appropriate methods and so I can't totally recommend the text to a microbiological audience. However, it is still a very useful resource, which I'll no doubt refer to for teaching purposes as many of the methods are generic and organism-independent. I also learnt that I've been mispronouncing Entrez for over a decade!

GAVIN THOMAS, University of York

Molecular Genetics of Bacteria, 4th edn

By L. Snyder, J.E. Peters, T.M. Henkin & W. Champness

Published by American Society for Microbiology (2012)

US$129.95 pp. 728

ISBN 978-1-55581-627-8

This is the 4th edition of a highly successful, fairly advanced text on bacterial genetics. It does not disappoint. Tina Henkin and Joseph Peters have joined forces with Larry Snyder and Wendy Champness to produce a highly relevant, up-to-date, accurate, readable and comprehensive text. No other text on the genetics of bacteria has the experimental background to support the knowledge that this book provides. New material, such as the sections on bacterial cell biology and the cell cycle, phage genomics, phage defence and an expansion of the chapter on homologous recombination, is all to be applauded. Although there is some historical material left out, detailed descriptions of some remain, such as Crick's brilliant elucidation of the triplet nature of the genetic code. There is also quite a lot of re-organisation; all the information on gene regulation is now together in one chapter and all the content on protein secretion is together in another. Importantly, the book is not all about *E. coli*; there is a broad range of paradigms described from other bacteria (cell cycle, sporulation, global regulation) and, where relevant, useful comparisons of processes within their eukaryotic counterparts. This is a book for teachers, microbiology research students and early career researchers and PIs. As with the previous editions of this book, I cannot recommend it too highly.

MARGARET SMITH, University of York

COMMENT

Sepsis – barriers to treatment and solutions to overcome them

Sciepro / SPL

RON DANIELS

Sepsis is defined as the body's response to an infection, which, if not treated promptly causes multi-organ failure and death in over one-third of sufferers. Infections causing sepsis are typically community-acquired conditions, such as pneumonia, with healthcare-associated infections making up a minority.

Almost unknown by the public, this killer condition accounts for 37,000 lives lost annually in the UK – more than breast cancer, bowel cancer and prostate cancer combined. Sepsis consumes an estimated £2.5 billion of our NHS expenditure each year.

We might expect, therefore, that sepsis would be a high priority and on the radar of health professionals and commissioners, and that robust system-wide protocols and solutions should exist; in reality, this is not the case. International guidelines govern recommendations for basic care, such as the administration of the right intravenous antibiotic within the first hour after taking samples to identify the infecting organism. In those hospitals prioritising urgent sepsis care in the UK, a simple care bundle known as the Sepsis 6 is used to ensure that all urgent interventions are delivered rapidly. This treatment is associated with a more than 50% reduction in death rate, yet in the UK we currently achieve care to these standards for only 1 in 7 patients with sepsis. If we can transform our system to care appropriately for patients with sepsis, cost savings to the NHS of over £170 million per annum are achievable.

BARRIERS

To better treat sepsis demands more timely identification and a coordinated response. This is hampered by its often subtle onset and an overwhelming lack of awareness among healthcare professionals (sepsis is not a formal component of most undergraduate or postgraduate curricula) and members of the public. The result is that patients present to healthcare late, early symptoms are frequently missed by GPs and other community-based staff, and hospitals respond unreliably. There is also a need for improved coding; sepsis is currently under-recognised and under-reported.

The Department of Health has responded robustly to issues of avoidable harm through the National Outcomes Framework but has focused primarily on harm due to commission – actions by healthcare staff or organisations that have brought about adverse consequence. Harm from omission, conversely, describes episodes where patients are failed through a lack of adequate response or a failure to recognise deterioration. Public sympathy lies with both scenarios, since both cause avoidable harm, and it is about time our attention was also given to both.

A third issue has been the interpretation of the Department of Health's document *Start smart – then focus*. Addressing the very real problem of antimicrobial stewardship, this document has been misinterpreted as demanding a reduction in the use of antibiotics at all costs. Ministers have been under the impression that this document has resolved the issue of antibiotic management – it has not.

SOLUTIONS

Awareness must improve

Earl Howe has recently asked the Academy of Medical Royal Colleges to examine their training provision on sepsis. We need to ensure that this happens and that it is followed through.

Junior doctors, who are the eyes and ears of the medical profession, are exposed to college curricula only after 2–4 years of practise. Their training needs can be met through the national education programme *Survive Sepsis* but at present, undergraduate and early postgraduate training in sepsis is voluntary and unregulated.

It is of equal importance that we address the training needs of nurses, paramedics and other healthcare professionals if we are to deliver transformational change together with heightened public awareness of the early signs of sepsis.

Coding of sepsis can be improved upon. The recent development of the role of Medical Examiner and of the Professional Association of Clinical Coders allows opportunities to develop standard instruction sets in the coding of patients with infective illness, which should be explored.

Systems must change

Domain 5 of the *National Outcomes Framework* aims to improve safety. It is time that this is modernised to encompass avoidable harm arising from inaction. Sepsis is the ideal inclusion to initiate this high profile change, as it is of major impact in health and economic terms, cost-effective therapies significantly improve outcomes and it is measurable.

The UK Sepsis Trust has formed a coalition of professional and patient bodies to help drive change, including the Royal Colleges of Physicians, Surgeons and Nursing, the Intensive Care Society, the College of Paramedics and the Patients' Association. This coalition is ideally placed to work with the NHS Commissioning Board to ensure that a system-wide change is implemented and embedded.

The public message around antibiotics must change

The current interpretation of *Start smart – then focus* is that healthcare-associated infections should be prevented and that people should avoid troubling healthcare services with symptoms of viral infection. While laudable, this is not the only message of the document.

Professional bodies, including the UK Sepsis Trust, the Infection Prevention Society, the British Society for Antimicrobial Chemotherapy and the Intensive Care Society, are now uniting to ensure a common, sustained message is delivered.

We need to work with public bodies to ensure that the real messages of antimicrobial stewardship gets across: (1) no patient should suffer harm due to a preventable infection; (2) the preservation of effective antibiotics to treat patients with known or suspected bacterial infection is of the utmost importance; and (3) identifying and responding rapidly in cases of severe infection is of equal importance to reducing healthcare-associated infection rates.

If you would like to know more about the content of this article, or would like to help the UK Sepsis Trust with parliamentary or Ministerial questions or in a future All Party Parliamentary Group on sepsis, please contact DR RON DANIELS, Chief Executive, UK Sepsis Trust at **ron@sepsistrust.org**