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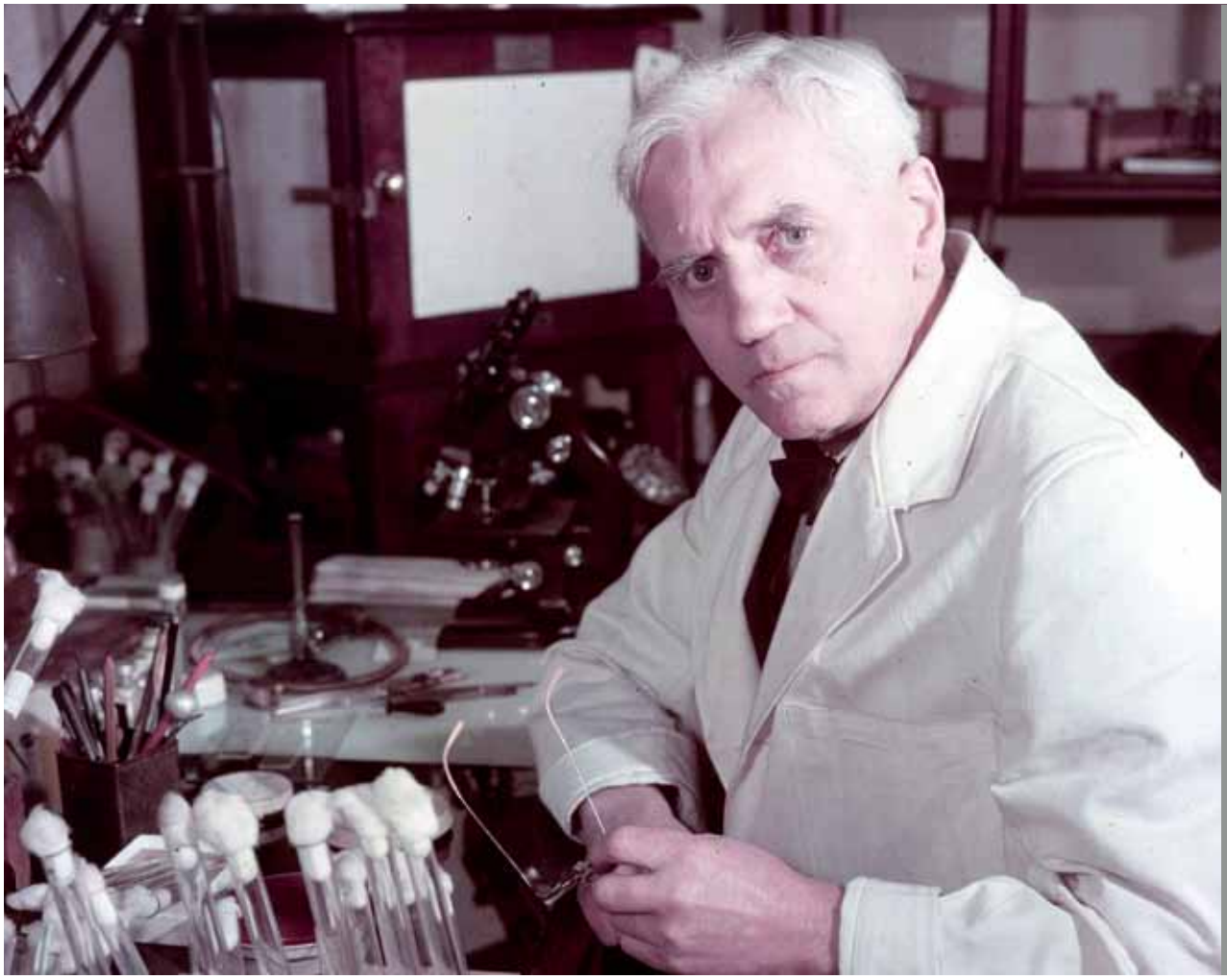

the legacy of fleming

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Cover image Alexander Fleming in his lab in 1943. *Popperfoto / Getty Images*

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SGM Prize Medallist 2009

Dr Stanley Prusiner is the first recipient of the SGM Medal, awarded annually to a microbiologist of international standing whose work has had a far-reaching impact beyond microbiology. He will deliver his talk *Prion biology and disease* on Wednesday 1 April 2009 at the Harrogate meeting.

Stanley B. Prusiner MD, is Director of the Institute for Neurodegenerative Diseases and Professor of Neurology and Biochemistry at the University of California, San Francisco, where he has worked since 1972. He received his undergraduate and medical training at the University of Pennsylvania and his postgraduate clinical training at UCSF. From 1969 to 1972, he served in the US Public Health Service at the National Institutes of Health. Editor of 12 books and author of over 350 research articles, his contributions to scientific research have been internationally recognized.

Dr Prusiner discovered an unprecedented class of pathogens that he named prions. Prions are infectious proteins that cause neurodegenerative diseases in animals and humans. He discovered a novel disease paradigm when he showed prions cause disorders in humans that can be manifest as (1) sporadic, (2) inherited, and (3) infectious illnesses. Dr Prusiner demonstrated that prions are formed when a normal, benign cellular protein acquires an altered shape. His proposals of multiple shapes or conformations for a single protein, as well as the concept of an infectious protein, were considered heretical. Prior to Dr Prusiner's discoveries, proteins were thought to possess only one biologically active conformation.

Remarkably, the more common neurodegenerative diseases like Alzheimer's and Parkinson's diseases have been found over the past two decades to be, like the prion diseases, disorders of protein processing.

Dr Prusiner is a member of the National Academy of Sciences, the Institute of Medicine, the American Academy of Arts and Sciences, the American Philosophical Society, and is a foreign member of the Royal Society, London.

He is the recipient of numerous prizes, including the Potamkin Prize for Alzheimer's Disease Research from the American Academy of Neurology (1991); the Richard Lounsberry Award for Extraordinary Scientific Research in Biology and Medicine from the National Academy of Sciences (1993); the Gairdner Foundation International Award (1993); the Albert Lasker Award for Basic Medical Research (1994); the Paul Ehrlich Prize from the Federal Republic of Germany (1995); the Wolf Prize in Medicine from the State of Israel (1996); the Keio International Award for Medical Science (1996); the Louisa Gross Horwitz Prize from Columbia University (1997); and the Nobel Prize in Physiology or Medicine (1997).

Dr Prusiner holds 50 issued or allowed United States patents, all of which are assigned to the University of California.

New scheme launched – Hayes-Burnet Award

This scheme is offered jointly with the Australian Society for Microbiology and supports the reciprocal exchange of one postgraduate student member to present their research at the other society's main conference, and a visit to a research laboratory in that country.

The award has been developed to strengthen a long lasting bond between the SGM and the Australian Society for Microbiology. It is designed to benefit PhD students in both countries by giving them the opportunity to present their work overseas and experience the best of microbiology in the partner country.

Postgraduate Student Associate Members of the SGM are invited to apply for a limited grant of up to £3,000 to present work at the Annual Scientific Meeting of the Australian Society for Microbiology and make a short research visit of up to 3 weeks at a laboratory in Australia.

The scheme was launched in early December and the closing date for applications for this year is **20 February 2009**.

For further details, see **www.sgm.ac.uk/grants/HB.cfm**

New Honorary Member

Professor Dr Volker ter Meulen

Council has been pleased to confer Honorary Membership on **Professor Dr Volker ter Meulen** in recognition of his long and distinguished service to microbiology and service to the SGM.

Professor ter Meulen was born in 1933 in Osnabrück, Germany, and attended medical schools at the Universities of Münster, Innsbruck, Kiel and Göttingen, qualifying as MD in 1960. Following an internship at the University of Göttingen, he received training in virology in the USA, in the Children's Hospital of Philadelphia. On returning to Göttingen in 1966 he specialized in paediatrics and was also Visiting Scientist at the Wistar Institute for Anatomy and Biology in Philadelphia and the Viral and Rickettsial Disease Laboratory in Berkeley, California. In 1973, on appointment as Assistant Professor and Head of the Department of Clinical Virology, he moved to the Institute of Virology, University of Würzburg, where he became a full Professor and Chairman of the Institute of Virology and Immunobiology in 1975. He retired from Würzburg in 2002 having been Dean of the Faculty of Medicine since 1998.

During his long research career, ter Meulen has worked on molecular and pathogenic aspects of viral infections in man and animals, in particular morbilliviruses, HIV/AIDS, coronaviruses and infections of the central nervous system. He focused on the study of virus persistence in brain tissue. In the late 1960s he was one of the virologists who identified measles virus as the aetiological agent of subacute sclerozing panencephalitis (SSPE) and measles inclusion body encephalitis (MIBE). His work on acute measles encephalitis (AE), MIBE and SSPE, in particular the molecular analyses of measles virus gene expression in brain tissue in these diseases, has provided important insights into the pathogenesis of these diseases as well as into the mechanisms contributing to the silencing of viral gene functions during the establishment of persistent infection in neural cells and to the restricted gene expression in the ultimate stage of the disease processes.

Since virus–cell/host interactions in human brain tissue can only be evaluated in autopsy material, animal models are required to study the events during a CNS infection. To meet this need, ter Meulen established a model in rats in which measles or coronaviruses induce acute or subacute encephalitides, which resemble, to some extent, acute or subacute encephalitides in man. In recent years, ter Meulen and his group have made a detailed study of the mechanisms of measles virus induced immunosuppression, a phenomenon of great clinical relevance.

Professor ter Meulen has been a member of many organizations and on the boards of a range of important international bodies, many of which he has chaired, including the World Health Organization Measles Task Force. Since 2003 he has been the President of the Germany Academy of Sciences, the Leopoldina. His work has also been recognized internationally by many awards and prizes. These include the Max Planck Research Prize (1992), the Emil-von-Behring Prize (2000), the Heinz Ansmann Prize for AIDS research (2002) and the Ernst Jung Medal for Medicine (2003). He served on the editorial board of *Journal of General Virology* from 1975 to 1980, 1982 to 1987 and 1990 to 1995.

MT in the news!

In 2005, member **Keith Jones** of Lancaster University contributed an article on birds and the spread of disease to an issue of *Microbiology Today* themed around 'Microbes in the air'. This was quoted in a recent *Sunday Times Magazine* (4 January 2009) article entitled *Gulls Aloud* which described how these increasingly common birds are becoming a public menace. Keith reported how gulls infected feeding troughs with *Salmonella* and caused an epidemic of abortion in sheep.

MT Editor **Matt Hutchings** has also been in the news. The findings of his research team into how nitric oxide sensors in pathogenic bacteria work at a molecular level were reported in *Times Higher* (11 December 2008).

SGM Council

Nominations 2009

Professors **Neil Gow** and **Petra Oyston**, retire from Council in September 2009. Under the new Articles of Association adopted at the AGM on 9 September 2008, there is one vacancy to fill, for which nominations are invited from Ordinary Members. All nominations must include the written consent of the nominee and the names of the proposer and seconder, both of whom must be Ordinary Members.

Members submitting nominations should indicate the main area of microbiological interest of their nominee, who must have been a member of the Society for at least 2 years.

Nominations should be sent to the SGM General Secretary, Dr Ulrich Desselberger (udesselberger@btinternet.com), or c/o SGM Headquarters to arrive no later than **30 April 2009**.

November meeting highlights

SGM Prizes 2009

Council approved the following awards.

Fleming Prize Lecture Dr Nicola Stanley-Wall, University of Dundee.

Colworth Prize Lecture Professor Geoffrey Gadd FRSE, University of Dundee.

Fred Griffith Prize Lecture Professor Jeffrey Errington FRS FMedSci, Director, Centre for Bacterial Cell Biology, University of Newcastle.

Further information on the recipients of the Fleming and Colworth Prizes is published in this issue on p. 6). Information on the recipient of the Fred Griffith Prize Lecture will appear in a future issue.

The Peter Wildy Prize was not awarded this year due to a lack of nominations.

IUMS Presidency

Warm congratulations were expressed to **Professor Geoffrey Smith FRS**, Imperial College, London, on his election as President-elect of the International Union of Microbiological Societies. He will be President 2011–2014. The announcement was made at the IUMS Congresses in Istanbul in August 2008.

Review of Council composition and functions

The changes proposed by Council (see November 2008 issue of *Microbiology Today*, pp. 160) were accepted at the AGM of the SGM in Dublin in September 2008 and will be implemented during 2009. To accommodate the recruitment of new Officers under the new system from September 2009, Council agreed that the President should chair a subcommittee to search for candidates. SGM Elected Members, Editors-in-Chief of SGM journals, Council Officers and members of the SGM staff are represented on the subcommittee. A report will be tabled and discussed at the next Council meeting in February 2009.

SGM finances

The Treasurer, **Colin Harwood**, reported on the present state of the SGM's finances. This was based on extensive discussions in Treasurer's Committee on the day before the Council meeting. Although the value of the equity component of SGM reserves has decreased due to the global financial situation, the damage has been limited due to the prudent diversification of investments during the year. Council will keep a very attentive eye on the financial situation.

New members of Council

The President welcomed **Professor Mark Harris**, University of Leeds, and **Dr Gary Rowley**, Institute of Food Research, Norwich, to their first sessions as new Elected Members of Council for a period of 4 years.

***Ulrich Desselberger**, General Secretary*

BA changes its name

The BA (British Association for the Advancement of Science) is now the British Science Association, with a new logo. The Association is a charity which works with members, supporters and partners towards a shared vision of a society in which people are able to access science, engage with it and feel a sense of ownership about its direction. The flagship event is National Science and Engineering Week which takes place in March. See **www.britishscienceassociation.org** for details.

BBSRC Industrial Impact Fellowships

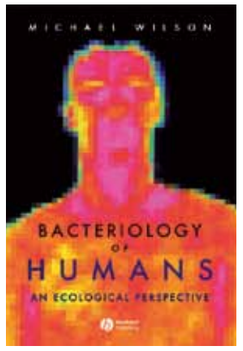
A new scheme to foster technology transfer between industry and academia has been launched by the BBSRC. Applications are now open for professionals in industry for a fellowship to work on the research council's funded projects, programmes and in BBSRC centres, to bring their knowledge, experience and networks to bear on the process of bringing innovations from research to market. The scheme builds on the existing BBSRC Industry Exchange Programme which supports the flow of researchers, in either direction, between the science base and industry. The deadline for applications for fellowships is **26 February 2009**. For further information see **www.bbsrc.ac.uk/business/people_information/industrial_impact_fellowships.html**

People

New Year's Honours 2009

Former SGM Council Member **Professor Anne Glover**, Chief Scientific Adviser for Scotland, has been made a CBE for services to Environmental Science.

Other microbiologists have been made OBEs for their services, including **Professor Philip Scott Mellor**, Head of Department of Arbovirology, Institute for Animal Health, and **Dr Geoffrey Ridgway**, Moortown, Ringwood, Hampshire.



Deaths

Sadly two Honorary Members have died.

An obituary appears on p. 59 of **Professor Naomi Datta**, London, a member since 1952. She was made FRS in 1985 for her discoveries whilst working at the Hammersmith Hospital of mobile genetic elements carrying antibiotic resistance genes in bacteria.

Virologist **Professor Patrick Meenan**, a member since 2002, former dean of the Faculty of Medicine at University College Dublin, and a former president of the Medical Council, has died aged 91. He was closely associated with Albert Sabin and Jonas Salk in developing the polio vaccine and carried out research into influenza, pneumonia and hepatitis as well as poliomyelitis.

The Society also notes with regret the death of:

Dr K.R. Cameron, Cockermouth, Cumbria (member since 1965), **Dr J.J. Cooney**, Plymouth, Devon (member since 1965), **Dr Ralph Lewin**, Scripps Institution of Oceanography (former member, joined 1953), **Joel Mandelstam FRS**, Emeritus Professor of Microbiology at Oxford University (member since 1951) and **Dr Mike Mayo**, Isle of Mull (member since 1969).

Professor Jim Baddiley, University of Cambridge, who joined the Society in 1957 and was a member of Council from 1973 to 1975, has died. An obituary appears on p. 58.

Dr Phil Jones (member since 1975). Mark Stevens writes:

Dr Phil Jones passed away on Friday 2 January 2009. Phil represented the Institute for Animal Health with considerable effectiveness, loyalty and professionalism.

After graduating from Surrey University he joined the Institute for Research on Animal Diseases (now the IAH Compton Laboratory) in 1972 to investigate the role of farm animal and human effluent in the transmission of bacterial diseases including salmonellosis to farm animals. He was appointed Head of the Division of Microbiology in 1990 and his scientific interests until retirement in 2005 included aspects of bovine mastitis, respiratory and enteric diseases of pigs, tuberculosis, gnotobiotics, transgenesis, and bioethics and biosafety. He was a prolific author of high-impact articles and a highly respected figure in the field of veterinary microbiology. Phil also acted as Head of Laboratory at Compton between 1992 and 2005.

Phil created and nurtured a nucleus of respected veterinary microbiology expertise at Compton to act in the national interest and deliver the needs of funders and government. He inspired great loyalty amongst his staff, many of whom now have successful careers in veterinary microbiology themselves. He was a very supportive and warm colleague with a great sense of humour and time for everyone.

Congratulations to …

Professor Michael Wilson, Eastman Dental Institute, has won first prize in the Society of Authors and Royal Society of Medicine Medical Book Awards category for a new authored book for undergraduates or postgraduates. He will receive £1,200 for his book *Bacteriology of humans: an ecological perspective*.

Professor Peter Borriello has been appointed Chief Executive of the Veterinary Laboratories Agency. He was formerly Director of the HPA Centre for Infections, Colindale, London.

Professor Fergus Priest, Heriot-Watt University, has been awarded the Bergey Medal by Bergey's Manual Trust.

Staff

Congratulations to **Ashreena Osman** on the birth of a baby daughter, Danika Rani, on 21 December 2008. Ashreena has been on temporary promotion to Senior Staff Editor of *JGV*, whilst Natalie Wilder has been on maternity leave. We welcome back Natalie to her former role, as Ashreena departs for her own spell of maternity leave.

We also bid farewell to **Lucy Goodchild**, who has been working in the External Relations Office to raise the profile of microbiology to the media. We wish her well in her new post in the press office at Imperial College London.

Prize Lectureships

Colworth Prize Lecturer

Professor Geoffrey M. Gadd FRSE (University of Dundee) will deliver his prize lecture, entitled *Metals, minerals and microbes: geomicrobiology and bioremediation* on Tuesday, 31 March 2009 at the Society's meeting at the Harrogate International Centre. The Colworth Prize Lecture is awarded for an outstanding contribution in any area of applied microbiology.

Geoff works on metal-mineral-radionuclide transformations by micro-organisms, mainly fungi, but also sulfate-reducing and other bacteria. The research has led to an understanding of processes underlying accumulation, detoxification and tolerance, as well as mechanisms that alter metal mobility and fate in the environment. The environmental and biotechnological significance of these phenomena is a consistent focus, particularly in biogeochemical studies on microbial metal and mineral transformations, and in the bioremediation of metal and radionuclide-polluted soil and water.

Geoff gained a BSc (1975) and PhD (1978) in microbiology, University College Cardiff, and after a postdoctoral fellowship in Dundee, with Professor Sir William Stewart FRS, was appointed to a Lectureship in Microbiology (1979). He was promoted to a personal chair in Microbiology in 1995 and became Head of the Department of Biological Sciences in 1999. From 2000, he was Head of the Division of Environmental and Applied Biology (until 2007) and Deputy Research Director (until 2006) in the newly formed School of Life Sciences at Dundee. He is currently Head of the new Division of Molecular and Environmental Microbiology. Publications include over 200 papers, 1 co-written book, 25 co-edited books, and over 40 book chapters. He is the current Chair of the Eukaryotic Microbiology Division of the SGM, and is the Treasurer and immediate past-President of the British Mycological Society. Geoff's research has been recognized by the Berkeley Award of the BMS, a DSc (1994), the Charles Thom Award of the Society for Industrial Microbiology, and Fellowship of the Institute of Biology, American Academy of Microbiology, Linnean Society, International Union of Pure and Applied Chemistry and the Royal Society of Edinburgh.

Fleming Lecturer

Dr Nicola Stanley-Wall (University of Dundee) will deliver her prize lecture, entitled *The complexity of biofilm formation by Bacillus subtilis* on Monday 30 March 2009 at the Society's meeting at the Harrogate International Centre. The Fleming Lecture is awarded for outstanding research by a microbiologist in the early stages of their career.

'My first exposure to micro-organisms came as a PhD student at the John Innes Centre while studying the Tat protein export system in *Escherichia coli* with Professor Tracy Palmer and Dr Ben Berks. During this time I became interested in bacterial behaviour, and after my PhD was awarded in 2001 I moved to Los Angeles to study the intricate methods used by bacteria to form biofilms – complex communities of micro-organisms – with Dr Beth Lazazzera. After almost 5 years in Los Angeles, I was awarded a BBSRC David Phillips Fellowship to establish my own laboratory and moved to Scotland in September 2005 to a lectureship at the School of Life Sciences, University of Dundee. Since then, work in my laboratory has focused on how multicellular behaviour processes are controlled in wild isolates of the Gram-positive bacterium *Bacillus subtilis*.

Grants

Travel and Meetings Grants

Postgraduate Student Conference Grants

All Postgraduate Student Associate Members are eligible to apply for a grant to support their attendance at one SGM meeting each year. Grants contribute towards travel, registration and accommodation expenses. The student need not be presenting their research, so it is an ideal introduction to scientific meetings at little cost to themselves or their supervisor. Applicants must be PG Student Associate Members resident and registered for PhD in an EU country. Closing date for the Harrogate meeting: **27 March 2009**.

President's Fund for Research Visits

Up to £3,000 is available to support early-career microbiologists who are planning a short research visit to another laboratory (minimum visit 4 weeks, maximum visit 3 months). Closing dates for applications: **20 March** and **25 September 2009**.

Retired Member Grants

Cover accommodation and the Society Dinner at one SGM meeting a year. Closing date for the Harrogate meeting: **27 March 2009**.

Scientific Meetings Travel Grants

Support for early-career microbiologists wishing to present work at a scientific meeting in the UK or overseas. Graduate research assistants and lecturers (within 3 years of first appointment in both cases), postdoctoral researchers (within 3 years of first appointment) and postgraduate students are eligible to apply. Retrospective applications are not considered.

SfAM/SGM Short Regional Meeting Grants

Contribution of up to £2,000 towards the costs of running a regional microbiology meeting.

Technician Meeting Grants

All Associate Members who are technicians are eligible to apply for a grant to support their attendance at one SGM meeting each year. Applicants need not be presenting work at the meeting. Some microbiology technicians who are not members of SGM may also apply for a grant to attend a Society meeting. Closing date for the Harrogate meeting: **27 March 2009**.

Education and Development Grants – National

Education Development Fund

Small grants to members for developments likely to lead to an improvement in the teaching of any aspect of microbiology relevant to secondary or tertiary education in the UK. Up to £1,000 is also available to support public engagement activities.

GRADSchool Grants

Postgraduate Student Members who are not eligible for a free place on a Vitae (www.vitae.ac.uk) personal development course (National GRADSchool) may now apply for a grant from SGM to cover full course fees. Retrospective applications are not considered.

Seminar Speakers Fund

Small grants to cover the travel and other expenses of up to two speakers on microbiological topics in annual departmental seminar programmes.

Student Society Sponsored Lectures

These cover the travel and other expenses of up to two speakers on microbiological topics per society each year at student society meetings.

Education and Development Grants – International

SGM-IUMS Fellowships

These provide funding for early-career microbiologists from developing countries to pursue, or complete, part of an on-going research programme in a laboratory in a developed country and/or acquire theoretical or technical knowledge in their particular area of research. See **www.iums.org/Grants/index.html** for details. Closing date: **15 March 2009**.

International Development Fund

The Fund exists to provide training courses, publications and other help to microbiologists in developing countries. In 2008 awards were made to **Professor Simon Cutting**, Royal Holloway, University of London, and **Dr Claude Sabeta**, Onderstepoort Veterinary Institute, Pretoria, South Africa. Closing dates: **20 March** and **25 September 2009**.

The Watanabe Book Fund

Members who are permanently resident in a developing country may apply for funding to acquire microbiology books for their libraries. These annual awards are available as a result of a generous donation from Professor T. Watanabe of Japan. In 2008 an award was made to **Dr S. Gopalakrishnan**, International Crops Research Institute for the Semi-Arid Tropics, Pantancheru, India. Applications for 2009 are invited. Closing date: **25 September 2009**.

Medical Microbiology Support Grants

Elective Grants

Funding for medical/dental/veterinary students to work on microbiological projects in their elective periods. Closing dates for 2009 applications: **20 March** and **25 September**.

Trainee Support Grants

Funding for SGM members carrying out small lab-based microbiology projects during either foundation or speciality postgraduate medical training. Up to £3,000 is available towards the consumables costs of a project. Closing dates for applications in 2009: **20 March** and **25 September**.

SGM has a wide range of grant schemes to support microbiology. See **www.sgm.ac.uk/grants** for details and closing dates.

Enquiries should be made to the:
Grants Office, SGM, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (t 0118 988 1821; f 0118 988 5656; e grants@sgm.ac.uk).

Check out the current schemes, to ensure that you don't miss any deadlines.

Divisional Committee Elections 2009

Under the new system for planning SGM's scientific meetings (described in the November 2007 issue of *Microbiology Today*, p. 146), members of Divisional Committees serve for 3 or 4 years. Some of the founding members of the Committees are due to retire in September 2009, so the time has come to start selection of replacements. There are two routes: the Divisional Committees themselves may nominate candidates, and Ordinary Members of the Society may make nominations. For the Virology, Eukaryotic Microbiology and Prokaryotic Microbiology Divisions nominations must be in the cross-cutting theme in which the vacancy arises. The Irish and Education Divisions do not have cross-cutting themes. All nominees must be members of the Society.

Nominations are now invited for the vacancies shown in the table.

Division: / *Cross-cutting theme*	Virology	Eukaryotic Microbiology	Prokaryotic Microbiology
Microbial diversity and evolution	1 vacancy	1 vacancy	1 vacancy
Fundamental microbiology	1 vacancy		1 vacancy
Translational and applied microbiology	1 vacancy	1 vacancy	1 vacancy
Infectious disease	1 vacancy	1 vacancy	1 vacancy
Division:	Education	Irish	
	2 vacancies	1 vacancy	

All nominations should be seconded by another Ordinary Member of the Society, and include a statement that the candidate is willing to stand, as well as which Division and, where appropriate, cross-cutting theme the nomination is for. A nomination form is available on the Society website at **www.sgm.ac.uk/meetings/divisions.cfm**. Where the number of nominations from the Divisional Committees and Ordinary Members exceeds the number of vacancies, elections will be held.

Nominations should be sent to the Chief Executive, Dr Ron Fraser, at Society for General Microbiology, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (e r.fraser@sgm.ac.uk), to arrive no later than **17 April 2009**.

A list of current members of Divisional Committees is available on the Society website at **www.sgm.ac.uk/meetings/divisions.cfm**

A Royal Society of Biology?

For some years, the Institute of Biology (IoB) and Biosciences Federation (BSF) have operated in parallel, both claiming to be the 'Voice of British Biology'. Many felt it would make more sense, and give a more focussed approach, if the two organizations were to merge, to give a single UK voice for advocacy on generic issues in the biological sciences. Accordingly, an implementation group of representatives of the governing councils of the IoB and BSF has been discussing the way forward, and has drawn up a draft business plan for a combined organization. This was put to Extraordinary General Meetings of the two organizations in early December 2008, and the proposal to move towards dissolving the IoB and BSF, and forming a new single organization, was agreed in principle. Further progress is subject to due diligence by both organizations and satisfactory agreement on the details required to build a sustainable organization with its objectives aligned to the joint inherited objectives of the two precursors.

It is hoped that the new organization will, like the IoB, be incorporated by Royal Charter, and that it may be allowed to use the name 'Royal Society of Biology (RSB)'. The new organization will continue to offer chartered status to individuals who require it, analogous to the CBiol offered by IoB at present to its MIBiols and FIBiols. There are undoubtedly challenges, not least the difficulty of fusing an organization like IoB which has around 12,000 individual members, and BSF where the members are learned societies which are mostly limited companies and registered charities in their own right. But the biggest challenge facing the 'RSB' will be to achieve financial stability, as neither parent is well endowed.

SGM Council recognizes the sense of having a single 'Voice for British Biology' to speak on generic issues, but will continue to speak out for microbiology. SGM is also committed to maintaining its full programme of independent activities in support of our members and the discipline of microbiology. Further Extraordinary General Meetings of the IoB and BSF will be required to agree the next steps, when the governing document of the 'RSB' and refined business plan have been drawn up. An interim council of the 'RSB' has been formed to progress this.

***Ron Fraser**, SGM Chief Executive*

microshorts

Faye Stokes takes a look at some recent microbiological research stories, whilst **Janet Hurst** finds out about Alexander Fleming in *J Gen Microbiol*.

Dirty cash

Liquid Library / Jupiter Images

Bank notes may be reservoirs for 'flu, according to scientists from the National Influenza Research Centre at Geneva University Hospital, Switzerland, who found the human influenza virus survived on Swiss franc notes for as long as 17 days. Although the virus was found to survive on the notes, the researchers did not study whether it could pass from the money onto fingers and cause 'flu.

As banknotes differ in composition from country to country, the scientists couldn't predict whether the findings, published in *Appl Environ Microbiol*, will translate to other currencies.

www.sciam.com/blog/60-second-science/post.cfm?id=dirty-money-can-the-flu-be-passed-o-2009-01-05


Liquid Library / Jupiter Images

Fungal pill could provide asthma relief

Up to 150,000 people suffering from severe asthma in the UK could benefit from taking antifungal medication already available at pharmacies, according to researchers at the University of Manchester. In the study, published in the *Am J Resp Crit Care Med*, the oral antifungal drug itraconazole greatly improved symptoms of asthma in those patients who had allergic reactions to one or more fungi such as *Aspergillus*, *Cladosporium*, *Penicillium*, *Candida*, *Alternaria* and *Trichophyton*. 25–50 % of asthma sufferers probably have an allergy to fungi, but a change in clinical practice to identify them is required before the therapy could be used.

www.eurekalert.org/pub_releases/2008-12/uom-fpc122808.php

Cranberry beats bugs in burgers

Concentrated cranberry has been found to significantly reduce the levels of bacteria in minced meat by scientists in the US. Researchers from the University of Maine found that when cranberry concentrate was added to minced beef inoculated with *Listeria*, *Salmonella*, *Staphylococcus* or *Escherichia coli* O157:H7, the number of bacteria found after 5 days was greatly reduced. Many people already rely on the antimicrobial effects of cranberry to help relieve or prevent urinary tract infections. The research, published in *Food Microbiol*, found that taste-testers noticed no difference in the appearance or flavour of the burgers. The findings could help reduce the risk of food poisoning from burgers and other processed minced-meat products.

www.meatinfo.co.uk/articles/69800/Cranberry-reduces-Ecoli-risk-in-burgers.aspx

Phages used for toxin transfer

Scientists have found a new way that harmful bacteria pass on virulence factors, including toxins and antibiotic resistance. Bacteria are well known for using plasmids to transfer genetic material between species, but a recent study published in *Science* has shown that they may also be able to enlist the help of bacteriophages. Researchers at New York University Medical School used phages for the first time to pass the toxic shock toxin from *Staphylococcus aureus* to *Listeria monocytogenes*. The scientists were surprised when the experiment worked, as this wasn't expected. Phages are normally species-specific, but the findings have raised concerns about other phage-mediated virulence gene transfers.

www.eurekalert.org/pub_releases/2009-01/nlmc-nsd010609.php

Historical highlight

JGM 1955 – Fleming's obituary

Sir Alexander Fleming was the first president of the Society in 1945. On his death on 11 March 1955, the discoverer of penicillin merited a 13-page obituary in *JGM*. The author was Dr V. D. Allison, who commenced work with Fleming at St Mary's Hospital in 1921 and over the next 34 years grew to know him very well as both colleague and friend. No doubt it has been mined before by Fleming's biographers, but here are a few insights into the great man that might not be so well known.

As a person, he seems to have been keen on sports, from student days to retirement. In his early years he was a fine rifle shot and keen swimmer; a member of both the hospital shooting team and the water polo team. In middle life he played billiards and could beat more experienced players at tennis, golf and croquet. His interests in culture extended beyond the laboratory bench and, no mean water-colourist and draughtsman himself, he was a member of the Chelsea Arts Club, an expert photographer and a devotee of second-hand bookshops. He collected Georgian silver and old English cut glass. Gardening was one of his greatest pleasures. He had two homes, a flat in London and a country residence in Suffolk where he experimented with plant breeding and grafting. Much of the produce he grew went to the wards at St Mary's.

Allison reveals much about Sir Alexander's personality that goes beyond his public image of taciturnity and shyness, noting that Fleming '*could not remain inactive for more than half an hour or so*'; this trait no doubt accounting for the quantity and diversity of his achievements and activities at work and at leisure. He enjoyed a good argument and liked to provoke debate with colleagues, especially encouraging students to think clearly and reason well.

Details of Fleming's humble beginnings in Scotland, his early work in London as a shipping clerk and his education are familiar, but his reason for choosing St Mary's Medical School as the place to train as a doctor in 1902 may not be. It was simply because he had played water polo against the hospital team! If it were not for this chance decision, the course of medical history may well have been very different.

On qualification Fleming began work in Almroth Wright's Inoculation Department at St Mary's, where, with a break for war service, he stayed until retirement in what became the Wright–Fleming Institute. Fleming spent a lot of time developing laboratory techniques, recounted in detail by Allison, but back in the early 1900s he was working on infectious diseases that still cause problems today. In 1909 he developed a medium for isolating the 'acne bacillus' which led to the successful treatment of cases with vaccines. Shortly after, he began the work on the new drug Salvarsan for the treatment of syphilis. This marked the beginning of chemotherapy and Fleming's lifelong interest in the investigation of chemical antiseptics in the treatment of infection.

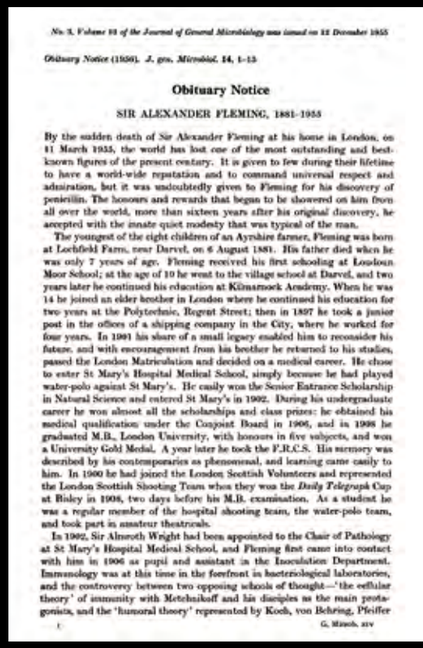
There was a break during World War I, when Fleming joined the RAMC and worked with Wright in a lab set up in Boulogne. The obituary describes their researches into infected war wounds, to foster which Fleming devised an 'artificial wound' in a glass test-tube with 'several conical spikes drawn out in its lower half, filled with serum and infected with faecal matter'.

Back at St Mary's, in 1921 when the obituarist joined his lab, Fleming discovered lysozyme, which he always considered more important than the discovery of penicillin. He continued to research the effects of antiseptics on bacteria in infected wounds.

Even in 1955, the penicillin discovery story was so familiar that Allison felt no need to repeat it in detail, but he did note that despite being unable to develop it for clinical use, Fleming used penicillin constantly in the laboratory for selective culture. He developed a medium for isolating *Haemophilus influenzae*, amongst other species of bacteria. Other scientists followed his lead and various papers of the 1930s and 40s are cited.

With the advent of World War II, interest in treatments for war wounds was revived, and Fleming played an important role in the research, mainly into the effectiveness of the new sulfonamides and acridines. Although Fleming was not involved in Florey and Chain's Oxford group's development of penicillin to treat infections, he did bring the drug to the notice of the Minister of Supply, which led to the setting up of the Penicillin Committee. This became instrumental in stimulating production of the antibiotic on a commercial scale.

In the late 1940s Fleming's research included the development of methods of estimating penicillin in blood, but he increasingly spent much time away from the bench delivering lectures and receiving numerous honours. Ever eager to try anything new, he used phase-contrast microscopy to study *Proteus vulgaris* and produced evidence to support the traditional theory of flagella being regarded as the organs of motility in bacteria. According to Allison, to the end Fleming remained his own technician.


No. 3, Volume 16 of the Journal of General Microbiology was issued on 15 December 1955

Obituary Notice (1956). *J. gen. Microbiol.* **14**, 1–13

Obituary Notice

SIR ALEXANDER FLEMING, 1881–1955

By the sudden death of Sir Alexander Fleming at his home in London, on 11 March 1955, the world has lost one of the most outstanding and best-known figures of the present century. It is given to few during their lifetime to have a world-wide reputation and to command universal respect and admiration, but it was undoubtedly given to Fleming for his discovery of penicillin. The honours and rewards that began to be showered on him from all over the world, more than sixteen years after his original discovery, he accepted with the innate quiet modesty that was typical of the man.

The youngest of the eight children of an Ayrshire farmer, Fleming was born at Lochfield Farm, near Darvel, on 6 August 1881. His father died when he was only 7 years of age. Fleming received his first schooling at Loudoun Moor School; at the age of 10 he went to the village school at Darvel, and two years later he continued his education at Kilmarnock Academy. When he was 14 he joined an elder brother in London where he continued his education for two years at the Polytechnic, Regent Street; then in 1897 he took a junior post in the offices of a shipping company in the City, where he worked for four years. In 1901 his share of a small legacy enabled him to reconsider his future, and with encouragement from his brother he returned to his studies, passed the London Matriculation and decided on a medical career. He chose to enter St Mary's Hospital Medical School, simply because he had played water-polo against St Mary's. He easily won the Senior Entrance Scholarship in Natural Science and entered St Mary's in 1902. During his undergraduate career he won almost all the scholarships and class prizes: he obtained his medical qualification under the Conjoint Board in 1906, and in 1908 he graduated M.B., London University, with honours in five subjects, and won a University Gold Medal. A year later he took the F.R.C.S. His memory was described by his contemporaries as phenomenal, and learning came easily to him. In 1900 he had joined the London Scottish Volunteers and represented the London Scottish Shooting Team when they won the *Daily Telegraph* Cup at Bisley in 1908, two days before his M.B. examination. As a student he was a regular member of the hospital shooting team, the water-polo team, and took part in amateur theatricals.

In 1902, Sir Almroth Wright had been appointed to the Chair of Pathology at St Mary's Hospital Medical School, and Fleming first came into contact with him in 1906 as pupil and assistant in the Inoculation Department. Immunology was at this time in the forefront in bacteriological laboratories, and the controversy between two opposing schools of thought—' the cellular theory ' of immunity with Metchnikoff and his disciples as the main protagonists, and the 'humoral theory' represented by Koch, von Behring, Pfeiffer

G. Microb. xiv

Fleming's last published work appeared in 1951. His medical career spanned 49 years and he published 90 scientific papers. Of these, only two were in *JGM* (founded in 1946). Although the obituary appears in this publication, there is no mention of Fleming's role in the SGM other than his presidency, buried in a long list of honours including his knighthood and Nobel prize!

Please note that the entire back-catalogue of J Gen Microbiol will soon be online.

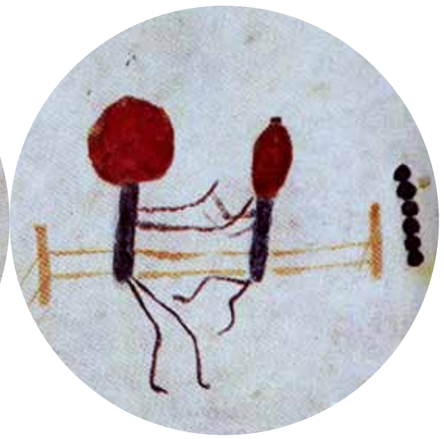
◀ Alexander Fleming in his laboratory with *Penicillium* cultures in 1944. *Alexander Fleming Laboratory Museum (Imperial College Healthcare NHS Trust)*

In 1928, by chance, Alexander Fleming discovered penicillin, which was subsequently developed and saved millions from death by infectious disease. **Kevin Brown** recounts the story of this amazing antibiotic and tells something of the man, later to become first president of the SGM, who found it.

'*That's funny!*': the discovery and development of penicillin

In many ways Fleming could have only discovered the original wonder drug in his musty, dusty, overcrowded, cluttered laboratory at St Mary's Hospital. After all, if there was no possibility of contamination there could have been no penicillin. Some might argue that without Fleming, there would have been none either. Certainly, the chance contamination of culture plates was common, but Fleming's genius was to notice something unusual and act upon it. As a scientist, he was very much in the tradition of the 19th-century lone researcher interested in unusual phenomena. This approach was to pay dividends when in September 1928 he returned from a 6-week holiday to find not only that a plate of staphylococci, he had been working on before his holiday had become contaminated by a fungus, but that there was the now classic zone of inhibition around the mould. Ever the master of understatement, Fleming's response was typical of the man: '*That's funny!*'

Fleming had the type of mind that was receptive to the quirky and unusual and an eye that could detect patterns that were out of the ordinary. One of his hobbies was painting, but he did not use oils or watercolours, preferring to use his skills as a bacteriologist to produce germ paintings in which different pigmented bacteria were used to colour in his sketches. It could indeed be argued that this interest helped to make possible his discovery. Fleming had recently read a paper by Joseph Biggar of Trinity College Dublin, which suggested that interesting staphylococcal variations could be produced by incubating the culture plates at room temperature, and that the pigmentation of a bacterium could be an indicator of its virulence. He had been asked to write a paper on staphylococci for a Medical Research Council volume on bacteriology and had made up some culture plates for observational purposes. It made sense to incubate some of the plates at room temperature to test Biggar's observations, but his artistic interests would have also encouraged him to investigate pigmentation of bacteria. Had he heated his plates in the incubator, the temperature would have inhibited the mould and there would have been no signs of inhibition of the bacteria in the area surrounding the fungus.



◄ ▼ ► The art of microbiology: Fleming used differently pigmented bacteria for his germ paintings.

► *From left to right:* Alexander Fleming, Ernst Chain and Howard Florey receive their Nobel Prize for Medicine at the 1945 ceremony in Stockholm.

Alexander Fleming Laboratory Museum (Imperial College Healthcare NHS Trust)

Contamination of a culture plate was commonplace, but what interested Fleming was the zone of inhibition, which recalled to him his first great discovery of lysozyme. He had discovered this in November 1921 when he had a cold and a drop of nasal mucus fell on to a plate of an as yet undiscovered microbe which Fleming was to name *Micrococcus lysodeiktikus* (now *M. luteus*). He wondered what would happen if he mixed the mucus in with the bacteria and after a few weeks found signs of lysis. He always admitted that his best scientific work had been done on lysozyme, but the problem with it was that it did not act against the most pathogenic of bacteria. When he saw what penicillin, or mould juice as he originally dubbed it, could do, his first thought was that it might be a much more powerful enzyme than lysozyme. By the time that he had established that it was not an enzyme, he was interested in it for itself.

He had an advantage that most modern researchers could only envy. He had the freedom to pursue something that was merely of interest rather than tied to current work. It was the ideal situation for him to take advantage of a chance contaminant. However, one person could not have all the skills and knowledge needed to develop penicillin. A different research strategy was needed to do this with a multi-disciplinary team behind him. However, all the help Fleming had was of two young research assistants who learned the chemistry that was needed from basic school textbooks and worked at a sink in a corridor outside a ward, blocking the way to a sluice. They were unable to purify or stabilize the penicillin, although they came close to finding the answer to these difficulties. In publishing his findings in his now classic paper of 1929, Fleming pointed out that there was a clinical potential if these problems could be overcome. It was left to other researchers to accomplish this.

Had Fleming not investigated his chance contaminant, not published his findings, not kept the fungus alive nor disseminated it, penicillin would have been relegated to the status of an interesting observation, but nothing more. However, penicillin was useful as what Fleming called a 'bacterial weed killer' for the isolation and selective culture of resistant strains of bacteria. He himself used it to isolate Pfeiffer's bacillus, then believed to be the cause of influenza, to produce an anti-influenza vaccine as part of a programme of vaccine production that underpinned the funding of the department in which he worked. Other laboratories obtained samples of the penicillin mould, including the Sir William Dunn School of Pathology at Oxford.

Developing the wonder drug

In 1939, Howard Florey, Professor of Pathology at Oxford, and the biochemist Ernst Chain, a German Jewish refugee from the Nazis, had just finished a research project on lysozyme when they decided to turn their attention to penicillin because of its apparent similarities to an enzyme, just as this had been what originally interested Fleming. Their initial interest in penicillin was purely academic, but as their work progressed, they became increasingly aware of its clinical potential as a life-saving drug that could prove invaluable to the Allied cause as Europe moved deeper into the Second World War. When invasion seemed imminent in the summer of 1940, Florey, Chain and their colleagues smeared samples of the mould into the linings of their suits with the intention of escaping to the free world and continuing their work in the British Empire or the US.

Wartime conditions with everything in short supply made their task more difficult. Norman Heatley, a biochemist on the Oxford team and a master of improvisation, devised equipment worthy of a Heath Robinson design, using milk churns, bath tubs, fridge coolants, Huntley and Palmers biscuit tins, bicycle pumps, library book racks and hospital bed pans. When it became possible to commission specially made culture vessels, Heatley based their design on that of a bedpan, possibly allied with that of the biscuit tin. Chain was later to comment unfairly that more could have been achieved if there had been more professionalism and less improvisation, but in the circumstances of the time there was no choice. By March 1941, using back-extraction, alumina column chromatography and freeze-drying techniques, the Oxford team were able to produce penicillin that was pure and stable enough to use on a patient; later it was realised that the penicillin injected into a 41-year-old Oxford policeman, dying from septicaemia contracted from a scratch when gardening, was actually 97% impure. They had so little penicillin that they had to extract anything usable from the man's urine to re-inject it. Eventually there was no active penicillin left and the first patient, Albert Alexander, died.

By now penicillin production was seen as of importance to the war effort. Increasing production to an industrial scale was difficult in wartime Britain where pharmaceuticals took second place to munitions. Florey took penicillin to North America with its greater industrial capacity and at the United States Department of Agriculture Northern Regional Research Laboratory at Peoria, Illinois, an improved production method using submerged culture that became the basis of modern industrial penicillin production was developed by Heatley and the American microbiologist Andrew Moyer. The new methods of production were taken up and developed by the pharmaceutical companies, initially working together in an unprecedented flurry of collaboration prompted by the needs of modern warfare.

Honours

Fleming, Florey and Chain shared the 1945 Nobel Prize for Medicine for their respective roles in the discovery and development of penicillin. It was a fair enough division of the honours in so far as it went, but credit was also due to many other researchers. Indeed, the key to the Oxford success had been multi-disciplinary teamwork, the bringing together of expertise from different fields to solve a common problem and this was to be a pointer to the future of medical research. Different research strategies and approaches, as well as different individual contributions, were needed at different stages of the development of penicillin. It is something that we would do well to remember today, 80 years on.

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Further reading

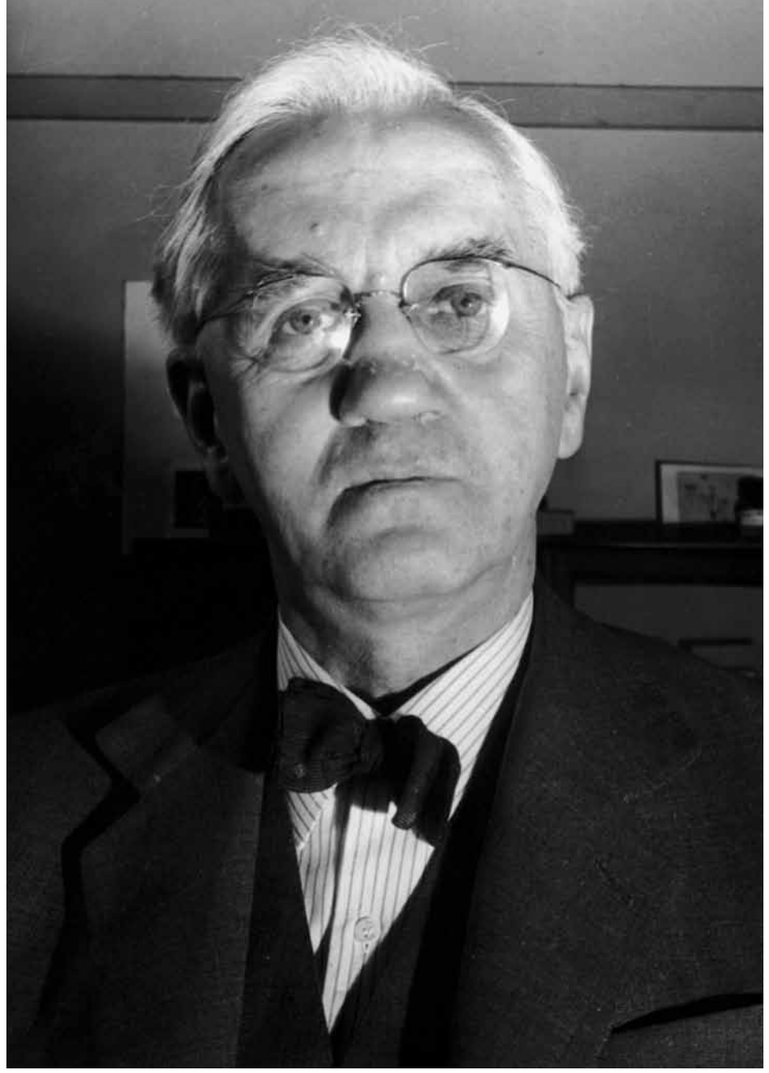
Brown, K. (2004). *Penicillin Man: Alexander Fleming and the Antibiotic Revolution*. Stroud: Sutton Publishing.

Bud, R. (2007). *Penicillin: Triumph and Tragedy*. Oxford: OUP.

Fleming, A (1929). On the antibacterial action of cultures of a *Penicillium* with special reference to their use in the isolation of *B. influenzae*. *Br J Exp Pathol* 10, 226–236.

What manner of man was Alexander Fleming?

Almost everyone has heard of Alexander Fleming though it is now 80 years since he discovered penicillin and over 50 years since he died. **Philip Mortimer**'s brief description of the character and career of the SGM's first president offers a novel perspective on Fleming's achievements.



◀ Alexander Fleming in 1951. *Hulton Archive/ Getty Images*

There is little prospect of further testimony from people who actually worked with Fleming. However, the existing accounts by those who knew the able but taciturn Scot well make it easier than it might otherwise be to reconcile Fleming's rather private personality with his eventually very public image as the internationally acclaimed discoverer of penicillin. Moreover, that discovery can now be seen in a historical perspective that acknowledges the contribution made by others to its realisation, and also takes account of Fleming's other, less well known, research achievements.

When, in the late 1940s, Fleming's fame rose to dizzy heights, it was largely as a result of his clinical colleagues' efforts to capitalize on the miracle of penicillin for the benefit of their medical school, St Mary's. This generated some resentment among scientists elsewhere whose work had brought the drug to the bedside. With Fleming being compared to Newton and Pasteur, a reaction was bound to follow; but that reaction has now perhaps swung too far, so that Fleming's justifiable reputation deserves to be revived.

The historical perspective

Fleming's laboratory career spanned nearly 50 years. It covered much of the chemotherapeutic era, from the introduction of salvarsan almost to the first semi-synthetic penicillins. Along the way it intertwined with Almroth Wright's and Leonard Colebrook's careers and, more controversially, with those of Howard Florey and the Oxford team. The Oxford scientists purified penicillin and they were the first to apply it experimentally and clinically. In their various ways these people all helped to transform surgical practice in the first half of the 20th century. They rejected Listerian antisepsis and they promoted the aseptic approach. They investigated the sources and nature of wound infections and they drew on specific vaccine, serum and chemotherapies to overcome them. Fleming's discovery of penicillin was the single most important contribution to that transformation in surgery, as well as enabling much more in the medical treatment of infectious disease.

Fleming's early years

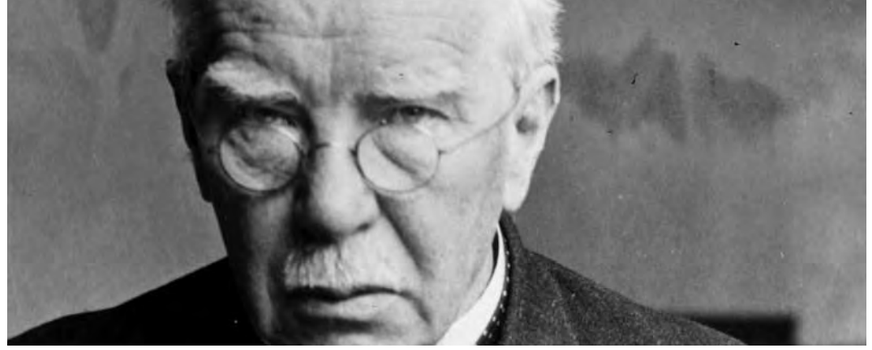
Alexander Fleming grew up on a farm on the bleak uplands of Ayrshire in south-west Scotland. He was one of a close knit family of five brothers and three sisters, and was educated at small local schools and Kilmarnock Academy. At 16 he left Scotland to join an older brother, Tom, in London. There he worked for 3 years as a shipping clerk, a job which may have given him the taste for international travel that he indulged towards the end of his life.

Office work did not extend Fleming's extraordinary capacity for disciplined and focussed observation of natural phenomena, however, and when he received a small family legacy he enrolled in 1901 as a student at the medical school of St Mary's Hospital, Paddington. There his academic career was outstanding. Contemporaries recalled him passing examinations without apparent effort, and the scholarships and gold medal he won testify to this ability. Very soon after qualification he also secured the fellowship of the Royal College of Surgeons – no mean feat.

A fruitful partnership

By then Fleming had been recruited to Almroth Wright's 'Inoculation' Department, a branch of the St Mary's Medical School dedicated to therapeutic applications of the new science of immunology. This admirable enterprise attracted, trained and financially supported clever young graduates like Fleming. Wright's interest was in therapeutic vaccines, and whatever Fleming's reservations may have been about the efficacy of some of these preparations (his famous uncommunicativeness may have served him well in this regard), it must be said that the sale of these vaccines financed the department right up to Wright's overdue retirement in 1946 at the age of 84. The income allowed Fleming, whose habits were in any case frugal, to pursue various unrelated interests without the usual constraint of lack of funds. Furthermore, Almroth Wright's capacity for 'networking' and his reputation as a controversialist willing to offer an opinion on any matter whatever kept his department in the public eye and the reclusive Fleming 'in the swim'.

Fleming quickly became Wright's right-hand man and silent foil. The delegation to him of routine responsibilities such as management of the production of the vaccine preparations that were sold to private patients through Parke Davis may not have been welcome, and they possibly hindered Fleming's own original work; but his chief's ebullience and flair probably generated many of the research ideas, and this must have benefited Fleming. While Fleming was not necessarily an



◀ Almroth Wright, October 1929. *Hulton Archive/Getty Images*

▶ Alexander Fleming, December 1951. *Time and Life Pictures/Getty Images*

original thinker, he was a deft, and became a very experienced, bench worker. Over a period of 36 years in Wright's department he turned out a series of important contributions to laboratory medicine. The semi-protected environment of the crowded Paddington laboratory well suited this perceptive but reserved man, whose abilities were complementary to those of his extrovert chief. Fleming also owed something to his friend and contemporary, Charles Wilson, later Lord Moran. It was Moran, the consummate medical politician who, in lifting St Mary's from its Cinderella status among the London medical schools, promoted Fleming's reputation.

Treating syphilis

So what was the substance of Fleming's career? In 1910 Wright's friendship with the famous German chemist Ehrlich secured the gift of samples of the new anti-spirochaetal drug, salvarsan ('606'), for clinical use. These were handed on to Fleming who put them to good effect.

Fleming's first scientific work had involved the application of von Wasserman's ground-breaking laboratory test for syphilis. That test has never been a laboratory exercise for the faint-hearted, and back in the 1900s the technical tinkering needed to get it to work must have been an appealing challenge for Fleming. That achieved, Fleming's next success was in devising satisfactory means of administering the salvarsan he had acquired. This synthetic compound was unstable and poorly soluble; and when given intramuscularly it was painful and necrotizing for tissue. Fleming overcame this by infusing the drug intravenously. Consequently, he developed a private practice discreetly treating cases of syphilis with '606' and its successor, '914'. These were universally used to cure syphilis for the following 30 years, and had seen it off as an endemic disease long before penicillin, the present drug of choice, made its clinical debut.

World War I

The next phase of Fleming's work had a terrible and lasting relevance. It concerned the management of war wounds, and raised an issue that has yet to be resolved even in modern peacetime surgical practice. In France, between 1915 and 1918, Fleming showed that most battlefield injuries became infected, first with anaerobic and then with aerobic organisms. The problem, a forerunner of today's hospital-acquired clostridial and MRSA infections, was superimposed on grossly contaminated war wounds, and Wright, sustained by Fleming's supportive research findings, railed against the incontinent application of disinfectants to these wounds.

From lysozyme to the conquest of sepsis

Returning to St Mary's in 1919, Fleming made his first major scientific discovery, that human tears and nasal secretions contain 'lysozyme' (the word was coined by the classically educated Wright). Lysozyme rapidly dissolves a wide range of bacterial cells in the laboratory, and it was found to be widespread in nature. It was assumed to be a common animal defence against bacterial infections. For Fleming it opened up a path of discovery semi-independent of Wright's scientific interests, and it would alone have assured Fleming a place in the history of microbiology. However, the achievement was (or more accurately was later judged to be) overshadowed by the discovery of penicillin in 1928. That story has often enough been told not to be repeated here (but see Kevin Brown's specially commissioned article on p. 12).

In retrospect, Fleming should obviously have persevered with penicillin longer than he did; but he was, according to his younger colleague Hare, 'no chemist'. However, Fleming's interest in antibacterial substances did not flag, and he pursued the general goal of finding effective, non-toxic antibacterial substances that might be of clinical use. In the later 1930s he studied the sulfonamides as they appeared and, like Colebrook, used them successfully to treat streptococcal infections, whether pneumonic, puerperal or other. Wright, Fleming and Colebrook shared the view that antisepsis had been a crude weapon dependent on the use of tissue-toxic chemicals. Conversely asepsis needed, in order to maintain it, non-toxic antibacterials that were specific for particular infections.

Fleming's biographers

Fleming has been lucky in his many biographers. The most distinguished, the French writer Andre Maurois, produced a literary triumph in 1959. He obtained written testimony from a host of Fleming's acquaintances, none of them willing to criticize a recently dead national treasure. And Maurois himself, already the biographer of several French notables, was anxious to expiate some incautious remarks he had made in 1940 on the subject of British perfidy. However, the British hero he chose to write about was far removed from his own culture and, not really understanding Fleming's world, Maurois was too generous to his subject. His was an uncritical, even hagiographic, account.

Posterity is more indebted to Ronald Hare who both wrote the best book on the penicillin phenomenon and drew attention to Fleming's other scientific achievements. Hare wrote affectionately about 'Flem', admiring his technical ability and modest demeanour, but acknowledging his pawky humour, extreme economy with words, and child-like pleasure in games and tricks such as painting with chromogenic bacteria. These latter characteristics may have diminished Fleming in the eyes of the English scientific establishment; they almost certainly led its members to undervalue his intellect.

A later biographer, Gwyn Macfarlane, was an Oxford physician who had previously written about Florey and understood the politics of the controversy that arose between Florey's Oxford group and Fleming's St Mary's based associates concerning where the credit for penicillin lay. The Londoners, abetted by the Beaverbrook press, had special reasons for claiming the triumph of penicillin as their own, and they antagonized some of the Oxford scientists. Nevertheless, Macfarlane gives a balanced assessment of Fleming's part in what was a huge shared achievement that also had important American involvement. Fleming's own way of dealing with the contention between Oxford and St Mary's was to stay aloof, though he enjoyed – and why not? – the belated public and academic acclaim accorded to him.

During his semi-retirement, Fleming travelled widely by plane and ocean liner, latterly with his second wife, Amalia. There is here an amusing parallel with the outstanding laboratory worker of the previous generation of microbiologists, Robert Koch. Both men, once freed of their laboratory responsibilities, circled the world accepting academic plaudits, accompanied by their young wives. Macfarlane quotes an anecdote describing the sort of reception Fleming was often given abroad

'*In Spain, when he was walking in procession from the graduation ceremony to a bullfight, members of the crowd fell to their knees to kiss the hem of his latest colourful robe. He later resented a cynical suggestion that he had been mistaken for a new cardinal.*'

Significance as a scientist

Though Fleming was a gifted laboratory-based doctor, he was, again like Koch, neither articulate nor gregarious enough to occupy a leading place in his country's medico-scientific establishment. British scientists do not rank their peers according to the esteem in which they are held by the lay public – this is more likely to attract envy than respect. The more ungenerous of Fleming's scientific contemporaries viewed his observation of a mould on a discarded plate in 1928 as a kind of fluke; but they perhaps ought to have taken the opportunity to read his other scientific articles, virtually all published before he became a household name. These are skilfully written and varied in content, and several have been influential.

Fleming's descriptions of the Wasserman test and of an apparatus for infusing salvarsan have already been referred to. His studies on the bacterial flora of war wounds focused on the haemolytic streptococci, and Fleming was one of the first to use beta haemolysis of blood agar as the touchstone of streptococcal pathogenicity. In 1919 he published a paper on the collection of blood into citrate solution for subsequent transfusion which anticipated and partially solved several of the difficulties that the first generation of professional blood bankers encountered some two decades later. Thereafter, as well as his well-known papers on lysozyme and penicillin, Fleming wrote papers on the use of the sulfonamide M&B 693.

Harking back to his experience of treating neurosyphilis, Fleming, in 1942, successfully treated a case of pneumococcal meningitis intrathecally with precious penicillin given him by Florey. Long after it was necessary to minimize its consumption, clinicians still chose to give penicillin in a small intrathecal dose to begin the treatment of meningitis, and Fleming's influence may also have been a factor in choosing the same route to administer streptomycin to children with tuberculous meningitis. The latter was frequently a life-saving intervention.

Conclusion

Fleming made not one but several important contributions to the development of chemotherapy. Taking the long perspective, he ranks not on a solitary pedestal but equal among several pioneers of antibiosis, and this, to be fair, is where he would probably have placed himself. He would also have pointed to the ironies that the first organism he showed to be sensitive to penicillin, *Staphylococcus aureus*, was the first to develop resistance to it (over 50% of hospital isolates by 1950), and that those who later met that problem with newer antibiotics did not, and have not since, been accorded the recognition he got.

Lord Moran, who knew Fleming as well as anyone, later wrote: '*Alexander Fleming had lived in obscurity and in some disfavour … He seemed to his profession to be disgruntled by criticism and by neglect, a sour, rather silent Scot. And then, on the verge of old age, he discovered penicillin. He, too, had found a place in the sun … Fleming seemed to spend the rest of his days travelling over the world, making modest little speeches … everywhere he went he won their hearts by his happy simplicity.*'

In fact, Fleming was very good at whatever he chose to do, and perhaps being aware of his weakness as an exponent of his work he accepted the long-delayed praise showered on him with dignity but few words. What more could one ask of a rather unlikely hero than that he should have known his limitations and not bored his audiences by reading out long speeches?

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Further reading

Hare, R. (1970). *The Birth of Penicillin and the Disarming of Microbes*. London: Allen and Unwin.

Macfarlane, G. (1984). *Alexander Fleming: The Man and The Myth*. London: Chatto and Windus.

Maurois, A. (1959). *Alexander Fleming* (trans. G. Hopkins). London: Penguin.

◀ Actinomycetes isolated from a soil sample growing on agar plates. *Linda Cavaletti, Instituto Insubrico di Ricerca per la Vita, Gerenzano, Varese, Italy*

Antibiotics and *Streptomyces*: the future of antibiotic discovery

Novel classes of antibiotics are constantly required due to the expanding population of patients at risk and the growing prevalence of resistant pathogens in hospital- or community-acquired infections. Despite this need, major pharmaceutical players seem to be reducing their efforts to discover new antibiotics. This is due to a combination of factors such as the maturity, great competition and increased genericization of the antibiotic market. Unrealized expectations from high-throughput screening, combinatorial chemistry and pathogen-genome-derived targets have also had a negative effect. The perception prevails that the discovery of novel antibiotics is a very rare event. On the other hand, past and present successes speak for a return to microbial product screening.

What are antibiotics?

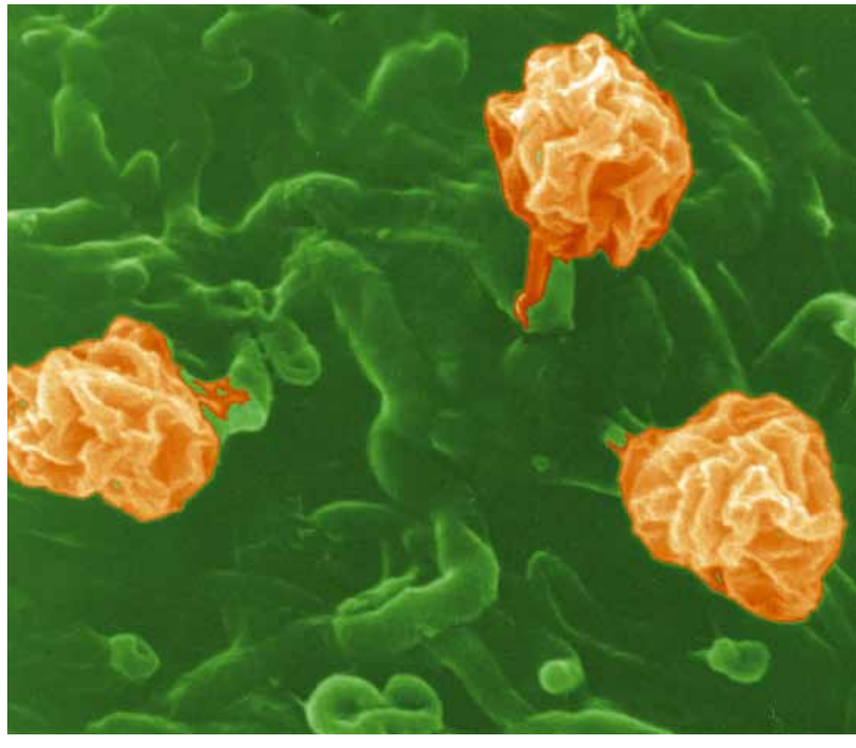
Antibiotics are defined as low-molecular-mass microbial metabolites that at low concentrations specifically inhibit the growth of other micro-organisms ('magic bullets'). Drugs obtained by chemically modifying the microbial metabolites are termed semisynthetic antibiotics.

From the point of view of the producing microbes, antibiotics belong to the wider category of the so-called secondary metabolites. J.D. Bu'Lock in 1961 was the first to explicitly introduce the term 'secondary metabolite' in microbiology, taking it from previous studies of plant physiologists on cellular components not essential for cell life and not found in every growing cell. Microbial secondary metabolites are not essential for vegetative growth of the producing organisms, at least under laboratory conditions, and they are biosynthesized from one or more general (primary) metabolites by a wider variety of pathways than those involved in general (primary) metabolism. They are mainly produced by a relatively restricted group of bacteria and fungi, but their intergeneric, interspecific, and intraspecific variation is extremely high. Many of them are endowed with biological activities; these include antibiotics, toxins, ionophores and bioregulators, and also activities such as intra- and interspecific signalling (see the article by Julian Davies on p. 24). Most of the known antibiotics are produced by differentiating microbes such as filamentous actinomycetes and fungi, which have in common a non-motile, saprophytic lifestyle in a complex habitat, such as terrestrial soil, where they lead an intensive social life and are subject to great competition with other inhabitants.

As the search for new antibiotics seems to be declining, despite a greater need than ever for effective antimicrobial agents, **Flavia Marinelli** shows that many options for drug discovery are still available to researchers.

'Magic bullets': past and present

The majority of antibacterial and antifungal agents in clinical use nowadays were discovered during the 'Golden Age' of antibiotics in the 1940s–1960s through massive isolation and screening of soil actinomycetes and fungi. It has been estimated that almost 12,000 bioactive secondary metabolites were discovered during that time, and about



▲ Colonies of the model organism *Streptomyces coelicolor*. *Andrew Davis, John Innes Centre, Norwich*

▲ Scanning electron micrograph of sporangia of the actinomycete *Actinoplanes* sp. 21954. *Giorgio Toppo, Instituto Insubrico di Ricerca per la Vita, Gerenzano, Varese, Italy*

160 of them then reached clinical use as natural products per se or as semisynthetic derivatives. In fact, 55% of them were produced by the genus *Streptomyces*, 11% from other actinomycetes, 12% from non-filamentous bacteria and 22% from filamentous fungi.

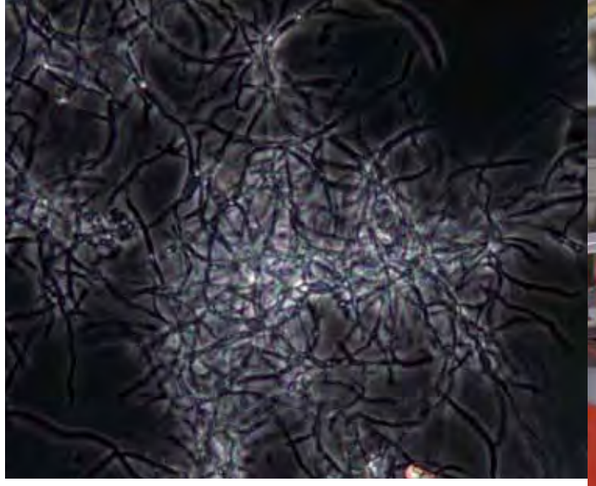
Penicillins, cephalosporins, tetracyclines, aminoglycosides, glycopeptides, macrolides and polyenes were all discovered in that period and have been useful in the battle against bacterial and fungal infections over the past 50 years. From 1960 to 1980 major pharmaceutical efforts were directed towards the incremental improvement of existing chemotypes, increasing potency, stability, and pharmacokinetics or reducing adverse reactions by medicinal chemistry. This led to the development of five generations of penicillins, four generations of cephalosporins, two generations of carbapenems (the first carbapenem thienamycin produced by the novel species *Streptomyces cattleya* was discovered in the early 1970s), three generations of tetracyclines, a dozen of aminoglycosides, five of macrolides and three of glycopeptides.

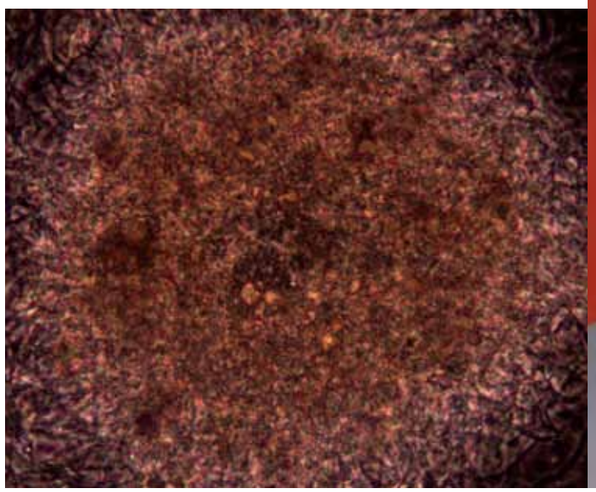
Research groups which continued to invest in microbial product screening were rewarded by the discovery of new and interesting chemotypes, such as thienamycin, daptomycin and echinocandins (the latter being launched on the market since 2000, see below) but the increasing frequency of re-isolation of known compounds posed serious challenges to the screening system. It was time to renew the empirical screening procedures that had been in use since Fleming's discovery of penicillin, based on the detection of pathogen growth inhibition on agar plates. In the 1960s and 1970s, many diverse microbes were then re-screened against biological targets other than microbial pathogens.

Screening for cytotoxicity toward rapidly proliferating eukaryotic cell lines led to the introduction of the armamentarium of anticancer drugs currently in use, including actinomycin (the first stretomycetes antibiotic discovered in Selman Waksman's lab in 1940), doxorubicin, daunorubicin, mitomycin and bleomycin, all of which are produced by *Streptomyces* spp. Screening for *in vivo* inhibitory activity versus nematodes or coccids was key to the identification of the avermectins from *Streptomyces avermitilis* and polyether antiparasitics from other actinomycetes.

The introduction of novel assays (based on cell-free enzymes, receptor-binding inhibition tests, or on specific cell lines) promoted the discovery of immunosuppressor drugs (cyclosporin A from a fungus, and the more active ones – tacrolimus and sirolimus from *Steptomyces* spp.), agricultural antibiotics (bialaphos from *Streptomyces* spp.), the β-lactamase inhibitor clavulanic acid (from *Streptomyces clavuligerus*) and the cholesterol-lowering fungal statins.

Notwithstanding these achievements, the introduction of cell-free assays in anti-infective screening and later on the





▲ Pellets of vegetative mycelium of *Actinoplanes teichomyceticus* growing in liquid cultures.

▶ Growth of the actinomycete *Nonomuraea* sp. in a 3-litre fermenter.

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emphasis on a high-throughput mode of screening – more suitable for chemical libraries than for microbial products – did not generate the expected pipeline of antibiotics over the past 20 years. Most of the molecules discovered through the era of high-throughput screening are potently active against selective cellular targets, but very often they do not penetrate microbial pathogen cells or they are inactivated *in vivo*. Furthermore, the genome sequencing of pathogens appeared to open Pandora's box by offering a plethora of novel targets. This attracted huge investments by the pharmaceutical companies, but for one reason or another, it did not provide the expected results in terms of novel chemotypes acting on emerging diseases and increasingly resistant pathogens. In the last few decades, only two novel antibiotic classes, discovered in the 1970s and 1980s, have been launched: the antibacterial lipopeptide daptomycin produced by *Streptomyces roseosporus*, which acts on membranes of multi-drug-resistant Gram-positive agents responsible for complicated skin and soft tissue infections; and the family of fungal echinocandins/pneumocandins, cyclic lipopeptides, which block fungal cell wall biosynthesis and are being used to treat increasingly occurring fungal systemic infections.

Streptomyces and the future of antibiotic research

The fame of streptomycetes as versatile producers of secondary metabolites started with the discovery of actinomycin in 1940, followed by streptomycin in 1943. Two-thirds of the marketed microbial drugs are produced by streptomycetes (see above). The genus *Streptomyces* belongs to the order *Actinomycetales* (high-G+C Gram-positive bacteria), which include unicellular and filamentous microbes, the latter having complex life cycles and forming hyphae, spores and secondary metabolites. Recent estimates indicate that nearly 50% of the 20,000 bioactive secondary metabolites described from 1900 onwards are produced by filamentous actinomycetes that originated in the soil. Among them, the easiest to isolate from soils are *Streptomyces* species. It follows that they have been extensively isolated since 1940, and today the chance of rediscovering known antibiotics from them is increasing. Thus, novel elements have to be introduced to streptomycetes screening. Isolation can be extended to peculiar habitats, assuming that unknown species of endophytes, extremophiles or marine streptomycetes may produce novel chemotypes. Or novel assays may be used to tease out previously undetected activities, as in the recent case of platensimycin, a novel fatty acid biosynthesis inhibitor discovered in *Streptomyces platensis*.

An additional strategy is the genome-guided discovery of novel metabolites based on the recognition of silent or cryptic genes encoding secondary metabolism, followed by the use of uncommon cultivation conditions to trigger their expression. The genome sequences of *Streptomyces coelicolor*, *S. avermitilis*, *S. griseus*, and *Saccharopolyspora erythraea* have shown a larger number of biosynthetic gene clusters (containing all the genes for secondary metabolite production, regulation, transport and auto-resistance) than those already characterized in fermentation extracts. In *S. coelicolor*, about 23 clusters of genes, representing about 4.5% of the genome, have been assigned to the production of secondary metabolites, only half a dozen of them having previously been identified. Similar potential has been confirmed in the other 'sequenced' actinomycetes.

Industrial isolation programmes have been driven towards the less-exploited groups of actinomycetes (*Actinoplanes*, *Nonomuraea*, *Microbispora*, *Planomonospora*, etc.), which are taxonomically close enough to streptomycetes to share the complex life cycle and versatile secondary metabolism. It has been demonstrated that once a selective isolation method is set up, a huge number of 'rare actinos' can be isolated. However, by using standard isolation procedures they are out-competed by the faster-growing streptomycetes.

For example, when a method to select *Actinoplanes* by recovering their peculiar motile spores from centrifuged soils was developed, thousands of members of this genus were isolated and then screened against a validated target, such as cell-wall synthesis. This led to the discovery of many novel molecules such as the glycopeptide teicoplanin, the lantibiotic actagardine and the depsipeptide ramoplanin. The problem is that as these rare actinos still remain difficult to cultivate and genetically engineer; exploiting them may require heterologous expression and combinatorial biosynthesis in the easier-to-handle *Streptomyces*, again confirming them as the real and trustworthy workhorses in the discovery of new antibiotics!

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Further reading

Baltz, R. (2005). Natural product discovery and development at Eli Lilly and Company. *SIM News* **55**, 5–16.

Bu'Lock, J.D. (1961). Intermediary metabolism and antibiotic synthesis. *Adv Appl Microbiol* **3**, 293–342.

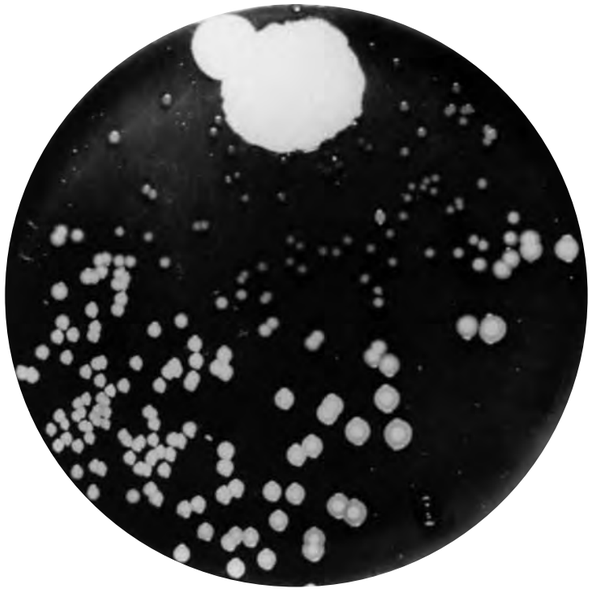
Castiglione, F., Cavaletti, L., Losi, D. & others (2007). A novel lantibiotic acting on bacterial cell wall synthesis produced by the uncommon actinomycete *Planomonospora* sp. *Biochemistry* **46**, 5884–5895.

Hopwood, D.A. (2007). *Streptomyces in Nature and Medicine: The Antibiotic Makers*. USA: Oxford University Press.

Lancini, G. (2006). Forty years of antibiotic research at Lepetit. *SIM News* **56**, 192–212.

Newman, D.J. & Cragg, G.M. (2007). Natural products as sources of new drugs over the last 25 years. *J Nat Prod* **70**, 461–477.

Wang, J., Soisson, S.M., Young, K. & others (2006). Platensimycin is a selective FabF inhibitor with potent antibiotic properties. *Nature* **441**, 358–361.



When antibiotics were discovered, they were considered only as miracle cures for infections. But as **Julian Davies** describes, these and other natural products also have important roles in microbial physiology as intercellular signalling agents.

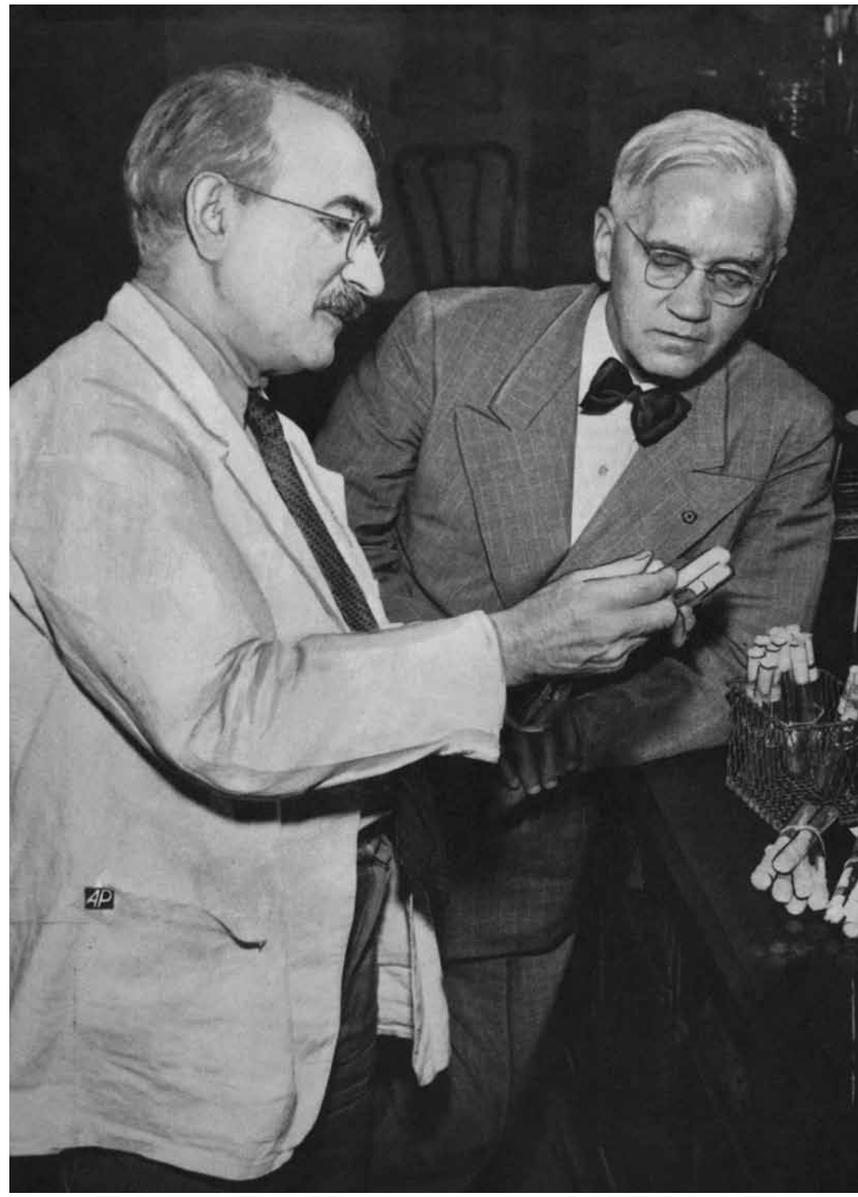
Look who's talking!

For thousands of years mankind has used natural products, chemicals produced by plants, fungi, bacteria and other living organisms, in a variety of applications: drugs, food, hallucinogens, etc. In more modern times this has led to investigations of the active compounds and their chemistry. The analysis of natural products, the basis of organic chemistry, contributed greatly to development of the methodology of structure determination and the art of total synthesis. Since the early 1900s, many organic chemists have honed their skills in natural product chemistry by characterizing plant compounds with a wide range of real and proposed curative properties. Microbial products were little studied until Alexander Fleming's fortuitous discovery (or was it rediscovery?) of their antibacterial properties, published in 1929. The chance finding of a stray fungal spore that produced a substance (subsequently shown to be penicillin) that caused lysis of a *Staphylococcus* strain became the all-time most famous photograph of a Petri plate (Fig. 1)!

The introduction of penicillin and streptomycin as the first potent antimicrobial agents derived from natural products in the early 1940s had global implications for the treatment of infectious disease. Penicillin was remarkably successful in saving lives in the Second World War, and streptomycin, discovered in the laboratory of Selman Waksman in 1944, turned out to be the first successful treatment for tuberculosis, the 'white plague' that has been a major cause of morbidity and mortality throughout human history. These two events also heralded the antibiotic era, when bioactive molecules produced by microbes became the silver bullets that completely transformed the treatment of disease. Since then, tens of thousands of antibiotic compounds have been discovered and tested, and medicine currently has an armamentarium of more than 100 approved antibiotics of some dozen different chemical classes. The legacy of Fleming and Waksman (Fig. 2) has been survival from the ravages of infectious diseases for billions of humans and animals over the past 60 years.

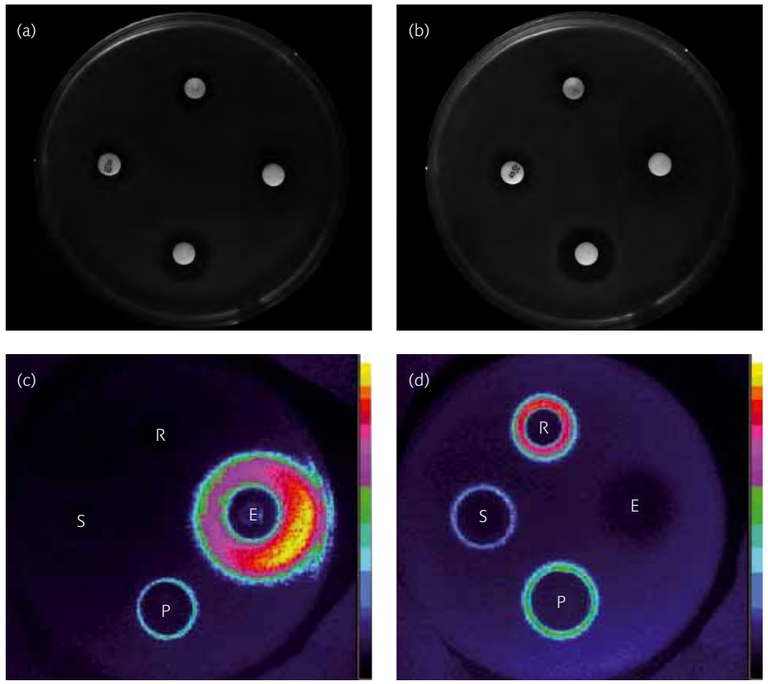
'Antibiotics'

It was Waksman who coined the word antibiotic: 'a chemical substance of microbial origin that possesses antimicrobial properties'. The word 'antibiosis' had been used previously but not in reference to purified chemicals. Waksman's definition has not been strictly adhered to and frequently includes compounds from any living source and even completely synthetic molecules. Microbial products with antibiotic activity exhibit many other types of bioactivity; the word antibiotic describes a specific function, but the compounds are multifunctional. The fact that a particular product has inhibitory activity in the laboratory does not mean that it plays such a role in nature. Antibiotics have a number of effects on bacterial physiology; for example they may affect the ability to swarm or form biofilms, or act as mutagens and induce bacterial lysogens to produce phage. Less well-appreciated is the fact that they also affect the function of plant cells and those of human hosts, and may cause undesirable side reactions; these secondary effects often occur at sub-inhibitory concentrations. Our laboratory has long been interested in the roles of antibiotics and other bioactive compounds of low molecular mass (<3000 Da) produced by microbes, etc., in biochemical evolution, and in the early 2000s we decided to examine their diverse activities by looking at transcription effects using promoter-reporter bacteria. The results were surprising (and colourful) Fig. 3; for example, rifampicin, the well-known antibiotic inhibitor of bacterial transcription (used for the treatment of TB), actually stimulated the transcription of a significant number of bacterial genes at low concentrations. This led us into detailed studies of



◀ Fig. 1. A photograph of Fleming's original culture plate, showing the zone of inhibited staphylococcal growth around the *Penicillium notatum* colony. *St Mary's Hospital Medical School / Science Photo Library*

▲ Fig. 2. Selman Waksman (left) and Alexander Fleming (right) in 1951. *Science Source / Science Photo Library*



▲ Fig. 3. Antibiotic growth inhibition (top) and transcription responses (luminescence) (bottom) of *Salmonella* Typhimurium 14028 carrying *ilvLG*::*luxCDABE* (a, c) and *nafC*::*luxCDABE* (b, d) transcriptional reporters. The colour scale on the right of (c) and (d) ranges from white, indicating high *lux* expression, to dark blue, indicating low *lux* expression). *Julian Davies*

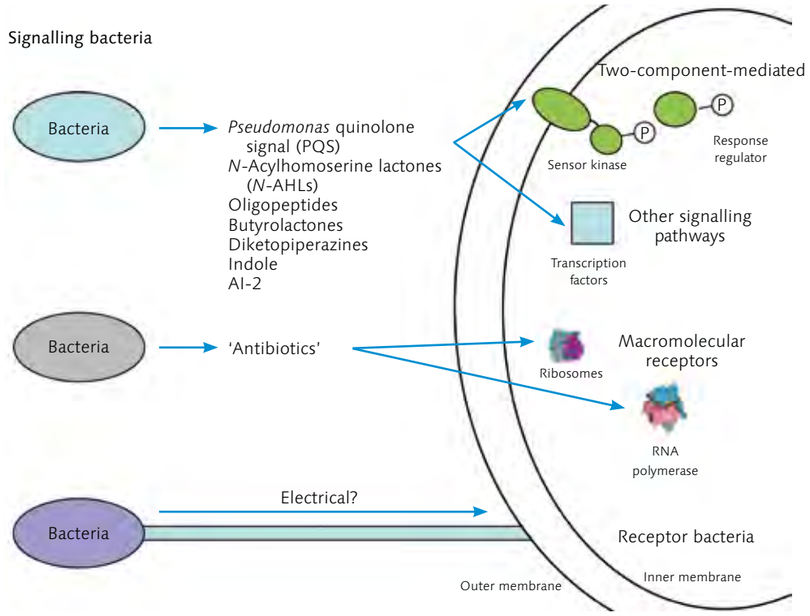
the effects of different inhibitors on pathogenic bacteria such as *Salmonella* Typhimurium and *Staphylococcus aureus*; to our surprise we found that at low concentrations all antibiotics modulate bacterial transcription in compound- and promoter-dependent ways. What does this tell us about the natural roles that antibiotics play in cell physiology? What might be their properties in the environment? The fact that these effects were seen at quite low concentrations suggested to us that so-called antibiotics act as intercellular signalling agents. We have been working on this ever since.

Signalling in bacterial communities

Bacteria in the environment exist in immense numbers, variety and genetic diversity. The microbial content of the biosphere approaches 10^{31}, a number beyond comprehension even when compared to the US national debt. The content of 1 gram of a typical soil is around a billion microbes. (These numbers are not yet accurate and vary with environment.) What is astonishing is that more than 95% of the population cannot be grown in the laboratory and cannot be classified (named) correctly; it is estimated that there are upwards of 1,000 different species in a gram of a rich soil. Our gastrointestinal tract contains a correspondingly huge number of microbes, most unidentified.

Bacterial populations normally grow as stable communities unless they are disturbed in some way. How do such mixed cultures maintain their stability with environmental changes? For example, therapeutic concentrations of antibiotics seriously deplete the bacterial population in the human GI tract, but once treatment stops, the population returns to its original state in a relatively short time. (Just imagine the burst of activity in soil bacteria after rain!) More and more evidence suggests that intercellular signalling maintains community growth and metabolism in a homeostatic manner, but what are the signals that modulate this? How do different types of bacteria communicate? And why? It is most likely that bacterial cross-talk occurs through the medium of small molecule and/or electrical signalling. An illustration of the signalling processes is shown in Fig. 4. In many cases the process involves modulation of transcription (RNA synthesis) either directly or indirectly, but other mechanisms may exist. The ribosome is an excellent example of a macromolecular receptor, possessing specific RNA and protein binding sites for small molecules that modulate metabolic processes essential for bacterial growth. On the other hand, at high concentrations these same molecules lead to translation inhibition, the basis of their antibiotic activity. Signalling by sub-inhibitory concentrations of natural compounds is mediated through interactions between ligands (small molecules) and different types of receptors. These take place at both the molecular and macromolecular level as indicated.

Given the large number and diversity of bacteria, one might expect that there would be myriads of different signalling molecules, so it is not surprising that bacteria have evolved many processes for small-molecule biosynthesis. The biosynthetic gene clusters are everywhere! In some prokaryotic families, such as the actinobacteria, pseudomonads and bacilli, each individual strain has devoted hundreds of kilobases of DNA to encode the production of dozens of different polyketides, non-ribosomal peptides, and hybrids of



◀ Fig. 4. Mechanisms of intermicrobial signalling. *Julian Davies*

these types, plus other unknown compounds. What is important is that signalling takes place at low concentrations.

Interbacterial signalling is essential in the formation of biofilm communities in disease and health, as has been demonstrated in the case of quorum-sensing agents. Signalling within the microbial communities of the GI tract is essential to human health; these complex microbiomes play important roles in protection against disease and their disruption is associated with a number of human pathologies. The gut bacteria cross-talk with their environment, which includes the host cells in the gut mucous membranes.

What about natural antagonistic reactions resulting from antibiotic activity? These have been clearly demonstrated in certain bacterial and fungal interactions in the lifestyles of ants and other insect species. Some natural products, such as the enediynes, are the most cytotoxic compounds known; they kill bacteria at nanomolar concentrations. One wonders if this is their only function in nature. Nevertheless, compounds with a range of activities are common; the bioactivity of natural products is exquisitely dose-dependent, yet we have no idea of their active concentrations in nature.

Antibacterial preparations from microbes underwent testing and even clinical use long before the introduction of penicillin, a good example being the substance 'pyocyanase', a small-molecule product of a *Pseudomonas* strain. Only recently have we begun to understand how they work. Diane Newman's laboratory has shown that the pyocyanins influence redox responses in bacterial populations; they are essentially acting as interbacterial signals in this case.

Conclusion

In the year in which we celebrate the anniversary of Darwin's *The Origin of Species* and Fleming's publication of the discovery of penicillin, it is interesting to consider how these monumental events have influenced our understanding of microbiology. Microbes evolved cell-to-cell interactions to ensure that their complex communities operate most efficiently for function and survival and for the benefit of their hosts. And in a typical Darwinian genetic response to antagonism (antibiosis), resistance developed in bacterial pathogens such as *S. aureus* – by mutation or by inheritance of antibiotic resistance mechanisms found in environmental bacteria. This is another evolutionary story; Darwin knew little about microbes and never envisioned horizontal gene transfer. Likewise, Fleming and Waksman could not have anticipated that small molecules and the antibiotics they discovered would prove to be so vital in the life of microbes!

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Further reading

Davies, J., Spiegelman, G.B. & Yim, G. (2006). The world of subinhibitory antibiotic concentrations. *Curr Opin Microbiol* **5**, 445–453.

Dietrich, L.E.P., Teal, T.K., Price-Whelan, A. & Newman, D.K. (2008). Redox-active antibiotics control gene expression and community behavior in divergent bacteria. *Science* **321**, 1203–1206.

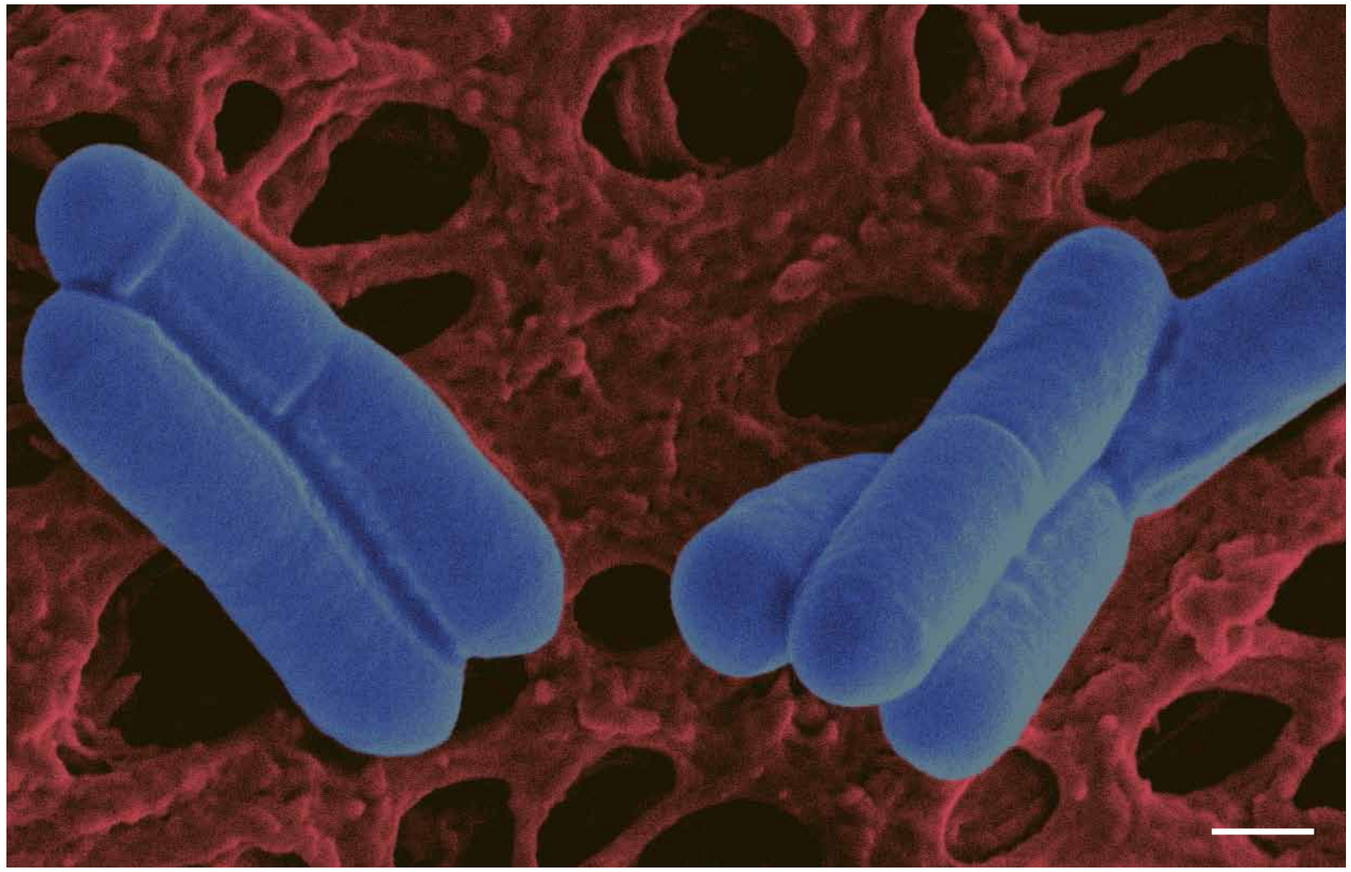
Fajardo, A. & Martínez, J.L. (2008). Antibiotics as signals that trigger specific bacterial responses. *Curr Opin Microbiol* **11**, 161–167.

Florey, H.W., Chain, E., Heatley, N.G., Jennings, M.A., Sanders, A.G., Abraham, E.P. & Florey, M.E. (1949). *Antibiotics. A Survey of Penicillin, Streptomycin, and Other Antimicrobial Substances from Fungi, Actinomycetes, Bacteria and Plants,* Vols I and II. London: Oxford University Press.

Nicolaou, K.C. & Montagnon, T. (2008). *Molecules That Changed the World*. Weinheim: Wiley.

Yim, G., Wang, H.H. & Davies, J. (2006). The truth about antibiotics. *Int J Med Microbiol* **296**, 163–170.

When good bugs fight bad



With few new antibiotics in the pipeline and many pathogens resistant to antimicrobials, **Roy Sleator** looks at some alternative therapies in the fight against infectious disease.

As we reach the 80th anniversary of Fleming's discovery of penicillin, the wonder drug which heralded a new era in the fight against infection, the medical establishment is now faced with a new challenge in the form of antibiotic resistance – the bugs are fighting back! Moreover, the superbugs, such as MRSA (meticillin-resistant *Staphylococcus aureus*) and C. diff. (*Clostridium difficile*) appear to be winning.

With life-cycles measured in minutes as opposed to years, bacteria have an extraordinary ability to evolve and adapt rapidly to changes in their environment. Thus, in a world where only the fittest survive, those bacteria which have developed resistance to antibiotics will predominate. This is particularly apparent in hospital environments where bacteria are in constant contact with many different antibiotics; such repeated exposure has facilitated the development of resistance to multiple antibiotics and what we now refer to as hospital-acquired or nosocomial infections.

Probiotic therapy – a possible solution?

Faced with an emerging pandemic of antibiotic resistance, clinicians and scientists alike are now struggling to find viable therapeutic alternatives to our failing antibiotic wonder drugs. One such alternative may be bacteria themselves – the application of probiotics – so-called 'good bugs', for therapeutic effect. While the exact mechanisms by which probiotic bacteria inhibit pathogens are, as yet, poorly understood, some advances have been made in our understanding of probiotic function. In addition to competing with pathogens for niches and nutrients, 'competitively excluding' disease-causing microbes from the host, certain probiotic bacteria have also been shown to employ a kind of chemical warfare, producing potent antimicrobial peptides (bacteriocins) which effectively wipe out the invading pathogen. However, despite their potent anti-pathogenic effect, a significant limitation of this approach is that probiotic bacteria tend to be physiologically fragile, often not surviving to sufficiently high numbers during prolonged storage in delivery matrices such as foods (yogurt and probiotic drinks) or tablet formulations. Furthermore, following ingestion, the already depleted probiotics must face the considerable physiological defences of the host (gastric acidity, bile, low iron, elevated osmolarity and temperature) in order to colonize the gastrointestinal tract in sufficient numbers to exert a therapeutic effect.

Patho-biotechnology – making good bugs better

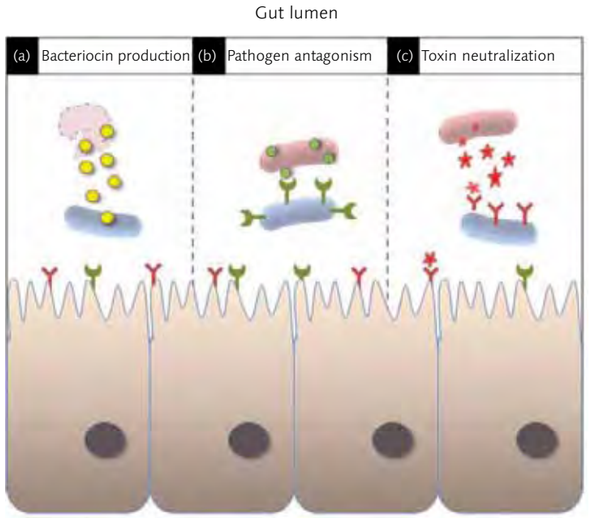
One approach to overcoming the limitations of physiological fragility is patho-biotechnology. Essentially, this novel approach involves the generation of 'improved' probiotic strains, using stress survival systems mined from more physiologically robust pathogenic microbes. The physiological versatility of pathogenic genera, oscillating between the external environment and the host, makes them a veritable treasure trove of genes that could potentially be used to improve the technological robustness of less well-adapted probiotic strains. Indeed, recent work in our lab has shown that cloning and heterologous expression of a single bile resistance gene, from the food-borne pathogen *Listeria monocytogenes* in the probiotic strain *Bifidobacterium breve*, not only improves gastrointestinal colonization and persistence, but also significantly bolsters the clinical efficacy of the probiotic.

Therapy

In addition to improving their physiological stress tolerance, resulting in improved delivery and persistence within the gut, recent studies have led to the development of 'designer probiotics' which specifically target enteric infections by blocking crucial ligand–receptor interactions between the pathogen and its target host cell. Many disease-causing bacteria exploit oligosaccharides displayed on the surface of host cells as receptors for toxins and/or adhesions, enabling colonization of the mucosa and entry of the pathogen or secreted toxins into the host cell. Blocking this adherence prevents infection, while toxin neutralization ameliorates

◀ Scanning electron micrograph of the probiotic strain *Lactobacillus salivarius* UCC118. Bar, 1 µm. *False colour added by Pat Casey*

symptoms until the pathogen is eventually overcome by the host immune system. 'Designer probiotics' have been engineered to express receptor-mimic structures on their surface. When administered orally, these probiotics bind to and neutralize toxins in the gut lumen and interfere with pathogen adherence to the intestinal epithelium – thus essentially 'mopping up' the infection. A particularly attractive feature of this toxin neutralization strategy is that, unlike antibiotic therapy, it applies no selective pressure for evolution of resistance by the pathogen. Blocking toxin-mediated host injury by the receptor mimic would negatively affect the capacity of the pathogen to survive and reproduce. Furthermore, mutations in a toxin sequence that prevents binding to a receptor mimic would logically also prevent the toxin from interacting with its natural target, thereby attenuating virulence. Therefore, widespread use of such agents in a therapeutic setting should have negligible long-term adverse consequences. As well as treating enteric infections, 'designer probiotics' are among the most recent conscripts in the war against AIDS, expressing HIV receptors which compete with host-cell receptors for the virus, thus providing a natural innate barrier to HIV attachment and infection.



▲ Overview of the antibacterial potential of designer probiotics. Bacteriocin produced by the probiotic (blue) can lyse invading pathogens (red) (a) while heterologously expressed receptor mimics on the surface of probiotic cells can antagonize pathogen adherence to the host (b) and neutralize toxin production (c). *Reproduced, with permission, from Sleator & Hill (2008),* J Med Microbiol *57, 793–794*

Prophylaxis

In addition to infection control, probiotics can also be engineered to function as novel vaccine delivery vehicles which can stimulate both innate and acquired immunity, but lack the possibility of toxicity which exists with more conventional vaccines that rely on live attenuated pathogens. Probiotic vaccine carriers administered by the mucosal route (i.e. orally or by nasal spray) mimic the immune response elicited by natural infection and can lead to long-lasting protection. Mucosal vaccine delivery also offers significant technological and commercial advantages over traditional formulations, including a reduction in pain and in the possibility of cross-contamination associated with intramuscular injection, as well as the lack of necessity for medically trained personnel to administer the vaccine – important considerations for large-scale vaccination protocols in less well-developed countries. Furthermore, not only do probiotics circumvent *in vivo* sensitivity to gastric acidity associated with oral application of therapeutic or prophylactic compounds, they can also be produced cheaply, grown to high levels, dried and stored for years at ambient temperatures.

Beyond conventional antibiotic therapies

In conclusion then, 'designer probiotics' can be engineered to kill pathogens, neutralize toxins and facilitate re-colonization of the resident beneficial microflora while at the same time priming both the innate and adaptive immune system, strengthening the host against subsequent infection – an approach far beyond the reach of conventional antibiotic therapies. Thus, the war against antibiotic-resistant 'superbugs' may eventually be won by recruiting engineered 'good bugs' as our allies.

Acknowledgements

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Further reading

Sleator, R.D. & Hill, C. (2006). Patho-biotechnology: using bad bugs to do good things. *Curr Opin Biotechnol* **17**, 211–216.

Sheehan, V.M., Sleator, R.D., Hill, C. & Fitzgerald, G.F. (2007). Improving gastric transit, gastrointestinal persistence and therapeutic efficacy of the probiotic strain *Bifidobacterium breve* UCC2003. *Microbiology* **153**, 3563–3571.

Sleator, R.D. & Hill, C. (2008). Battle of the Bugs. *Science* **321**, 1294–1295.

Sleator, R.D. & Hill, C. (2008). Engineered pharmabiotics with improved therapeutic potential. *Hum Vaccin* **4**, 271–274.

Sleator, R.D. & Hill, C. (2008). Designer probiotics: a potential therapeutic for *Clostridium difficile*? *J Med Microbiol* **57**, 793–794.

Sleator, R.D. & Hill, C. (2008). New frontiers in probiotic research. *Lett Appl Microbiol* **46**, 143–147.

A precious memory

Very few people are still around who met Alexander Fleming, but **Norberto J. Palleroni** not only recalls his meeting with the great man, but also has a photograph of the occasion as a keepsake.

One of the International Congresses of Microbiology took place in Rio de Janeiro in the middle of 1950. I had then received my degree from the University of Buenos Aires and had accepted the invitation to become Professor at the University of Cuyo located in Mendoza, Argentina. Attending the Congress was for me a unique opportunity to be near the scientists who had participated in the development of the science of my choice, and added to the pleasure of spending a few days in a magnificent hotel located on one of the hills surrounding spectacular Rio de Janeiro.

Professors Santos Soriano and Alberto Sordelli asked me to be part of the group shown in the picture above. Unfortunately, I have forgotten the names of two of the persons who spent such happy hours with me, but the group is represented here, from left to right: unknown, myself, unknown, Professor Santos Soriano (my microbiology teacher), Sir Alexander Fleming, Dr Alfredo Sordelli and Dr Molina (whose first name I forget). Two of the great microbiologists present at the congress were Professor Albert J. Kluyver, and Professor Charles Thom, the *Penicillium* taxonomist who named Fleming's strain *Penicillium notatum*. These two scientists were not available when the picture was taken.

About 350 microbiologists were present at the meeting and I had fascinating conversations with many of them. Both the importance of the congress and the beauty of the Rio de Janeiro bay and the Petropolis area contributed to the attraction of the event from both the scientific and social points of view.

My conversation with Sir Alexander has remained imprinted on my memory for the rest of my life. Both the content of our talk and the fact that it was rather short had much to do with its persistence. Dr Fleming came to me and asked, "*What are you doing in your laboratory, young man?*" I had finished my thesis manuscript not long before, and my answer was related to my recent studies. I simply said, "*I am interested in yeast genetics.*" Fleming looked at me for a minute or two, and his answer clearly painted the great man as a humble admirer of life's diversity, "*I must confess to you that I do not know anything about yeasts or about genetics.*" At which, the microbiological part of our conversation came to an end. The rest of our talk had to do with the beauty of the region and the hotel, and some comments on the coming banquet.

Norberto Palleroni is a Research Professor at Rutgers University, New Jersey, USA. He was a pioneer in the use of molecular identification techniques in prokaryotic bacteriology and is well known for his work on *Pseudomonas* taxonomy. Three bacterial species and a genus (*Palleronia*) have been named in his honour, and Professor Palleroni was awarded the Bergey Medal in 1995 (**e** palleroni@aesop.rutgers.edu)

The Defra-commissioned independent review of bovine tuberculosis research

With the Randomized Badger Culling Trial (RBCT) at an end, Defra asked SGM to review research into bovine TB and identify some new approaches. Co-chairs of the expert panel **Mike Barer** and **Charles Penn** found it a fascinating but demanding exercise.

The SGM is regularly asked by government and other bodies to comment on reports, policy statements and proposals relating to all our areas of interest. In the summer of 2007, Council was approached by the Department for Environment, Food and Rural Affairs (Defra) to assemble a panel of experts to review research into bovine tuberculosis (bTB) (Table 1), advise on the current Defra-funded portfolio and make recommendations regarding appropriate investments over the next 10 years. The scale of this request was a new departure for SGM.

Council took a generally favourable view to the approach, but required clarification of a number of matters. Ron Fraser duly made enquiries and a number of key points were established: (a) SGM had been recommended by our late lamented past president Howard Dalton, who had recently completed his term as chief scientific adviser to Defra; (b) while Defra had specific questions, the process and the report were to be independent; (c) the report was to address research, not policy issues.

Table 1. Specific brief

In the light of the Wilsmore and Taylor (2008) review and including the independent review of the TB research programme in 2006 and the Independent Scientific Group on TB's published papers on the RBCT and final report of 2007, to identify progress in the ongoing research programme and advise on whether the current balance is correct and whether the recommendations and objectives from the Krebs review (1997) have been achieved.
Identify gaps remaining in the evidence base and ascertain whether they are relevant and important to policy development and possible to answer through further research. Provide recommendations on the timescale and scope of further research.
Identify areas of uncertainty that will not be answered by research and advise how these can best be handled/mitigated.
Provide recommendations on what direction the bTB research programme should take in the next 5–10 years (including economics, agricultural demographics and social science). This should include recommendations on what should be considered research priorities within areas, e.g. diagnostics, and overall research priorities. This should include consideration of what are the most urgent areas that should be examined and where there might be scope for the most progress within a realistic timescale.

Bovine tuberculosis (bTB) – background

- Tuberculosis in cattle is caused by the bacterium *Mycobacterium bovis*, a close relative of the human tubercle bacillus *Mycobacterium tuberculosis*. Following the introduction of statutory cattle control measures and the pasteurization of milk in the UK, human infections with *M. bovis* are very rare; however, bTB remains a significant animal welfare and economic problem.
- The disease develops slowly over months, principally affecting the lungs and lymph glands. Infection appears to be transmitted by droplets containing live bacilli. Infectious animals do not necessarily appear to be ill.
- Following a 30-year period of relative quiescence, there was a rapid increase in reported bTB in the 1990s from under 5,000 to over 20,000 cases per annum.
- Several wild animals are susceptible to bTB. In particular badgers are regularly found to be infected. The same *M. bovis* strains can be shown by DNA fingerprinting (Spoligotyping) to be present in both badgers and cattle within a particular area.
- The RBCT attempted to determine whether elimination of badgers in areas with high levels of bTB would control the disease in cattle.
- Opinion on the results is divided. While it seems likely that a comprehensive badger cull in geographically defined regions could be effective, consideration of the balance of economic, logistic, ecological, social and political issues has proven exceptionally challenging.

In effect, SGM was being asked to review the research situation 10 years on from the landmark Krebs report (Krebs *et al.*, 1997) which had recommended the Randomized Badger Culling Trial (RBCT).

These discussions with Defra were taking place more or less contemporaneously with the publication of the final report on the RBCT (Bourne, 2007), the taking of evidence concerning bTB control by the all party House of Commons Select Committee on Environment, Food and Rural Affairs (EFRA, 2008), and the Government Chief Scientist's own review (King, 2007). These three processes seemed remarkable, at least as represented by the associated publicity, for the lack of concordance of opinion, in particular with respect to whether badger culling would or would not be the answer to reducing the statutory annual slaughter of over 25,000 cattle dictated by bTB surveillance.

To be fair, while these points of controversy spiced up the menu, they did not feature prominently in Council's final deliberation on whether to accept the commission and, with reassurance from Ron's enquiries, we were asked as co-chairs to assemble a group of experts to respond to Defra's brief.

It seemed self-evident that SGM would have ample expertise to address what appeared at first glance to be a microbiological research problem. However, as emerges from the brief, we were specifically directed to research that might impact on the control of disease in cattle. Thus ecological, social, economic and epidemiological expertise beyond the core skills of microbiologists was also essential and, in spite of a few inevitable refusals, we were delighted to assemble the group listed (Table 2). It was important that group members had no direct conflicts of interest, for example by having current Defra-funded research grants.

Carrying out the review

The group met for the first time just before Christmas 2007 and established a working framework. In contrast to the focus of the other assessments published or in progress at the time, we did not take the role of the badger reservoir as the starting point for our considerations. Rather, responding to Defra's request that we take a fresh look and ask whether important alternative lines of investigation had not been appropriately pursued, we attempted a systematic review from the microbiological perspective. Was there any aspect of *M. bovis* biology or the pathogenesis of bTB that might open up opportunities for improved control? With three more meetings, site visits to the Veterinary Laboratories Agency (VLA) centre at Weybridge and the Laboratory of the Government Analyst Field Station at Woodchester Park, and a very substantial amount of electronic traffic, we formed our conclusions.

The outcome

The systematic review of a pathogen is a well-trodden path and daunting volumes testify to the academic careers sustained by this pursuit. However, the need to identify insights that could support practical disease control measures, leaves us with a far less certain, muddy and pot-holed path compounded by many dead-ended side routes. For example, the diagnosis of bTB is currently based on skin testing for a specific cell-mediated immune response to a crude *M. bovis* antigen preparation. Tests require multiple visits from a vet. Surely, the new generation of blood sample-based Interferon Gamma Release Assays (IGRA) could make this key step easier and more reliable? The recent appearance of VLA colleagues in the high court to defend the use of IGRA assays testifies to the difficulty of introducing change in such a field. It impacts on a human activity on which many livelihoods depend and where tests predict a risk as opposed to actual infectiousness.

So what about the badgers? There is no doubt that they are an important reservoir, but there are huge challenges in defining the risk they pose and in instituting effective control. To diagnose bTB in a live wild badger requires trapping and anaesthesia so that samples can be taken and this makes large-scale surveillance prohibitively expensive. Critically, in spite of good molecular epidemiological tools, we have no means of directly determining the number and direction of infections transferred between cattle and badgers. Farm-level control measures to prevent contact are clearly rational, but we have little systematic evidence to support them; there is a major gap in understanding how best to motivate farmers to implement controls and the economic models that could provide such motivation are poorly developed. Culling produces disturbances in population distribution whose consequences will take many years to determine. Finally, badger vaccination provides an approach that will not antagonize the ecological lobby but there are huge uncertainties about delivery, efficacy and economics.

Our report was published in September 2008 (www.Defra.gov.uk/animalh/tb/pdf/report-oct2008.pdf) and the general recommendations (*Crown copyright*) are reproduced in the box below. We did not come to any startling new insights but, as far as time and resources allowed, commented constructively on current and future Defra-funded research. The experience was a fascinating journey encountering all the issues of science in contemporary society.

Table 2. Review group

Professor Mike Barer (co-chairman) University of Leicester
Professor Charles Penn (co-chairman) University of Birmingham
Dr Greg Bancroft London School of Hygiene and Tropical Medicine
Professor Chris Garforth University of Reading
Professor George Gunn Scottish Agricultural College Inverness
Professor Tim Roper University of Sussex
Professor Neil Stoker Royal Veterinary College London
Professor Rick Titball University of Exeter
Defra support Wendy Middleton Fiona Stuart
Secretariat (SGM, Reading) Dr Ron Fraser Mrs Janet Hurst

Key general recommendations

We identify three priority areas in which we believe new or additional investment in research could impact on the control effort. Related recommendations are developed further under the specific points below.

1 Diagnosis. We recommend further work on the development of simple screening tests applicable to cattle, badgers and contaminated environments. Critically, such tests should support high throughput and be focused on sensitivity. Availability of such tests would allow more resource-intensive analyses with higher specificity to be deployed in confirmatory investigations that would lead to statutory intervention.

2 Farming practices. The evidence base related to relevant farming practices is weak. We have insufficient information regarding the levels of understanding that farm workers and managers have regarding key issues affecting the control of bovine tuberculosis (bTB) and how this and other factors translate into relevant farm-level and economic actions.

3 Existing resources. We recommend that several extant and developing sources of information should be fully exploited, monitored and analysed to extract maximum benefit. Most important in this regard is the continued analysis of the impact of the RBCT, where the net effects of interventions on bovine disease have yet to be resolved. Further, where they are relevant, maximum use should be made of the results of studies concerned with human TB to progress our understanding of bTB. Finally, there is a strong case for a comprehensive and authoritative description of the histories of the bTB epidemics in the UK and Ireland, and a comparison with historic bTB within these islands.

In addition to these points, we strongly endorse current efforts being made towards vaccination of badgers and cattle and comment on some specific aspects of the work.

A key aspect of our remit was to advise on the potential application of new technologies. In this regard, we note that newly established high-throughput genome sequencing technologies render much more extensive work in this area economically feasible.

References

Bourne, F.J. (2007). *Bovine TB: the Scientific Evidence. Final Report of the Independent Scientific Group on Cattle TB*. London: Defra. www.defra.gov.uk/animalh/tb/isg/pdf/final_report.pdf

EFRA Committee (2008). *Badgers and Cattle TB: the Final Report of the Independent Scientific Group on Cattle TB*. London: Stationery Office. www.publications.parliament.uk/pa/cm200708/cmselect/cmenvfru/130/130i.pdf

King, D. (2007). *Bovine Tuberculosis in Cattle and Badgers. Defra*. Unpublished report. www.defra.gov.uk/animalh/tb/pdf/badgersreport-king.pdf

Krebs, J.R. & others (1997). *Bovine Tuberculosis in Cattle and Badgers – an Independent Scientific Review*. London: MAFF Publications.

Wilsmore, A. & Taylor, N.M. (2008). *Bovine Tuberculosis: an Update*. University of Reading/Defra. www.defra.gov.uk/animalh/tb/pdf/wilsmore-taylor-feb08.pdf

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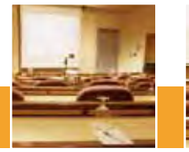

Spring**09** | Harrogate International Centre
www.sgmharrogate2009.org.uk

30 March–2 April 2009

Legacy of Fleming – Diagnosing, preventing, controlling and treating infectious diseases in the modern world

Programme booklet

A booklet giving full details of the programme is enclosed with this issue of *Microbiology Today*. Any changes will be posted on the SGM website.

Who should attend?

This will be the largest gathering of microbiologists in the UK in 2009. Attendance is essential for anyone who wants to keep up to date with modern microbial science.

Where is it?

Located in the heart of historic Harrogate, gateway to the Yorkshire Dales, the International Centre has excellent facilities. Harrogate is within easy reach of Leeds, Manchester, York and Newcastle, with convenient rail, air and transport links.

Grants

Conference grants are available to SGM Postgraduate Student Associate Members.

New SGM Prize Medal Lecture

Prion biology and diseases

Professor Stanley B. Prusiner (Institute for Neurodegenerative Diseases, University of California, USA)

Novel antimicrobials and therapies

Antibiotics and the environment

Impact of medical intervention on microbial evolution

Infection control

New ways of rapid diagnosis

Novel antimicrobial treatments for food production

Production, formulation and delivery of antimicrobials (*industry session*)

Multi-drug-resistant TB

Mechanisms of resistance (with BSAC)

Antibiotic resistance in staphylococci

The human microbiota

Infections in war wounds past and present

Virology

The programme will include symposia on *Molecular evolution of virus pathogens*, *Structural insights into virus biology* and *Prions*, 7 workshops (*Pathogenesis* | *Gene expression* | *Immunovirology* | *Epidemiology, evolution and modelling* | *Entry, trafficking and egress* | *Virus structure* | *Plant virology*) and poster sessions.

Other highlights

Careers and education workshops

Gala Dinner at the Old Swan Hotel

Evening poster sessions with wine

Prize lectures

Trade exhibition

Go to **www.sgmharrogate2009.org.uk** for programme details and online registration.

Autumn**09** | Heriot-Watt University Edinburgh

7–10 September 2009

Translational microbiology

The 200th anniversary of the birth of Darwin will be marked by a symposium at this conference, alongside a range of sessions that explore the many ways that microbes can be put to work, such as in food or drug production, cleaning up the environment, in industry and as model organisms. Topics include:

Darwin's Tree of Life | *Bacterial cell walls* | *Putting microbes to work* | *Conjugate vaccines* | *Contribution of the global N cycle to global processes* | *Alternative models to study mammalian pathogenesis* | *Meningitis* | *Cultivating and sensing microbes in micro-scale devices* | *Microbial foods* | *Microbial polysaccharides* | *Bioenergy fuel sources* | *Microbial factories* | *Polar microbiology*

Contact details of organizers are included in the meeting programme on the SGM website. Deadline for receipt of titles and abstracts for offered presentations: **8 May 2009**. A card to promote the meeting is enclosed with this issue. Please circulate it in your department. See **www.sgmheriot-watt2009.org.uk** for details.

Other**Events**

FEMS 2009 – 3rd Congress of European Microbiologists

Gothenburg, Sweden
28 June –2 July 2009

www.kenes.com/fems-microbiology

ASM/SGM Joint Meetings

Cambridge MA, USA, 1–4 July 2009
Prokaryotic Development

Aix-en-Provence, France
5–9 October 2009
3rd International Conference on Salmonella

Irish**Division**

23–24 April 2009

University of Cork, Ireland

Innovative models and systems for studying microbial pathogenesis

For further details, contact John Morrissey (e j.morrissey@ucc.ie).

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Suggestions for topics for future symposia are always welcome.

Meetings Administrator
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(t 0118 988 1805; f 0118 988 5656; e meetings@sgm.ac.uk).

Abstracts

Titles and abstracts for all presentations must be submitted through the SGM website by the advertised deadlines. For further information contact the Administrator.

www.sgm.ac.uk/meetings

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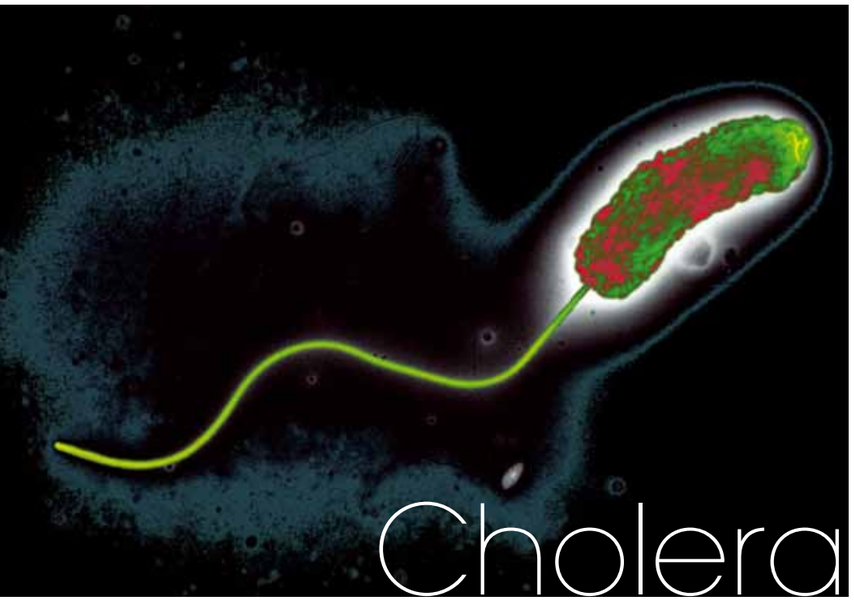

Cholera

With cholera in Key Stage 4 specifications as an exemplar of an infectious disease, teachers can use the recent outbreak in Zimbabwe to show how relevant it still is to everyday modern life. **Dariel Burdass** describes the disease and the course of the current epidemic.

Cholera is caused by the bacterium *Vibrio cholerae*. It affects the absorption of water in the small intestine. The bacteria multiply in the gut and produce a toxin. The toxin affects the cells lining the gastrointestinal tract and causes large quantities of fluid to be lost from the body.

Reservoir of infection

The bacterium is found in brackish water habitats where there is a mixture of sea and fresh water. When this water gets into the drinking supply, an outbreak of the disease may follow.

Epidemiology

Until the 1800s, outbreaks of cholera were confined to the Indian subcontinent. Since then pandemics have occurred around the world. Today cholera is common in Asia (particularly in Bangladesh and the Ganges Delta), Africa, the Middle East, Peru and some other South American countries. It is usually confined to countries with poor sanitation infrastructure.

▲ *Vibrio cholerae* bacterium. *Eye of Science / Science Photo Library*

History

It was originally thought that cholera was caught by breathing in bad air – miasma – and people believed that strong smelling substances such as herbs and camphor could offer them some protection from the disease.

John Snow did not accept this theory. He argued that cholera entered the body through the mouth, not the lungs. In 1849 he published his ideas in an essay *On the Mode of Communication of Cholera*. In 1854 he was finally able to prove his theory of transmission. Snow mapped cases of cholera during the 1853–4 outbreak in London and believed the source was a water pump in Broad Street, Soho. He identified a child living in Broad Street who had been ill with cholera, and suspected that the child's faecal matter had leaked from the sewerage system into the water supply. This became contaminated and infected anybody who drank water from the pump. John Snow recommended the removal of the pump handle so that people could no longer draw their water from it. This led to an immediate decline in the number of cases of cholera, proving his theory.

Thirty years later Robert Koch identified the organism that causes cholera.

Symptoms

The incubation period for this pathogen is very short: from 2 hours to 5 days. Some people with cholera are asymptomatic (they do not experience any symptoms) and most only have mild diarrhoea which is difficult to distinguish from that caused by other pathogens, such as viruses. However, all of these people carry the pathogen, excrete it and thus can spread it to others.

Severe cholera (cholera gravis), which accounts for fewer than 10 % of cases, is characterized by the rapid onset of violent watery diarrhoea, leg cramps, vomiting and dehydration. The diarrhoea is straw-coloured with flecks of mucus and looks similar to rice water. As much as 1 litre of fluid can be lost every hour.

As fluid is lost the blood thickens and the skin becomes blue/grey in colour. What makes cholera so dangerous is the rapid loss of fluids from the body in a short space of time. If untreated, the loss of fluid can be fatal within 24 hours of developing the disease. The fatality rate in untreated cases can be as high as 30–50%. If patients are given rehydration therapy, then the death rate is below 1%.

Transmission

As the bacteria are excreted in the faeces, cholera is spread by person-to-person contact via the faecal–oral route, for example if a person drinks from a water supply contaminated with infected faecal matter. The bacteria can also be spread to food if infected people don't wash their hands thoroughly after going to the toilet.

Shellfish living in contaminated water can transmit cholera too. They are filter feeders and as they strain the water the bacteria become concentrated inside them. Anyone consuming the shellfish without proper cooking can become ill.

Epidemics usually occur due to infected water supplies rather than by direct person-to-person contact.

Treatment

Clean water and rehydration salts are given to sufferers to alleviate symptoms. These are usually taken orally. However, if the person is very dehydrated then they may need to be hospitalizsed and given fluid through an intravenous drip. Some people are given antibiotics.

Prevention

Good sanitation, clean drinking water and improved hygiene practices such as washing the hands after visiting the toilet and before preparing food are all strategies that need to be followed to prevent outbreaks of cholera.

Vaccines

An oral vaccine, Dukoral, is available in the UK, but it does not protect against all strains of *Vibrio cholerae,* and is usually given to people working in areas where cholera is endemic and the risk of contracting it is higher than normal.

Websites

www.cdc.gov/nczved/dfbmd/disease_listing/cholera_gi.html

www.netdoctor.co.uk/travel/diseases/cholera.htm

www.un.org/ha/

www.who.int/topics/cholera/en/

Outbreak!
Cholera in Zimbabwe

Cholera is endemic in Zimbabwe. Outbreaks of the disease, according to the World Health Organization, have been occurring annually in the country since 1998, but this is the worst one since 2000. Previously, the disease had been kept under control by strategies that concentrated on both prevention and preparedness. In 2008, however, cholera bridged Zimbabwe's dry season when the incidence usually dies down, and it has been predicted that the crisis will worsen during the rainy season which runs from December through to March.

On 14 January 2009 the World Health Organization reported that the number of cholera cases in Zimbabwe since the outbreak began in August was 40,448; according to the United Nations the death toll was 2,106. The bulk of cases were in Harare, the country's capital. Some doctors have indicated that this death count is too low and that many have not been officially recorded as the government tries to hide the scale of the problem. The overall mortality rate in Zimbabwe is 4 %, but in some areas it has reached as high as 20–30 %. If the illness is treated quickly and

properly, the mortality rate is normally less than 1 % and the patient recovers completely.

The scale of this year's cholera epidemic has been caused by the breakdown in Zimbabwe's water supply network and sanitation system, and exacerbated by the collapse of the country's health service. Much of Harare is now without water because of a shortage of purification chemicals; the densely populated town of Chitungwiza has been without running water for 13 months. Out of desperation people are now drinking from contaminated wells and streams. Raw sewage is reported to be running through the streets of Harare and three hospitals in the capital have closed because of a shortage of drugs and staff.

Elizabeth Byers, a spokesperson for the United Nations Office for the Co-ordination of Humanitarian Affairs (OCHA) said,

> '*The rapid deterioration of the health service delivery system in Zimbabwe, lack of adequate water supply and inability to dispose of solid waste and repair sewage blockages in most areas will continue to contribute to the escalation and spread of the outbreak.*'

The United Nations Health Agency, on 1 December, called for $2 million to tackle the epidemic in Zimbabwe by providing health supplies, water purification equipment and trained personnel.

A major concern is that as infected refugees flee Zimbabwe looking for treatment, water and food, they will spread the disease across the border into neighbouring countries such as South Africa and Botswana, increasing the scale of the problem even further.

Dariel Burdass
SGM Education Manager

ASE at Reading 2009

The Association for Science Education (ASE) Annual Meeting was held at Reading University from 8 to 10 January, and the SGM took part in many activities. As well as having a stand in the exhibition shared with MiSAC, where staff distributed our microbiology teaching resources, gave advice on related topics and promoted schools membership and our practical training courses to teachers, technicians and consultants, we sponsored a speaker in the *Biology in the Real World* symposium organized under the NUCLEUS banner (see below).

Hands-on

Dariel Burdass, Janet Hurst and Jane Westwell also took part in the MiSAC drop-in microbiology workshop. We demonstrated simple and fun practicals on hand hygiene and the effects of antimicrobials tied in to the 'How Science Works' part of the curriculum, showed how to make a hay infusion and investigated the fascinating lives of algae and protozoa under the microscope. Other members of MiSAC showcased a wide range of microbiology observations and experiments. Four workshops were held over 2 days which proved very popular with delegates, each of whom was given an SGM rucksack packed with teaching goodies to take away.

▼ *From left to right*: Martin Adams (MiSAC), Jane Westwell, Yvonne Taylor and Janet Hurst (all SGM) manning the stand. *Dariel Burdass*

MiSAC is 40!

This year marks the 40th anniversary of the Microbiology in Schools Advisory Committee. A brief account of its history will appear in a future issue of *Microbiology Today*, but the gathering of bioscience education professionals at the ASE Annual Meeting provided an ideal opportunity for a party to celebrate the birthday! SGM, which provides the secretariat for MiSAC and administers the annual schools competition, hosted the event. About 50 friends, old and new, met for an evening reception in the Cole Museum at the University of Reading, which is located appropriately in the Animal and Microbial Sciences Department where MiSAC Chairman John Grainger spent most of his professional life.

▲ Guests at the MiSAC 40th birthday party listen to John Grainger's speech. *Dariel Burdass*

Biology in the Real World

This one-day event sponsored by members of NUCLEUS aimed to 'bring the curriculum to life'. Member organizations, which are all involved in promoting bioscience education, invite eminent speakers from their discipline to give talks on areas of their research which are linked to topics in the biology specifications. The speakers include cutting-edge research which allows teachers to update their knowledge and address the 'How Science Works' aspect of the curriculum.

The SGM invited Dr Helen Fletcher from The Jenner Institute, Oxford to give the presentation *Why do we need a new vaccine for tuberculosis?*

Helen first became interested in TB during her first postdoctoral position at University College London where she looked for tuberculosis (TB) in a collection of 18th century Hungarian mummies. She then moved on to a project to look at immune responses in TB patients and their household contacts in The Gambia, Zambia and Ethiopia. In 2002 Helen started work on a TB case-contact study in Senegal and to look at the immune response to vaccination with a new vaccine for TB which had been developed at Oxford. The new TB vaccine is a viral vector vaccine called MVA85A. Since it was first tested in humans in 2002 it has undergone a series of safety and dose finding trials in healthy adults, children, infants and in HIV and TB infected adults. In 2009 the group will be conducting a phase IIb efficacy trial with MVA85A in infants in Cape Town, South Africa. This study will recruit 3,000 infants and will be the first efficacy trial of a new TB vaccine.

Helen gave an excellent talk that was extremely well received by the 60 plus teachers in the audience. She gave an overview of vaccination and its effect on the immune system before moving on to explain why we need a new vaccine for TB, and describing current TB vaccine developments and vaccine efficacy testing for Phase II, III and IV. It was particularly exciting as Helen will be one of the members of the team going to Cape Town in February to start the phase IIb efficacy trial with MVA85A in infants.

Helen has kindly provided new information on the various vaccine strategies that are currently being investigated for TB in the SGM's updated teaching factfile *Tuberculosis: can the spread of this killer disease be halted?* due to be published soon. School members will receive a free copy of the revised resource.

Dariel Burdass & Janet Hurst
SGM External Relations Department

In brief

Survival Rivals

www.survivalrivals.org

Survival Rivals is a series of three experiments inspired by Darwin which provide opportunities for young people to carry out practical science. A kit will be available for each experiment which includes everything necessary to carry out the investigation. The topics are: *I'm a Worm, Get Me Out of Here* for 11–14 year-olds, *BrineDate* for 14–16 year-olds and *The X-Bacteria* for post-16 students. *X-Bacteria* investigates antimicrobial resistance and how it is spread by plasmids.

Sponsored by The Wellcome Trust, the kits will be available to all UK secondary schools later this year.

Practical Work in Science

www.score-education.org

This booklet has been created by SCORE (Science Community Representing Education) to encourage practical work in schools. It has sections on biology, physics and chemistry, each containing a range of investigations tied to particular age groups. SGM has contributed a secondary practical entitled *Microbes ate my Homework* which investigates how microbes break down cellulose (originally published in the SGM/MiSAC book *Practical Microbiology for Secondary Schools*). The booklet will be distributed free to all UK secondary schools and has been published to coincide with SCORE's Manifesto *Getting Practical: A Framework for Practical Work in Schools*, which is available on their website.

Gradline aims to inform and entertain members in the early stages of their career in microbiology. If you have any news or stories, or would like to see any topics featured, contact **Jane Westwell** (e j.westwell@sgm.ac.uk).

Funding your research – getting your hands on the money

There is no doubt that sourcing funds is one of the biggest issues facing researchers in universities and institutes – all the more so for those in the early stages of their careers. In August 2008 issue of Gradline, **Jane Westwell** reviewed sources of funding. This issue she considers strategies to maximize application success rate.

As outlined in the previous article, for early career microbiologists, the main options for funding independent research are the fellowships supported by some of the funding bodies (e.g. MRC, Wellcome Trust, BBSRC and Royal Society). The funding bodies provide guidelines for applicants that are available from relevant websites, but there are some common points to consider.

Before you start

Enlisting the support of a mentor is an excellent idea – someone who can give feedback on your ideas and the first draft of your proposal. You should allow yourself plenty of time to put together the grant application. Apart from giving yourself the chance to hone your science (and words), you will almost certainly be required to include counter-signatures from your Head of Department and Finance Office. It isn't just a matter of signing the form – the finance office will actually check your figures and will need a few days to turn the application around. Equally, your Head of Department will not appreciate a request for a supporting statement only a day (or hours) before the deadline.

Making your case

To maximize your chances of success you should consult and follow the published guidelines; ensuring that you meet all criteria and address all points.

Presenting your scientific case

- ☐ Is the science relevant to the grant scheme? Unless your idea fits within its remit, you will almost certainly be wasting your time.
- ☐ Projects should have a clear hypothesis.
- ☐ Put your proposal in context and show why it is important. Refer to current and past progress in the field and describe how your work will fit in. You should also indicate how your project will add value.
- ☐ The outline of the proposed work should be clear including experimental approach and techniques to be used.
- ☐ Including pilot data will show that the work is feasible.
- ☐ Identify potential problems and outline how you might overcome them.
- ☐ You should be aware of strengths and weaknesses of your proposal – the panel will certainly consider them.

General points

- ☐ The proposal will be read by several people.
- ☐ Whatever the scheme, your scientific track record is important – all the more reason to publish as much as possible from your PhD research and any postdoctoral projects.
- ☐ Take care with the costings and requests for resources – they must be realistic and accurate. Perceived value for money is also important.
- ☐ Don't apply for ineligible costs, there may be limits on expenditure on individual pieces of equipment.
- ☐ If the work involves people, human samples or animals, you will need to give consideration to arrangements for ethical review and research governance of the project.

Aim for perfection

You must make sure that you complete all relevant sections clearly and concisely. The proposal will be read by several people, some of whom will not be experts in your field of research. Your abstract should be very clearly written to attract the award panel's attention, and don't forget to introduce any acronyms. Proof-reading is essential to remove all spelling and grammatical errors. Some reviewers take the view that a sloppy application is an indicator of a sloppy scientist; you don't want unreliable spelling to create a poor impression. Enlisting the help of a colleague or friend to proof-read is a very good idea (you are likely to see the words you intended to write rather than mis-spellings). Also, make sure you comply with any maximum word / page allowances.

Assessment procedure

Each funding body will vary slightly in the assessment procedures, but generally applications are screened for eligibility and sent out to referees who consider proposals against a defined set of criteria such as:

- ☐ How important are the questions or gap in the knowledge being addressed by the proposal?
- ☐ Does the project offer potential for good scientific progress?
- ☐ Is the research plan feasible?
- ☐ Does the applicant have the relevant expertise or do they need a collaborator?
- ☐ Is the proposal relevant to funding body strategy?
- ☐ Is the project cost effective and does it offer good value for money?

Applications are then usually considered by an award panel, in light of the referees' comments, ranked and decisions over funding made.

Common reasons for failure

In the competitive world of grant applications there can be many reasons for failure. By the time the panel is allocating funds they are choosing between excellent proposals and weaker applications will have been eliminated before this stage. Reasons for rejecting applications include:

- ☐ The proposal is poorly written.
- ☐ There is no clear hypothesis.
- ☐ The proposed research does not appear to meet the aims of the project.
- ☐ The proposal is too expensive or offers poor value for money.
- ☐ The methodology is flawed or not enough information is provided for the panel to make a judgement.
- ☐ The applicant doesn't appear to be familiar with other research in the field.
- ☐ The applicant has an unpromising track record.
- ☐ There is a lack of expertise and no collaborators are identified.
- ☐ The proposal is unrealistic, i.e. too much work planned for the timescale.

Ablestock / Jupiter Images

Industrial support

Some research is not supported by the funding bodies because it does not fit their remit. Applied science is often funded by industrial sponsors via short-term research contracts. If your area of research falls in this category, you may need to consider obtaining funding from industry. The first thing to remember is that commercial organizations do not fund research grants. A successful funding proposal identifies a potential market opportunity and develops a programme of research to take the idea forward. Alternatively, it might answer a specific problem or question that the sponsor has identified. If you do apply for industrial funding, you should clarify your sponsor's policy about presenting work at meetings and publishing in journals. It is useful to find out who is involved in the decision-making process and what the likely timescale is.

Making initial contact can be hard. 'Cold-calling' with an unsolicited proposal will not meet with success. Instead you should take a long-term view and start by raising your professional profile. Exploiting colleagues' contacts is a good start, as is networking at scientific meetings attended by industrially employed scientists. If you are able to speak at a conference, this is an excellent way of getting you and your research noticed. Writing articles for specialist trade magazines is also a good idea.

If at first you don't succeed…

Applying for funding can be a disheartening process; it is intensely competitive and assessment is stringent. Very few people are lucky enough to obtain funding the first time they apply and it can sometimes take several attempts before you achieve success. However, as they say in the north-east of England 'if you don't ask, you won't get, so why not give it a go!

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Further information

www.sgm.ac.uk/pubs/micro_today/pdf/080807.pdf (Gradline article – *Funding your research*)

www.bbsrc.ac.uk

www.mrc.ac.uk

www.wellcome.ac.uk

www.daphnejackson.org.uk

http://homepages.inf.ed.ac.uk/bundy/how-tos/rsg-how-to-get-funding.html (*Writing a good grant proposal* by Alan Bundy and Simon Peyton Jones)

Harrogate HIC

Attention postgrads and postdocs attending the SGM Harrogate meeting!

Don't miss the free workshop for early career microbiologists: *Personality and career development*, followed by a buffet and drinks.

It takes place at 1915 on Monday 30 March 2009 and will give you some new ideas for your career development and planning. You will learn about a well-known personality inventory, the MBTI (Myers Briggs Type Indicator), and how it can help to decipher between different personality types. The session will give you the opportunity to spot some of the personality elements which describe you or that you recognize in your friends or colleagues, and will show the importance of considering personality in your day-to-day working life.

The workshop will be delivered by Sarah Blackford, Education & Public Affairs Officer for the Society for Experimental Biology, who is a qualified MBTI practitioner. She uses it as a basis for self-awareness in the career development programmes she runs which are specifically designed for life science postgraduates and postdocs.

addresses

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Science writer **Meriel Jones** takes a look at some recent papers in SGM journals which highlight new and exciting developments in microbiological research.

Candida and the Asuga beauties

Nagatsuka, Y., Kiyuna, T., Kigawa, R., Sano, C., Miura, S. & Sugiyama, J. (2009). *Candida tumulicola* sp. nov. and *Candida takamatsuzukensis* sp. nov., novel yeast species assignable to the *Candida membranifaciens* clade, isolated from the stone chamber of the Takamatsu-zuka tumulus. *Int J Syst Evol Microbiol* **59**, 186–194.

Fungi and bacteria are well-known for damaging works of art when growing on or into them. A Japanese collaborative team, consisting of researchers at the TechnoSuruga Laboratory Co. Ltd and the National Research Institute for Cultural Properties, Tokyo, has had an unusual problem to deal with in recent years that has led to the discovery of novel species of fungi growing in a most unfortunate position. The 7th or 8th century Takamatsu-zuka tumulus in Nara Prefecture was excavated in 1972. The contents were disordered and had been looted in the past. However, the outstanding discovery was the quality and cultural significance of paintings depicting guardian spirits, men, women and star constellations in vivid colour on its plaster walls and ceiling. They were designated National Treasures and measures were taken to prevent deterioration by maintaining water-saturated air at moderate temperatures around them within a protective facility.

Unfortunately, perturbations caused by restoration or building work have tended to coincide with the appearance of fungal colonies and viscous gels on the surface of the murals. To elucidate the cause of the biodeterioration of the mural paintings and to understand how to prevent these damaging microbes growing on the paintings, the team identified some of the fungi. After taking swabs from inside the tumulus, they were able to isolate many fungi, including 44 that grew as the single-celled form called yeasts. To identify the yeasts, the researchers carried out a series of physiological and biochemical tests and also determined the sequence of several regions within their DNA. They also checked whether the disinfectants that had been used within the tumulus had any effect on them.

Nineteen of the 44 yeast strains were members of the *Candida membranifaciens* group, but distinct from any previously known species. However, a search through the records of *Candida* DNA sequences pulled out two earlier reports of identical sequences. These came from unnamed *Candida* species isolated from a liquid sweetener in the Netherlands and from seawater taken in the Mid-Atlantic Ridge near the Azores. The Japanese yeasts fell into two groups, now named *Candida tumulicola* and *Candida takamatsuzukensis*, both characterized by the results from biochemical tests and DNA sequences. The disinfectants paraformaldehyde, ethanol and isopropanol had all been used in the tumulus, and interestingly, the two novel yeast species could not consume isopropanol. This therefore seems a good choice for keeping the newly identified yeasts away from the artworks.

► 1300-year-old mural paintings, with serious discoloration and blackening, in the small stone chamber of the Takamatsu-zuka tumulus in the village of Asuka, Nara Prefecture, Japan. Top, Part of the star constellations (*Seishuku*) on the ceiling (*Nara National Institute for Cultural Properties*); middle, a group of four women, called the Asuka beauties or the *Asuka bijin*, on the west wall plaster (*Agency for Cultural Affairs, Japan*); bottom, a group of four women on the east wall plaster with a black-stained region (near the bottom of their skirts) on which viscous gels (biofilms) have developed (*Agency for Cultural Affairs, Japan*).

► False-coloured scanning electron micrograph of *Bifidobacterium bifidum*. *B. bifidum* is a member of the large family of probiotic bifidobacteria which are present in mammalian gastrointestinal systems including humans and cattle, where they suppress pathogenic micro-organisms. Some are also present in the intestines of poultry. They are used by the dairy industry in addition to lactobacilli and lactococci to make yogurt and are also part of medicinal supplements. *Scimat / Science Photo Library*

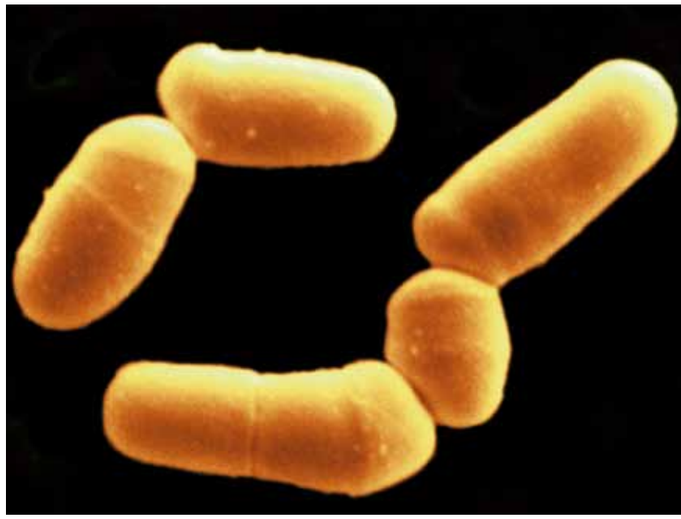
Enzymes from friendly bacteria

Searle, L.E.J., Best, A., Nunez, A., Salguero, F.J., Johnson, L., Weyer, U., Dugdale, A.H., Cooley, W.A., Carter, B., Jones, G., Tzortzis, G., Woodward, M.J. & La Ragione, R.M. (2009). A mixture containing galactooligosaccharide, produced by the enzymic activity of *Bifidobacterium bifidum*, reduces *Salmonella enterica* serovar Typhimurium infection in mice. *J Med Microbiol* **58**, 37–48.

Any visit to a supermarket, chemist or health-food shop reveals the expanding range of products for sale with the claim that they improve the balance of 'good' bacteria within the gut. As well as probiotics that contain live bacteria, there are also prebiotics, defined as non-digestible food ingredients that should benefit their consumers through stimulating the growth or activity of selected bacteria. Prebiotics are usually made from some of the more unusual types of sugar molecule, and galactooligosaccharides (GOS) have attracted considerable interest, partly because they are in normal human milk, which is most definitely good for the digestive health of babies.

An additional potential market for prebiotics is within agriculture to help control infections and improve growth of farm animals. Antibiotics used to be added to animal feed in the European Union for this purpose. Even though ones used in medicine have not been permitted as growth promoters since the mid-1990s because of concern about the spread of antibiotic-resistant bacteria, the European Commission finally banned the use of all antibiotics as growth promoters from January 2006, although they continue to be used in many other countries. European farmers now have to use different means to maintain the health and quality of their animals. As well as taking greater care in animal husbandry, there are opportunities for new products that affect the balance of microbes in the gut so as to maintain the animal's health and growth. This is therefore seen as a new, and potentially large, market for prebiotics.

Whether prebiotics really benefit healthy, well-nourished people or animals is still unclear. This report on the GOS prebiotic Bimuno is therefore a very interesting addition to the debate. It comes from research funded by Clasado Ltd and carried out by UK researchers at the Veterinary Laboratories Agency. Bimuno is manufactured by Clasado Ltd using



enzymes from the bacterium *Bifidobacterium bifidum* and has been marketed in the UK since 2007 as a health supplement (www.bimuno.com). The researchers carried out a series of tests to see whether Bimuno offered protection from *Salmonella enterica* serovar Typhimurium. This species of bacteria can be found in the intestines of farm animals and can be transmitted to humans on meat products where symptoms such as nausea, vomiting and diarrhoea are observed, being most severe in the very young and old. Young farm animals can also suffer illness and sometimes die; therefore, infections in animals and people constitute a public health problem. The question was therefore whether Bimuno might help prevent the gastroenteritis caused by the pathogen *S.* Typhimurium.

The researchers carried out their tests by feeding mice Bimuno and then bacteria half an hour later, or each alone. It was immediately obvious that Bimuno reduced every facet of illness in the mice, although the mechanism was not clear. It might have stopped the bacteria sticking to cells on the surface of the mouse gut, and thus prevented them entering the host to cause disease. Experiments in a more artificial situation using cultured human colonic cells indicated that Bimuno reduced the invasion of the pathogen; it is possible that protection could have been through triggered mechanisms within the colon cells to resist bacterial invasion, or the Bimuno might have concealed receptors on the colon cell surface from the bacteria by coating either the bacteria or the colonic cells. Regardless of the exact mechanisms of its action, the researchers are confident that the studies demonstrate that Bimuno reduces the severity of illness in mice and are a step towards discovering whether it can have a role in preventing conditions such as travellers' diarrhoea or salmonellosis.

Further studies are underway to determine the mechanisms of its action.

Biodiesel from fungi?

Strobel, G., Knighton, B., Kluck, K., Ren, Y., Livinghouse, T., Griffin, M., Spakowicz, D. & Sears, J. (2008). The production of myco-diesel hydrocarbons and their derivatives by the endophytic fungus *Gliocladium roseum* (NRRL 50072). *Microbiology* **154**, 3319–3328.

Renewable fuel sources are a hot topic, although bioethanol from microbial fermentations has been used for decades in several countries, notably Brazil and the USA. Increasing production from this industry has run into the problem that the fermentations need grain from good agricultural land, creating tension between food and fuel. Both academic and industrial researchers have been trying to make the process more efficient, and are looking around for alternatives. Gary Strobel and his group from Montana State University, USA, have now encountered the exciting possibility that biodiesel could be produced by a fungus from the Northern Patagonia forest. Although the project is still at an early stage, the recent report from his research group and collaborators in *Microbiology* holds very interesting potential.

A filamentous fungus, initially identified as *Gliocladium roseum*, was found growing within stems of an ulmo tree (*Eucryphia cordifolia*) without any obvious effect on it. This meant it was classed as an endophyte, a relatively unstudied type of fungal lifestyle for the very reason that it is neither harmful nor beneficial to the plant within which it is concealed. As the researchers studied the fungus, they realized that it had very unusual properties in that it liberated volatile compounds into the air. Their initial experiments showed that these compounds had antimicrobial properties, but their most recent analyses have detected something even more interesting.

Diesel, used as fuel in cars and lorries, consists of hydrocarbons produced by the petrochemical industry from oil. These are smaller than the hydrocarbons produced by most bacteria, fungi or plants that have been tested. Surprisingly, *G. roseum* produces a mixture very similar to diesel even when growing on oatmeal in the laboratory. Yields were even higher when access to oxygen was limited, perhaps mimicking the organism's natural environment within a tree. It could even do this when grown on cellulose, the most abundant natural organic compound in the world. Indeed, the researchers speculate that some hydrocarbons in fossil oil deposits might have originated from endophytic fungi like *G. roseum* growing on decomposing trees in the distant past.

The researchers have coined the term 'myco-diesel' for the volatiles from *G. roseum*. It may not be a commercial proposition now, but it certainly provides new insight into microbial biosynthetic capacity that might eventually lead to an economically viable product.

▲ Top. A culture of *Gliocladium roseum*. Bottom. The author, Gary Strobel, with the host plant, *Eucryphia cordifolia* (ulmo tree). *Gary Strobel*

Fighting hepatitis infection with gamma interferon

Thirion, G. & Coutelier, J.-P. (2009). Production of protective gamma interferon by natural killer cells during early mouse hepatitis virus infection. *J Gen Virol* **90**, 442–447.

Mouse hepatitis virus causes disease of the liver and nervous system in mice, with symptoms similar to those in human illnesses. It is also one of the coronaviruses, which have gained a high international profile since another member of this group was identified as the cause of the severe acute respiratory syndrome (SARS) epidemic in 2003. Therefore, there are several good reasons for investigating exactly how this coronavirus causes disease.

Different strains result in different symptoms, suggesting that they do not all affect the same systems within the body. Gamma interferon (IFN-γ) is among the important proteins produced during an infection to resist the virus. It is required to protect the liver against the lethal A59 strain of mouse hepatitis virus (MHV-A59). The level of IFN-γ in mouse blood reaches a maximum 2 days after the start of an infection and then decreases to undetectable levels 2 weeks later. Without a rapid increase in IFN-γ, the mice die from hepatitis, so it is clearly very important for protection.

Researchers already know that IFN-γ is synthesized by lymphocytes, but there are several types of lymphocyte. Both T lymphocytes and natural killer (NK) cells produce IFN-γ following a viral infection. The authors of this paper have now shown very convincingly that NK cells within the liver are the main producers of IFN-γ in the first days of MHV-A59 infection. The protection occurs through a direct effect of IFN-γ on cells infected by the virus, rather than any indirect route. The next question for the researchers is to see whether this protective mechanism works in the same way for other viruses that damage the liver, such as the hepatitis B virus that affects humans.

SGM aims to promote microbiology to a whole range of audiences. In this issue we describe some schemes to help scientists wishing to get started in public engagement, cover a conference on schools biology outreach, see images of famous people in microbes and go to Ireland to narrow the gap between microbiologists and politicians.

Getting the word out

In November 2008 the Biosciences Federation presented its annual science communication awards. The winners of the new researcher and established researcher categories both spoke about the help scientists who talk to the general public can get by talking to each other. **Ed Hutchinson**, whose nomination for the new researcher category of the award was sponsored by the SGM, spoke to some of the people who are trying to make this possible.

The importance of communicating science to the general public as well as to one's peers is now widely recognized, and as regular readers of *Microbiology Today* will be aware many scientists are engaging in this with great enthusiasm. In recent years, various schemes have been set up to help scientists integrate public engagement with their work. Thanks to these innovative projects, scientists interested in outreach work can now receive training, and can share their expertise and experience with each other at the click of a mouse.

It comes as no surprise that a lot of science communication work is based in universities, where large numbers of staff and students have a winning combination of knowledge, enthusiasm and fairly flexible working hours. Cambridge is a good example of this, with literally thousands of staff and students regularly volunteering their time to share their enthusiasm for their subjects. This outreach work is often supported directly by the university and its colleges, who provide resources and facilities for everything from small-scale events to the university's annual *Science Festival*, the largest free science festival in the UK. Like many others at Cambridge who have enjoyed the chance to be involved with science communication, I was interested to hear about *Rising Stars*, an HEFCE-funded training course set up by the university to assist people in communicating their subjects.

Rising Stars – fostering public engagement

'*Underlying the scheme is the need to create dialogue between the University and the wider community, and to communicate what goes on at the University and its contribution to society*,' explains Nicola Buckley, the university's Festivals and Outreach Co-ordinator. '*We see* Rising Stars *building on the success of initiatives such as the* Science Festival*, and fostering talent within the University by tapping into the huge energy and enthusiasm that exists among staff and students for sharing their subject interest.*'

◀ Visitors at the University of Cambridge's *Science Festival 2008*. *University of Cambridge*

Rising Stars was set up in early 2007 to enable staff and students intending to pursue an academic career to develop their public engagement skills. '*The scheme is wide ranging, covering working with 'hard-to-reach' communities, methods of engagement, identifying and creating opportunities to communicate, publicity, evaluation, clear communication of technical subjects and print and broadcast media*,' says Emma Wenborn, Community Affairs Officer at the university. '*The course is multidisciplinary, integrating the sciences with the arts, humanities and social sciences and participants put their new skills into practice by organizing a real-life public activity.*'

Interest in the course has been overwhelming, both from within Cambridge and also from members of

the public. Nearly 60 staff and students have been trained so far, and entry to the course is highly competitive. '*There is clearly a demand for training in this area*,' Emma observes. *Rising Stars* is the first university-run course of its kind in the UK, and she notes that its impact has been seen across the University with course participants embarking on a variety of public engagement activities.

As someone already involved in science communication, I found the course immensely helpful, and not just because of the training it provided. By discussing our outreach work, our group of trainee communicators benefited from each other's experience, and we were encouraged to think about new ways of communicating our own subjects. Unexpectedly, the most useful thing of all was a mailing list. Participants in the course signed up to receive email updates about outreach events, allowing anyone organizing an outreach activity to contact a group of interested people and invite them to join in. If you enjoyed science communication, it was often very hard to say 'no', and the list provided a way to get involved in a wide range of outreach work.

SciConnect – custom-made communications training

Schemes of this sort, though fairly new, are not limited to Cambridge. In 2006, Jon Copley (winner of this year's BSF science communication award for established researchers) and Claire Ainsworth (an award-winning science journalist) founded *SciConnect* (www.sciconnect.co.uk), a company dedicated to providing science communication training to researchers and science students. Jon and Claire have both been involved in research as well as working in science journalism, and between them have a huge amount of experience in communicating science to the public. Through *SciConnect* they have been passing on this experience, with courses held at universities and institutions across the UK and Europe.

'*It seemed that everyone, from the House of Lords and the Royal Society to the research councils, was telling scientists they had to engage with the public*,' says Jon. '*But no-one seemed to be teaching them how to do it, or showing them how to get started.*' Jon brought in Claire, a colleague from *New Scientist* magazine, to help provide training in this area. Demand has grown rapidly, and *SciConnect*'s range of tailor-made training courses has since expanded to include core science communication skills, performing schools outreach and delivering compelling public lectures. It also covers the use of recently-developed media. '*Tools such as podcasts and blogs have created a fantastic opportunity for scientists to reach huge audiences and interact directly with them*,' says Jon. '*We're entering a new era of public engagement.*' To train scientists to use these opportunities effectively, *SciConnect* arranges for experienced practitioners to pass on their skills – podcast training is given by a BBC radio and podcast journalist, and schools outreach training by a school teacher.

The founders of *SciConnect* emphasize that public engagement is a skill that can be learned. '*A lot of people bash scientists for being poor communicators*,' says Claire, '*but I don't think they are. Most communicate very effectively with their peers, but academic writing and presentations demand a very different approach to engaging with non-specialists. Anyone can pick up the basics of how to engage and inspire the public in a day or two's training.*' And as Jon points out, the skills involved are highly transferable. '*The same skills are required to write that increasingly important non-specialist summary for a grant proposal, or when talking to colleagues from other disciplines to forge new collaborations.*'

◀ Ed Hutchinson and Emma Wenborn at a *Rising Stars* event. *University of Cambridge*

Connecting Science

Like members of the *Rising Stars* group in Cambridge, participants in *SciConnect* found that they needed somewhere to share ideas. '*The feedback I get from our courses suggested that researchers needed a place to help them get started, exchange ideas and experiences, and find out what resources and public engagement activities are out there*,' recalls Claire. It was also concerning that some researchers still felt their outreach efforts were not supported, or even discouraged, by their institutions and their peers. Keen to establish a forum where scientists could pass on advice and encouragement about science communication, Claire recently set up *Connecting Science* (www.connectingscience.org). This free online community is open to any scientist or science student who might find themselves talking to the general public, the media or non-specialists – in other words, to anyone with any involvement in science.

'*There's a lot of great science communication going on in the UK*,' says Claire, '*but it can be hard to keep track of it all.*' *Connecting Science* provides space for members to post information about their interest and public engagement activities, and they can search the site to find resources or link up with colleagues. Just as on networking sites like Facebook, users can form groups to discuss or network about particular interests, such as outreach in schools. Claire's hope is that members will network and form connections and collaborations they may not otherwise have done, creating new outreach ideas and opportunities.

Talking to non-specialists is increasingly seen as a key component of research, and the chance to share your enthusiasm for your subject can be one of the most rewarding opportunities that scientific work provides. But for scientists to talk successfully to people outside their field, it helps if they can also talk to each other. Groups like *Rising Stars* and *Connecting Science* now provide places to do just that.

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Useful Links

www.bsf.ac.uk
The Biosciences Federation, which presents annual awards for science communication.

www.cam.ac.uk/communityaffairs
University of Cambridge's Office of Community Affairs, with details of the *Rising Stars* course and community engagement events.

www.sciconnect.co.uk
Science communication and media skills training courses.

www.connectingscience.org
Online community, helping scientists reach wider audiences.

Illuminating the eminent with the invisible

Absent to a large extent from lectures or exhibitions at the country's leading science communication forums, and all too often with their less desirable activities highlighted in news headlines, bacteria suffer from a serious public relations problem.

The Bioluminescent Photobooth, a collaborative project between myself and artist Anne Brodie, has provided a unique opportunity to introduce and engage people with some of the wonder that living bacteria can instil. The installation is essentially a darkened and portable booth into which people enter to have photographic portraits taken using only the light generated by the bioluminescent bacterium *Photobacterium phosphoreum*. The Photobooth has made appearances at the Royal Institution, where it was used to photograph past speakers, including Lord Krebs and Professor Marcus Du Sautoy, and at the DANA Centre of the Science Museum, where portraits of Professor Chris Rapley CBE (Director of the Science Museum) and Sir Christopher Frayling (Chair of the Arts Council) were taken.

Not only has the spectacle of the ethereal blue-light emitted by 10 litres of liquid culture and 200 agar plates of glowing bacteria enthralled many public visitors, but the Photobooth has also provided an opportunity to expose leading proponents, in both the sciences, science communication and the arts, to the unexpected beauty of bacteria, and maybe in some small way to influence them.

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The author would like thank Pattie Hendrie for her invisible but invaluable contribution to the project.

◀ Portraits of (*from top left and going clockwise*) Lord Krebs, Richard Ashcroft, Marcus Du Sautoy and Kevin Warwick taken using the Bioluminescent Photobooth. *Anne Brodie*

Biology outreach in schools

Biosciences Federation Education Colloquium

What is effective outreach in biology and how can we deliver it? These were the questions posed by Sue Assinder at the beginning of the 2008 Biosciences Federation (BSF) Education Colloquium. Hosted by the National Science Learning Centre (NSLC) in York on 28 October, the Colloquium brought together around 60 delegates from a variety of backgrounds to explore the outreach and enrichment provision offered to schools and colleges by the biology community.

Sue set the scene by giving a brief overview of the importance of biology outreach from the perspective of the different stakeholders. For deliverers of outreach, such as learned societies and universities, working with schools offers an opportunity to enthuse the next generation of bioscientists and can be invaluable in recruitment to bioscience degrees. From the school perspective, outreach providers can play a key role in enriching and enhancing biology teaching, in particular support of the *How Science Works* strand of the curriculum.

There followed a keynote address by Professor John Holman, Director of the Government-initiated Science, Technology, Engineering and Mathematics (STEM) programme. He described the approach the STEM programme is taking to bring better cohesion nationally to activities in support of STEM teaching both inside and outside the public sector. This was followed by two talks showcasing successful outreach initiatives. The first, by Dr Karen Bultitude (Development Director in the Science Communication Unit at the University of the West of England) concentrated on a specific aspect of the STEM programme – the Enhancement & Enrichment (E&E) agenda – and highlighted the recently published *STEM Directories* that provide a 'one-stop-shop' for information relating to appropriate E&E providers. Dr Jeremy Pritchard then gave an academic perspective by describing a variety of outreach events in which he has been involved at the University of Birmingham, including *Plants of the World* for primary schools, the *Big Biology Quiz* for year 10 pupils and a range of activities to mark Darwin's 200th anniversary in 2009.

Delegates then chose from concurrent workshops on the themes of Teacher Scientist Networks, the Researchers in Residence initiative, working with STEMNET, running a Junior *Café Scientifique*, outreach delivery by universities, the Undergraduate Ambassadors Scheme and the role of Science Learning Centres. As well as learning about the particular activity involved, delegates were asked to identify why it worked, what were the challenges and how we might gather evidence of success. Several common themes emerged from the workshops. Characteristics shared by successful activities included an innovative and engaging approach, a clear vision of intended outcomes, interactivity and sustainability. Challenges identified were the frequent over-reliance on the goodwill and enthusiasm of volunteers, the lack of 'joined-up thinking' across different outreach providers and securing continuity of funding. The importance of evaluating the long-term impact of outreach activities was widely recognized, but this is an area where there is a scarcity of effective practice on which to build.

The outcomes from the workshops were fed into the afternoon plenary discussion, which sought to make recommendations for achieving excellence in biology outreach from the perspectives of learners, teachers, providers and policy-makers. For learners, it is essential that outreach has a 'wow factor' and is relevant to everyday life. To help the learners to engage, teachers in turn must be given clear information about what is available, be able to understand the relevance to the curriculum and be supported by their school. Providers should understand the needs of the school when planning and designing outreach and make sure that they have thought about how to evaluate success in order to be able to build on effective practice. Policy-makers need to put in place mechanisms that encourage integration and joined-up thinking between providers and enable the identification and sharing of best practice. Universities in particular need to consider how participation in outreach activities can be formally recognized within academic career structures.

The Colloquium received very positive feedback from participants, the only disappointment being the relatively low number of teacher delegates. A summary of the recommendations for how to achieve excellence in biology outreach will be published jointly by the BSF and the NSLC. The BSF is very grateful for the support given to the Colloquium by the SGM – Dariel Burdass organized the exhibition, Janet Hurst was a member of the Steering Group and the Society supported the Colloquium financially.

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SGM Education Officer and
Chair, BSF Education Committee
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MAC in Ireland

22 October 2008, Royal College of Physicians of Ireland, Dublin

The latest stage in the Society's Microbiology Awareness Campaign looked at microbiology issues that affect Ireland. The event was orchestrated by members of the Irish Division and was intended to bring together scientists and parliamentarians from both Northern Ireland and Eire.

SGM President, Professor Robin Weiss, began by telling the delegates about the role and activities of SGM and the importance of microbiology worldwide. Almost 10 % of SGM membership comes from Ireland, so in terms of microbiology output 'Ireland punches above it's weight'. Dr Evelyn Doyle (UCD) and Chair of the Irish Division, went on to describe the all-encompassing remit of the Division, promoting microbiology research and education within the whole island.

Professor Colin Hill (Cork) then gave two examples where bacteria isolated in Ireland have demonstrated their potential as positive agents in human health. He explained that the human genome does not encode enough information for a fully functional human being and that the missing component is the microbiome, the microbial passengers who supply an enormous genetic and metabolic component to the human 'superorganism'. He finished with the fact that it has been conclusively demonstrated that the microbiome plays an important role in health and disease, and so it represents a possible point of intervention for the maintenance of human health.

Dr John McGrath (Belfast), explained how micro-organisms can be exploited for environmental protection. He described the considerable expertise within Ireland and its application to bioenergy production, wastewater treatment, environmental clean-up, and waste recycling and reuse. He stressed that a key strength lies in the close association enjoyed between academic institutions and industrial partners throughout Ireland.

Professor Martin Cormican (Galway) described using microbiological methods to see how closely related a salmonella from a patient in Cork is to that from another patient in Donegal or to salmonellae from food or animals in Dublin. In July 2008, his lab showed that salmonellae from 6 patients in Ireland were of an unusual type and genetically very similar to each other. This was a first signal of an outbreak that may have otherwise been missed.

Dr Kevin Kavanagh (Maynooth) described microbiology education in Ireland, where a wide range of qualifications in the subject (e.g. certificates, diplomas and degrees) are available. Microbiology graduates find employment in a wide range of sectors and this has been instrumental in attracting many pharmaceutical, biotechnological and health care companies to Ireland in recent years.

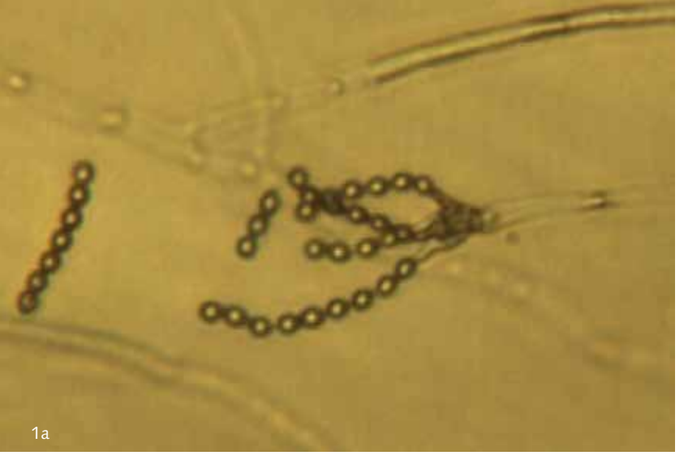
The event was brought to a close by David McClarty, MLA for East Londonderry and Deputy Speaker for the Northern Ireland Assembly, who expressed his interest in MAC and the education of Ireland's next generation of scientists. He announced that funding for hundreds of new science and technology PhD posts had been secured. Research investment, worth £14.5 million, will enable universities in Northern Ireland to collaborate with those in Eire on projects of social and economic relevance to all Ireland.

The delegates were then treated to a buffet lunch and the opportunity to view an exhibition from various groups and organizations, who are working on many fascinating and hugely important areas of microbiology.

Faye Stokes
Public Affairs (e pa@sgm.ac.uk)

Staff at SGM HQ would like to take this opportunity to thank all of those involved in putting together the exciting programme for this event.

▼ Delegates at MAC Ireland. *From left to right* Senator Paddy Burke, Senator Maurice Cummins, Senator David Norris, Dr Kaye Burgess, Professor Colin Hill, Denis Naughten TD and Dr Martin Collins. *Dr Kaye Burgess*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2a


2b

Kay Yeoman and **Jaeger Hamilton** describe how they have used a grant from the SGM Education Development Fund to set up an online educational photographic resource to aid communication of their passion for fungi. http://biobis.bio.uea.ac.uk/fungi/index.html

Images and stories to inspire a joy of fungi

As a society we have interacted with fungi for thousands of years, as exemplified by the mushroom stones of the ancient Mayans and Palaeolithic rock paintings. We have built up a fascinating folklore (ethnomycology) surrounding these organisms and put them to good use as medicines, dyes, cosmetics, as food and in ritual.

Recently a report by the BBC stated that there are only eight mycologists left in Britain. This is a somewhat pessimistic view (as they meant fungal taxonomists), and one which doesn't accurately reflect the many scientists working on interdisciplinary studies with fungi as animal and plant pathogens, and their use as a model organism to understand our own biochemistry and genetics. It is unfortunately true that fungi are not given much room in the undergraduate syllabus, despite their crucial role in the carbon cycle, as mutualistic symbionts, plant pathogens and also their increasing importance as human pathogens.

I want to showcase fungi and their wonderful interactions, life cycles and uses, in the hope that it will inspire more of us to teach to undergraduates and school children about fungi in a social as well as a scientific context. I was delighted to receive an Education Development Fund grant from the SGM to capture images and videos of fungi in action. The fungi and their associated images chosen for this report were those where there was interesting social or environmental context and represent just a few included in the project. There are many more examples of still images and movies available free to download on the accompanying website which can be used to illustrate lectures, public talks or projects with school children.

◀ Fig. 1. (a) The asexual structure of *Penicillium camemberti* which forms the white crust on cheeses such as brie and camembert. (b) *P. camemberti* growing on malt extract agar.

▲ Fig. 2. (a) The hard fruiting body of *Daldinia concentrica*. (b) Ascospores developing inside the sac-like ascus.

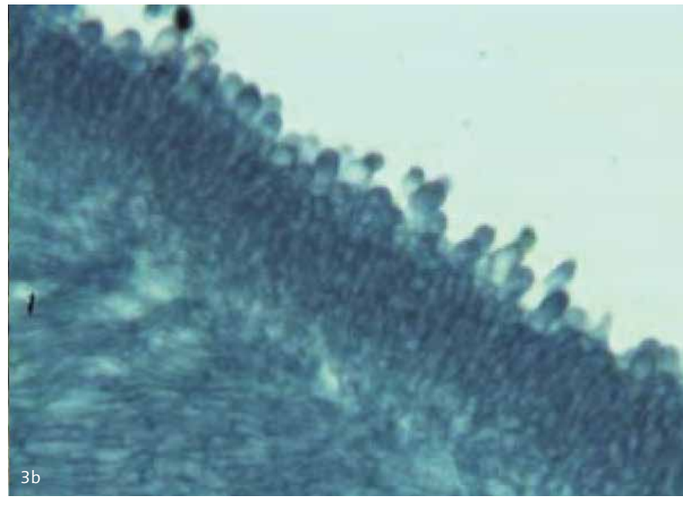
▶ Fig. 3. (a) A young fruiting body of *Amanita muscaria* taken at Felthorpe, Norfolk. (b) Maturing basidiospores of *A. muscaria*.

Medicinal fungi

The most famous example of the use of fungi in medicine is of course the discovery of penicillin by Alexander Fleming in 1928, although without the pioneering work of Howard Florey and Ernst Chain, who actually worked out how to purify penicillin, it would have remained a scientific curiosity. In folklore, the use of mouldy materials such as bread, cheese and apples as poultices to wounds has had a long history. *Penicillium* spp. are also used in food production to flavour cheese (Fig. 1). An easy way to observe fungal asexual structures is to place a piece of clear tape sticky side down on a fungal plate culture; this can be lifted off and placed on a microscope slide, still sticky side down, and observed under low power.

An interesting example of superstitious belief and treatment is the fungus *Daldinia concentrica*, also known as 'cramp balls'; people believed that by putting these hard fruiting bodies into your clothing it would protect against cramp. They are also known as 'King Alfred's cakes' after the Saxon King. Taxonomically, these fungi belong to the phylum Ascomycota; they produce their spores in a sac-like ascus (Fig. 2). The asci and spores are quite large, which makes them easy to see under a light microscope. They have an intriguing spore dispersal mechanism, which is inhibited by light, so the spores are released at night. In an interesting twist, it has been known for some time that species of *D. concentrica* produce antimicrobial compounds and steroids, and in 2006 Qin *et al.*, described the isolation of concentricolide, a benzofuran lactone and its effect as an anti-HIV agent. The tough fruiting bodies (Fig. 2) are quite persistent in the environment; they are easy to see and to collect and make interesting organisms for study at any level.


3a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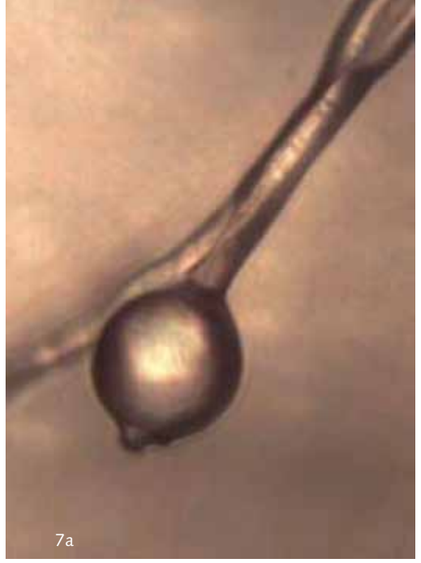
Fungi as mutualistic symbionts

One of my favourites is *Amanita muscaria*, its iconic bright red colour and white spots means it is often used to depict toadstools in fairy tales. Its common name is the 'fly agaric' and it belongs to the phylum Basidiomycota, which produce their spores on a club-shaped basidium (Fig. 3b). This fungus contains a toxin called ibotenic acid, which is decarboxylated to muscimol and was thought to have insecticidal properties. People used to bring the dried fruiting bodies into their houses, or use milk steeped in *A. muscaria* to keep the flies away. This represents a possible root for the common name, and surprisingly the 'fly agaric' name is equivalent in many cultures across the world. Interestingly, work suggests that muscimol is not insecticidal and that the effect on the flies is due to its hallucinogenic nature – they simply nod off! The

fungus itself, most of which exists in the soil as a network of hyphae, can form an ectomycorrhizal association with the roots of trees, for example birch. Mycorrhizal associations are such important, fascinating interactions; plants would literally not be able to survive without this mechanism of nutrient acquisition.

Lichens are also a mutualistic symbiosis between fungi and, most commonly, algae. They are so intertwined as to produce a single body or thallus. Beatrix Potter, the children's author and a keen naturalist, was one of the first people to realize that they were in fact two separate organisms living together in a symbiosis; her work, however, received little attention.

Fig. 4 shows stained, thin cross-sections of a lichen thallus; the layers can clearly be seen and a scanning electron microscope image shows very clearly the two separate organisms which comprise the thallus. Lichens are slow-growing and exquisitely sensitive to sulfur dioxide levels in the air, and thus have been used as biological indicators of pollution. They have also been exploited as indicators of pH in the form of litmus paper. The mycobiont of lichens can be easily isolated by attaching a small piece of the lichen to the underside of a petri dish lid; the spores then drop onto the medium below.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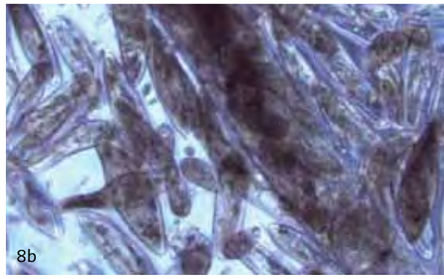
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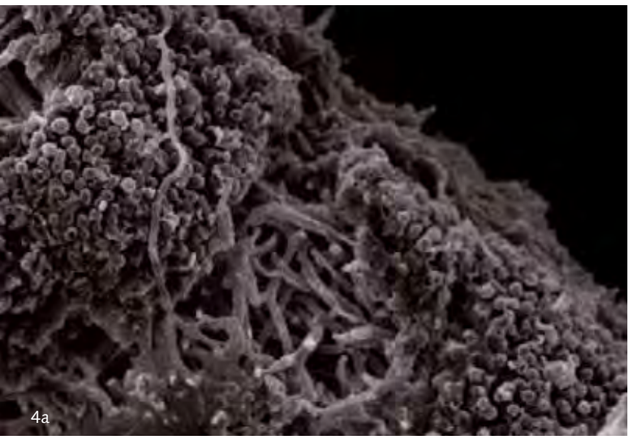
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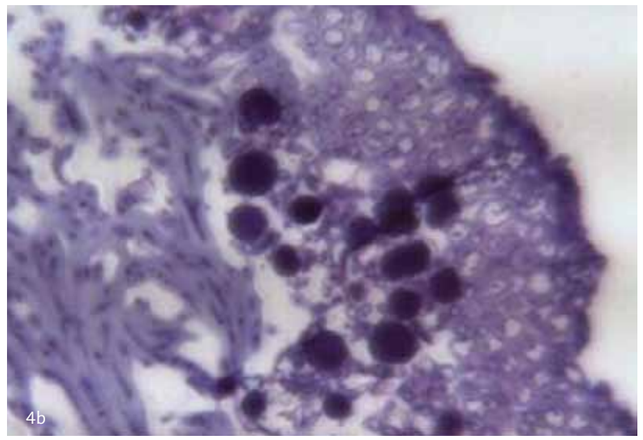
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6b

▲ Fig. 4. (a) Scanning electron microscope image of a lichen. (b) Thin lichen cross-section stained with methylene blue.

◀ Fig. 5. Fruiting bodies of *Armillaria mellea* bursting from the trunk of a tree in the UEA grounds.

◀ Fig. 6. (a) *Phycomyces blakesleeanus* growing on malt extract agar. (b) Mature zygosporangium.

▶ Fig. 7. (a) The lemon-shaped zoosporangium of *Phythphora infestans*. (b) Zoospores maturing in the zoosporangium.

▶ Fig. 8. (a) *Vorticella* sp. attached to *Saprolegnia* sp. hyphae. (b) *Paramecium* sp. attracted to the hyphae.

Fungal luminescence

Armillaria mellea, a member of the phylum Basidiomycota, also known as the 'honey' or 'bootlace' fungus, is a serious pathogen of trees (Fig. 5). It is also faintly luminescent, possibly due to the presence of luciferin, which when combined with oxygen in the presence of the luciferase enzyme can generate light. It is possible that this attracts insects at night, which then aid in spore dispersal. Fungal luminescence has a fascinating social history; decomposing leaf litter can have a faint glow, known as 'foxfire' or 'faerie fire'. Soldiers in the trenches used to make crude lanterns from rotting, luminescent wood.

How can fungi inform us about ourselves?

Phycomyces blakesleeanus belongs to the phylum Zygomycota, often termed the 'pinhead' fungi, and are representative of a more ancient lineage. It reproduces sexually by forming a zygospore (Fig. 6). Recent work on this fungus has given rise to an interesting insight into the evolution of our own sex chromosomes.

The oomycetes

Oomycetes are water moulds and they are curious organisms; they are not true fungi, as they have cellulose in their cell walls rather than chitin, but they behave in a similar way to fungi and are taught as part of mycology. They produce motile zoospores as a means of asexual reproduction. One example of an oomycete which has had devastating social consequences is the causative agent of potato blight, *Phytophthora infestans*, responsible for the Irish potato famine of 1845–1849. The motile zoospores are formed inside a lemon-shaped zoosporangium (Fig. 7).

Another oomycete of interest is *Saprolegnia* spp. If you've ever kept an aquarium, you will be familiar with this organism as it is a common fish pathogen. William Arderon, a Norfolk naturalist, first observed it as a causative agent of vertebrate disease in 1748 (published in *Transactions of the Royal Society*).

A simple experiment to do with students is to drop some sterile hemp seeds into pond water. The motile zoospores of *Saprolegnia* spp. are attracted to the food source, where they encyst and form long, thin hyphae. The zoosporangia form at the end of the hyphae and they are cigar-shaped. The hyphae of *Saprolegnia* provide an ideal habitat for other single-celled protozoa, such as *Vorticella* sp., as shown in Fig. 8(a), which can anchor its stalk to the hyphae. The *Paramecium* sp. shown in Fig. 8(b) simply can't resist the potential food source surrounding the hyphae!

Production of images

Macro images were taken using a Fuji FinePix S8000 fd. Microscopic images were taken using a MOTIC 2000 camera.

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SGM Education Development Fund

The Fund provides support for (a) relevant science promotion initiatives, or (b) to support developments likely to lead to an improvement in the teaching of any aspect of microbiology relevant to secondary or tertiary (including postgraduate) education in the UK. See ***www.sgm.ac.uk/grants/dtf.cfm***

Further reading

BBC (2008). Fears over fungi expert demise. http://news.bbc.co.uk/1/hi/uk/7752103.stm

Dobkin de Rios, M. (1974). The influence of psychotropic flora and fauna on Maya religion. *Curr Anthropol* **15**, 147–164.

Dugan, F.M. (2008). Fungi, folkways and fairy tales: mushrooms and mildews in stories, remedies and rituals, from Oberon to the internet. *N Am Fungi* **3**, 23–72.

Idnurn, A., Walton, F.J., Floyd, A. & Heitman, J. (2008). Identification of the sex genes in an early diverged fungus. *Nature* **451**, 193–197.

Michelot, D. & Melendez-Howell, L.M. (2003). *Amanita muscaria*: chemistry, biology, toxicology and ethnomycology. *Mycol Res* **2**, 131–146.

Money, N.P. (2007). *The Triumph of the Fungi – a Rotten History*. Oxford: Oxford University Press.

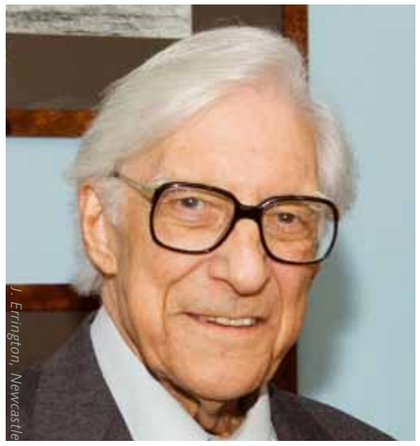
Qin, X.-D., Dong, Z.-J. & Liu, K.-J. (2006). Concentricolide, an anti-HIV agent from the ascomycete *Daldinia concentrica*. *Helv Chim Acta* **89**, 127–133.

Spooner, B. & Roberts, P. (2005). *Fungi*. New Naturalist Series Vol. 96. London: HarperCollins.

obituaries

Professor Sir James Baddiley FRS

(15.05.**1918**–18.11.**2008**)



Jim Baddiley died at Addenbrookes Hospital, Cambridge in November after a short illness. His friends and colleagues were particularly fortunate to be with him at the inauguration of Newcastle University's Baddiley Lecture in June. He was in great form and none of us imagined it would be our last opportunity to meet. He is remembered with great affection by all who worked with him, for his incisive mind, his warmth and dry sense of humour. Despite scientific honours too many to list, and a knighthood awarded in 1977, Jim was a modest man who kept his primary commitment to good science throughout his life.

Jim studied chemistry at Manchester, where a year later Alexander Todd took over the chair of Organic Chemistry and established research into the chemistry of nucleotides and nucleic acids. Jim joined Todd's group as a PhD student, moving with him to Cambridge in 1944. There he made a series of important contributions to nucleotide chemistry which culminated in the first structurally definitive chemical synthesis of ATP.

He consolidated his reputation through research fellowships in Stockholm and at the Lister Institute in London. At Fritz Lipmann's invitation, the Baddiley group at the Lister took up the problem of the structure of coenzyme A, resulting in their final determination of its complete structure. He subsequently collaborated with David Hughes on the biosynthesis of coenzyme A in *Lactobacillus arabinosus* and became convinced of the value of working with bacteria as model cells. During the work with *Lactobacillus*, one of Jim's group, Tony Mathias, partly characterized two novel cytidine nucleotides.

In 1954, at the age of 35, Jim took up the Chair of Organic Chemistry at Newcastle University. There he pursued the hypothesis that cytidine nucleotides were the precursors of unknown bacterial phosphate-containing polymers. In the light of biochemical knowledge in 1954, this was a brilliantly novel idea. Nothing was known of the role of nucleotides in nucleic acid synthesis, and Leloir's discovery of UDP-glucose was newly published. The hypothesis led Baddiley's group to the discovery of 'membrane' and cell-wall-linked teichoic acids. Investigations of their structure, function and biosynthesis, and wider aspects of bacterial cell walls, engaged him for the whole period of his work at Newcastle, latterly in his Microbiological Chemistry Research Laboratory (MCRL). The work carried out there made a major contribution to our understanding of the Gram-positive bacterial cell wall. Jim had a keen interest in the idea that a transmembrane biochemical 'machine' was responsible for cell-wall assembly.

Achievements included the development of techniques for characterizing sugar and alditol phosphate-containing compounds, identification of the role of teichoic acids in ionic balance in the cell envelope, the biochemistry of the linkage between teichoic acid and peptidoglycan, and the use of continuous culture to study the regulation of cell-wall assembly.

The MCRL was a hugely stimulating place to work. Researchers enjoyed a freedom inconceivable nowadays. Jim did not believe in disciplinary boundaries and would enthusiastically encourage the pursuit of good ideas whether of a chemical, biochemical or microbiological flavour.

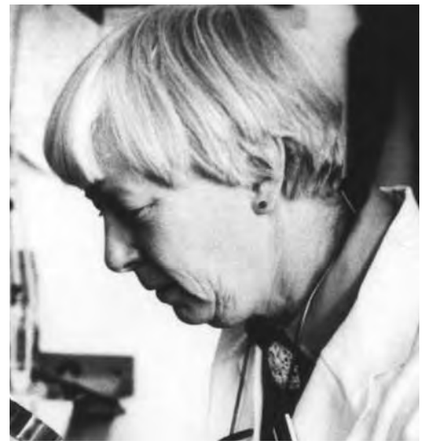
He had connections in a wide range of scientific disciplines through his work for Research Councils and scientific groups. He was elected to the Royal Society in 1961 and was a member of its council from 1977 to 1979. At various times he was a member of the Councils of the Chemical Society and the SGM, and a member of the Committee of the Biochemical Society. He sat on SERC's Enzyme Chemistry and Technology Committee and the Biological Science Committee.

In 1981 Jim and his wife Hazel (whom he had married in 1944) moved back to Cambridge where Jim took up an SERC Senior Research Fellowship in the Biochemistry Department and became a Fellow of Pembroke College. There, with a PhD student, he continued to research aspects of teichoic acid and cell-wall synthesis, and as recently as 2003 published with Frank Neuhaus, with whom he had first collaborated 43 years before, a stimulating and insightful review of teichoic acid function. He took up various duties for the College and the University and was particularly involved in the establishment of the Institute of Biotechnology. Jim and Hazel continued to give a friendly and sociable welcome to past colleagues in their delightful cottage in Hildersham until Hazel's death in 2007.

Ian Hancock, Glen Lodge, Northumberland

Professor Naomi Datta FRS

(17.09.**1922**–30.11.**2008**)



Naomi née Goddard was born in London, the youngest daughter of a chartered surveyor. She attended St Mary's School, Wantage, Oxfordshire. She studied at the Sorbonne, returning to England to enrol at University College London (UCL), followed by Medical Studies at the West London Hospital Medical School. Naomi was the first in Europe to demonstrate that resistance to antibiotics could be transmitted from one species of bacteria to another. She decided that she wanted to study medicine, partly due to the influence of her older sister Helen who married a pathologist.

Naomi started her studies at the Sorbonne, but her father asked her to return home when war broke out. After a short spell of hospital work, in 1940 she started the Medical Foundation course at UCL. For the first year the female students were evacuated to Bangor. In the second year both sexes studied together and were based at Leatherhead. It was there she met Prakash Datta, whom she married in 1943.

Prakash went on to study medicine at UCL. Naomi went to the West London School of Medicine as at that time UCL admitted very few women to their medical course. She completed her medical degree in 1946 and worked for a year as a junior doctor. She joined the Public Health Laboratory Service (PHLS) in Colindale in 1947 as a Senior Bacteriologist and studied part-time for a Diploma in Bacteriology which she was awarded in 1950.

In 1957 Naomi was appointed as an assistant lecturer in bacteriology at the Royal Postgraduate Medical School (RPMS), Hammersmith Hospital. In 1978 she was appointed as Professor of Microbial Genetics at the University of London, retiring as Emeritus Professor in 1984. London University was the parent body of the RPMS. This responsibility transferred to Imperial College in 2007.

Lecturers were expected to undertake some independent research, as well as teaching. In 1959 there was an outbreak of infection in the Hammersmith Hospital caused by *Salmonella* Typhimurium, affecting staff and patients. Naomi collected 309 cultures from affected people. She tested the cultures to see if any of the characteristics had changed over the course of the outbreak. She found that 25 cultures were drug-resistant, 15 of which were resistant to sulfonamides, streptomycin, and tetracycline – an unexpected result.

In 1961 a Japanese research team published their results on the transfer of drug resistance between enterobacteria. Naomi tested her strains in a mixed culture to see if there was any transfer of resistance to *Shigella sonnei* and discovered this occurred in a significant number of cases. The resistance could also transfer back from *Shi. sonnei* to *Sal.* Typhimurium. Naomi published her results in 1962 in the *Journal of Hygiene*.

The next query was how this resistance was transferred. She and other researchers thought that plasmids were responsible. Researching the biology of plasmids, their structure, genetics and function became the focus of her work. She built up a team of researchers and worked with many microbiologists from abroad. She devised a classification of plasmids, led conferences and contributed chapters to major texts.

Though fully employed, her family were the focus of her life. Some help was employed to help care for the children when they were at school, but once home from her scientific work she readily took up the role of mother. She was an excellent cook and enjoyed entertaining. Family holidays were important, as they had been in her own childhood. She enjoyed travelling to conferences worldwide. When she retired she and Prakash travelled widely for enjoyment. She contributed two chapters to *But the Crackling is Superb: an Anthology of Food and Drink by Fellows of the Royal Society and Foreign Members*, published in 1988.

When she retired, Naomi studied linguistics at UCL, but was unable to take postgraduate exams as she did not have an undergraduate arts degree. She took a 2-year part-time postgraduate course in human evolution at the Department of Anthropology. She wrote a dissertation on Y chromosome variations in Greeks, Turks, Greek Cypriots and Turkish Cypriots and was awarded a Master's degree. At 75 she was the oldest in the group and thoroughly enjoyed being in a learning situation.

In 1985 she was elected as a Fellow of the Royal Society. She joined the SGM in 1952 and was made an Honorary member in 1989. Naomi is survived by her husband and their two daughters. Their son died in 2006.

Catharine Haines, Lancaster

reviews

If you would like your name to be added to our database of book reviewers, please complete the book reviewer interests form at **www.sgm.ac.uk**. A classified compendium of reviews from 1996 to the present is also available on the website.

Medical London: City of Diseases, City of Cures

By R. Barnett & M. Jay
Published by Strange Attractor Press (2008)
£15.99
ISBN 978-0-9558761-0-3

Deadly Companions

By D.H. Crawford
Published by Oxford University Press (2007)
£16.99, pp. 250
ISBN 978-0-19-280719-9

The Medical Detective

By S. Hempel
Published by Granta Books (2007)
£9.99, pp. 308
ISBN 978-1-8620793-7-3

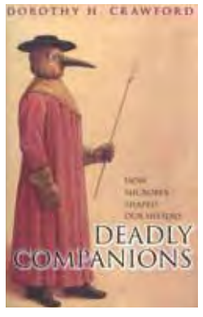
These three books take very different approaches to the history of infectious disease and medical science. Perhaps most ambitious, and very different, is *Medical London*, which aims to cover 'two thousand years of life and death in London'. The sturdy case binder holds a treasure-trove of information presented in a variety of formats. The pack comprises a hardback book, *Anatomy of the City: A Guide to Medical London*, complemented by six separate walk booklets which each include a map, and a softback collection of essays under the umbrella *Sick City.*

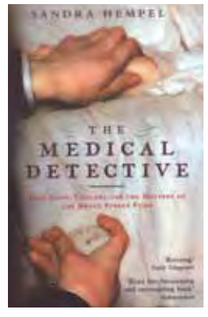
Anatomy of a City lists a huge range of key medical history locations, arranged by geographical region and within each region alphabetically. These include museums and other collections open to the public and full details of what they have to offer, plus opening hours and contact details, alongside 'Vanished London' sites which are significant but no longer visible. Every aspect of

medical history and public health from 55 BC to 2000 AD that you can possibly think of is covered. The titles of the 6 walks give a flavour of the amazing breadth of topics: (1) *Life and death by water: a walk along the medieval Thames*; (2) *In the footsteps of Daniel Defoe: a journey through the 'Plague Year'*; (3) *Gallows, ghosts and golden boys: a day in the life of an 18c medical student*; (4) *Tall ships and tropical diseases: medicine and the British Empire in Greenwich*; (5) *Pox and pleasure: Soho by night*; (6) *From homeopaths to psychopaths: Bohemian medicine in Chelsea*.

The last-named takes in 15 sights, including the Chelsea Physic Garden, the Science Museum and Chelsea Embankment, through three hospitals to the site of Thomas Crapper's water-closet manufactory. Even if you don't take to the streets and follow the clearly laid out maps, it is fascinating reading about the medical association of each sight in the accompanying notes. There is no space here to comment on the essays, save to say that the comprehensive scheme is continued under six subject headings: *City of Multitudes*, *City of Money*, *City of Madness*, *City of Pleasure*, *The bowels of the City* and *City of the World*. The authors of this monumental study are both professional medical historians who have written and/or lectured widely; they have an engaging style and are to be congratulated on a cracking read. Who could fail to find something of interest on dipping into this beautifully produced and clearly laid out work? An added bonus is, because it has been sponsored by The Wellcome Collection, the price is only a bargain £15.99.

Dorothy Crawford's book *Deadly Companions*, subtitled 'how microbes shaped our history', can be read like a novel, but of course, this story is true! It begins with SARS in the 21st century, itself a medical detective tale, and then the author goes back to describe the origins of microbial life 4 million years ago and explore the links between the emergence of microbes with the cultural development of humans. The impact of various 'plagues' in our history that have affected not only the populations of people but animals and plants as well are covered in depth, but the important role of microbes in maintaining the ecosystems of our planet also receives due credit and it is made clear that the majority of these tiny life forms co-exist with us quite harmlessly (despite the title of the book!). Our behaviour has also altered theirs and as all microbiologists know, no matter what the human race does, microbes are always a step ahead and will be around long after we are extinct. A side story is the history of microbiology and the work done and in progress to combat the negative effects of microbes, as well as exploit their potential. The descriptions of the immune response to disease and how vaccination works are particularly clear, but I did wonder why it was necessary to include the





R_o values of pathogens when covering epidemiology in a popular science book.

In fact, while I thoroughly enjoyed reading *Deadly Companions* and *Medical London*, I am not quite sure who they are aimed at. They are probably a bit intimidating to the general reader, but definitely not textbooks either. *Deadly Companions* also suffers from a paucity of illustrations and has no photographs at all, which is a shame. Both works deserve a wide readership.

Sandra Hempel, on the other hand, author of *The Medical Detective*, is a journalist, and her book on John Snow, cholera and the mystery of the Broad Street pump is definitely aimed at the popular market. Nevertheless, it is well-researched, as well as very readable. She describes the disease and the causative organism of cholera, and charts the course of the infection once it had emerged from India in 1817 to cause death and illness around the world in a series of epidemics. One of these hit Newcastle-upon-Tyne in 1831, where the young John Snow, a labourer's son, was apprenticed to a local surgeon. Hempel sets out the contemporary treatment for cholera, and puts the (unpopular) control measures imposed by local and national government into their political context. The story then moves on with Snow to his further training as a doctor in London and his success as a pioneer of anaesthesia. In 1853 he gave chloroform to Queen Victoria in her eighth confinement. Meanwhile, in 1848, cholera had once again appeared in London and Snow, who, after his early experiences in Newcastle had often pondered about the transmission of the disease, began to consider it in earnest. The rest of the story is familiar, but Hempel puts it in a broader context of the social conditions of the time and the attitudes of the medical establishment in this era before the germ theory of disease was proved. Snow died in 1858, but *Vibrio cholerae* did not and the story of cholera to the present day is recounted in the book.

***Janet Hurst**, SGM*

New Strategies Combating Bacterial Infection

Edited by I. Ahmad & F. Aqil
Published by John Wiley & Sons Limited (2008)
£90.00, pp. 304
ISBN 3-52732-206-0

The emergence of bacterial resistance to established antibiotics is a serious public health concern, and this book considers a variety of research approaches that might be employed to address the problem. The book covers a number of familiar strategies and concepts such as phage therapy, inhibition of bacterial resistance mechanisms and the prospects for antimicrobial peptides as new therapeutic agents. However, with the exception of some new anti-TB drugs, there is no general description of several other novel antimicrobial drugs in the glycopeptide, cephalosporin, fluoroquinolone and pleuromutilin classes that are being developed for therapeutic use against problematic organisms other than TB. Furthermore, the important role of structure-based drug design and associated molecular biology technologies are not addressed in this book.

Despite these omissions, the book does contain valuable information. For instance, there are few textbooks that cover non-antibiotic alternatives for the control of bacterial infections. Consequently, I found the chapters dealing with essential oils, honey and probiotics in the management and prevention of bacterial infection to be of particular interest.

Overall the book is well-presented, although the quality of some of the illustrations, particularly in Chapter 1 which deals with current antibiotic resistance mechanisms, is poor.

In summary, this book perhaps focuses too greatly on non-antibiotic approaches to infectious diseases and overlooks some of the recent important advances in the discovery and development of small molecule inhibitors as antibacterial drug candidates. Nevertheless, the book is a valuable source of information on the more esoteric possibilities for new antimicrobial therapies.

***Ian Chopra**, University of Leeds*

Twelve Diseases That Changed Our World

By I.W. Sherman
Published by American Society for Microbiology (2007)
US$29.95 pp. 219
ISBN 1-55581-466-3

'This book is about the lessons we have or should have learned from our past encounters with unanticipated outbreaks of disease and how such understanding can be put to use when future outbreaks occur.'

Sherman suggests that porphyria and haemophilia have influenced European politics and that late blight in potatoes impacted on US immigration. He proposes that many of our current disease control measures were established as a result of historical epidemics – cholera led to sanitary measures and oral rehydration therapy, while smallpox resulted in vaccines, plague in quarantine and syphilis in chemotherapy. Malaria and yellow fever outbreaks both led us to curb the spread of disease using vector control.

The final two chapters, on influenza and HIV, tell stories of diseases that have so far eluded our control. However, '*the future is not without hope or remedy.*' Sherman assures us that if we look to history for advice, we will succeed in the fight against emerging infectious disease. Control, he says, is more than just biology – it requires financing, national will, public trust, surveillance and ultimately a change in human behaviour.

This book is aimed at the general reader and is a very interesting read. However, the treatment of topics can be inconsistent, with widely variable content and length of chapters, making it arduous to read in one go; chapters are more entertaining when read as

essays. There is a stark difference between the historical stories and the sometimes very technical scientific content, which also makes for difficult reading. I would suggest that the book may be unsuitable for those with no prior knowledge of microbiology.

Although the historical stories are interesting, they are somewhat out of context and occasionally used anachronistically – the author is a scientist, not a historian. Despite this, the book has renewed my interest in the history of disease.

***Lucy Goodchild**, Imperial College London*

Vibrio cholerae: Genomics and Molecular Biology

Edited by S.M. Faruque & G. Balakrish Nair
Published by Caister Academic Press (2008)
£150.00 pp. 218
ISBN 1-90445-533-2

Research on the biology of *Vibrio cholerae* has come a long way in the past couple of decades and this book provides an updated review of this progress. The Editors have recruited leading researchers on cholera biology and therefore the content is up-to-date and authoritative. The reviews are generally useful, timely and well-written, although the quality and number of figures could be improved.

One of the main themes running through the chapters is the ecology of *V. cholerae* and the integration of data derived from the intestinal and aquatic environments. The book does what it says in the title as the focus of most chapters is on genomics and molecular biology. After an introductory overview, the book starts with a broad and interesting review of *V. cholerae* genomics; the lack of a discussion on comparative genomics is understandable as only two genome sequences are published and at least 14 are still in draft form.

The genomics review links well with a comprehensive chapter on *Vibrio* phage genomics. I particularly enjoyed reading the chapters on colonization and synchronized gene expression, despite the inevitable overlap in some of the content. The chapter on ecology links well with reviews on biofilm formation and polysaccharide biosynthesis. For many, population genetics can be a dull read, but I found this chapter to be cogent, combining well with a review on the evolutionary relationships of pathogenic clones. With a view to future disease risk there are two articles covering emerging hybrid variants and antibiotic resistance. The book closes with a chapter of conclusions and future prospects that highlights timely and emerging research areas.

The primary target audience is likely to be the *Vibrio* research community, for whom it would be well worth consideration. The hefty price tag makes it an unlikely purchase for other researchers and out of reach of most students. For some, a wait to compare with a book on the molecular and epidemiological aspects of cholera out next year might be considered. Would I buy this book? Yes, but tinged with the relief that I have now been saved the expense!

***Julian Ketley**, University of Leicester*

Forgotten People, Forgotten Diseases: The Neglected Tropical Diseases and their Impact on Global Health and Development

By P.J. Hotez
Published by American Society for Microbiology (2008)
US$39.95 pp. 248
ISBN 1-55581-440-3

At first look, this book is a review on infections in tropical and subtropical countries leading to severe disease. The infections are mainly parasitic [helminths – ascariasis, necatoriasis (hookworm disease), trichuriasis, schistosomiasis, filariasis, onchocerciasis; protozoa – leishmaniasis, Chagas's disease, trypanosomiasis], some are bacterial (trachoma, leprosy, leptospirosis) and viral (dengue, rabies).

On the other hand, the book communicates the much wider aspects of this disease burden: almost 40% of the world's population, preferentially the poorest people, are affected, and although the suffering in volume is similar to that from HIV/AIDS and malaria, only a fraction of the attention and funding has been given to these 'neglected tropical diseases' (NTDs). Many of the diseases are chronic, disabling, stigmatizing and promote poverty, but have been shown to respond favourably to drug treatment applied in mass drug administration (MDA) campaigns, at a fraction of the costs of treatment of AIDS and tuberculosis. Recently, joint initiatives from governments and private donors have set up a Global Network for NTD Control by MDA and also vaccine development. The transition from recognizing a medical problem of large proportions to developing a public health policy and searching for funding is described very clearly, with attention to detail and with the commitment of a pioneer in this field. The problems arising in the course of this work (development of drug resistance, difficulties in the logistics of delivery, etc.) are recognized.

Chapters are enriched by good illustrations and concluded with poignant summary points. A glossary of the numerous abbreviations used would have been helpful.

In my view, nobody reading this amalgam of scientific review, practical recommendations and political pleading can remain unmoved. The case for action is compelling. The book should gain wide distribution among students and practitioners of medicine, public health administrators and decision-makers.

***Ulrich Desselberger**, Cambridge*

Bacterial Resistance to Antimicrobials, 2nd edn

Edited by R.G. Wax, K. Lewis, A.A. Salyers & H. Taber
Published by CRC Press / Taylor & Francis Group (2008)
£99.00 / US$179.95 pp. 430
ISBN 0-84939-190-3

Either when new to a topic or seeking to refresh and gain up-to-date knowledge, I look for a single authoritative text. This book provides very good coverage of antibacterial resistance, but gaps exist. For instance, if you wish to seek information on pneumococci, enterococci, staphylococci, mycobacteria or enterobacteria, then this textbook provides comprehensive chapters and is consequently an excellent source. For pseudomonads, look elsewhere. The opening chapters are well-structured, supplying logical subject matter development. As a minor criticism, coverage of novel drug development is very superficial, although I recognize this is not the focus. So why include? Overall 8/10; not cheap though.

***Andrew Lamb**, Robert Gordon University*

Therapeutic Drug Monitoring Data: A Concise Guide, 3rd edn

Edited by C.A. Hammett-Stabler & A. Dasgupta
Published by AACC Press (2007)
US$59.00 pp. 241
ISBN 1-59425-075-0

Therapeutic Drug Monitoring and Management (as TDM is defined in this book) is benefiting from the ever-growing interest in personalized medicine, although the Editors rightly claim that TDM was about individualizing medicine long before pharmacogenomics and pharmacogenetics were to be found in the scientific lexicon!

The book uses several short introductory chapters to give a history and background to TDM and then focuses on 7 drug classes (anticonvulsants, cardioactives, antidepressants, immunosuppressives, antimicrobials/antivirals, analgesics, antineoplastics) with details on behaviour of individual drugs in each class. A concluding chapter on caffeine, lithium and theophylline rounds out the book. For SGM members, the introductory chapters and the discussion of TDM applied to antivirals and antimicrobials are likely to be the only immediately relevant text. However, members with a wider interest in personalization of medicines might also enjoy other descriptions. This short and inexpensive book provides a succinct and useful grounding in TDM and thus may find itself in individual collections rather than on library shelves.

***Edward D. Blair**, Cambridge*

Reviews on the web

Reviews of the following books are available on the website at www.sgm.ac.uk/pubs/micro_today/reviews.cfm

Evidence-based Laboratory Medicine, 2nd edn

Pathogenic Fungi: Insights in Molecular Biology

Accessing Uncultivated Microorganisms From the Environment to Organisms and Genomes and Back

Handbook of Human Immunology, 2nd edn

Disinfection and Decontamination Principles, Applications and Related Issues

Handbook of Food Spoilage Yeasts, 2nd edn

Practical Manual of Groundwater Microbiology, 2nd edn

Thermophiles Biology and Technology at High Temperatures

Fungal Pathogenesis in Plants and Crops Molecular Biology and Host Defense Mechanisms, 2nd edn

The Aspergilli. Genomics, Medical Aspects, Biotechnology and Research Methods

Microbial Food Contamination, 2nd edn

Handbook of Listeria monocytogenes

Helicobacter pylori*: Molecular Genetics and Cellular Biology*

Bacteriophage Ecology: Population Growth, Evolution, and Impact of Bacterial Viruses

Bacterial Physiology: A Molecular Approach

Membrane Structural Biology with Biochemical and Biophysical Foundations

Germ Stories

Food Microbiology: An Introduction, 2nd edn

Pasteurellaceae*: Biology, Genomics and Molecular Aspects*

Prion Protein Protocols

Plant Virology Protocols: From Viral Sequence to Protein Function, 2nd edn

Cumitech 45: Infections in Solid-organ Transplant Recipients

Clinical Infectious Disease

Bioinformatics Volume I: Data, Sequence Analysis and Evolution

Bioinformatics Volume II: Structure, Function and Applications

Phytophthora*: Identifying Species by Morphology and DNA Fingerprints*

Therapeutic Microbiology: Probiotics and Related Strategies

Avian Influenza

Chemical Biophysics: Quantitative Analysis of Cellular Systems

Genomes, Browsers & Databases: Data-mining Tools for Integrated Genomic Databases

Plant Pathogenic Bacteria Genomics and Molecular Biology

Neurotropic Viral Infections

Diagnostic Microbiology of the Immunocompromised Host

RNA–Protein Interaction Protocols, 2nd edn

Microbial Production of Biopolymers and Polymer Precursors: Applications and Perspectives

SARS – and Other Coronaviruses: Laboratory Protocols

Global Infectious Disease Surveillance and Detection. Assessing the Challenges – Finding the Solutions: Workshop Summary

Molecular Biomethods Handbook, 2nd edn

Plant Pathology Concepts and Laboratory Exercises, 2nd edn

comment

debating creationism

Charles Darwin came up with the theory of evolution. Yet in 2009, the year we celebrate the 200th anniversary of his birth, creationism is a topic of great public interest. **Lucy Goodchild** discusses the relevance of the science versus religion debate to microbiologists.

Just before Christmas I went to a show that was the atheist's dream at that time of year – *Nine Lessons and Carols for Godless People*. Perhaps unsurprisingly, atheist Richard Dawkins topped the bill with readings from three of his books. Considering the publicity atheist views of the relationship between science and religion have been given lately, it came as little surprise to see Professor Dawkins flanked by an assemblage of 'celebrities': Ricky Gervais, Jarvis Cocker, Mark Thomas, Robin Ince and Ben Goldacre to name a few. To see so many well-known performers together at Christmas to talk (and laugh) about the shortcomings of Creationist ideas would have been astonishing a few years ago. Now, Creationism, Intelligent Design and the so-called science versus religion debate have become topics of conversation over a quiet drink in the pub, no longer reserved for academics and theologians.

It is important to understand the distinction between religion and Creationism. In *God, the Big Bang and Bunsen Burning Issues*, The Reverend Dr John Polkinghorne, KBE said: '*If we think Genesis 1 and 2 is a divinely dictated scientific textbook that God wrote to save us the trouble of having to do science, then we're making a big mistake. These chapters are theological writings.*'

This argument is supported by a great many Christians, some of whom are leading scientists. Although Creationists are Christians, not all Christians are Creationists by default; in fact, like John Polkinghorne, most do not believe the Bible to be a literal account of what happened at the dawn of time and space. Some people believe that the Creation took place over millions of years and that the days described in Genesis represented ages. But the vocal minority, the Special Creationists, believe this view amounts to evolution. They are calling for 'equal' time in science class, with half given to their very specific brand of Creationism and the rest apportioned between everybody else.

Why should this matter to microbiology? Creationism draws on microbiology to support its beliefs, namely that the origin of life on Earth is so unlikely that it probably didn't happen without a guiding hand. Considering the stack of evidence in support of various scientific theories explaining the appearance of life, microbiologists are in a good position to contest the Creation, on these grounds at least.

So should we give equal time to Creationism? I don't think so, at least not in science lessons. I think religion and science go hand in hand; the disciplines we now recognize as science would not have come about without the input and support of religion. But this does not mean that one can be applied to explain the other – just as science cannot explain God, religion cannot be applied to science.

I happen to accept empirical science and evolution as true, but that's not to say that we must all make a choice – indeed, many scientists are devoted Christians who say science and religion are perfectly complementary. However, they are not the same.

Whatever we think of Creationism and its more recent manifestation, Intelligent Design, they exist and are here to stay. Silencing Creationists will not solve the issue – and will not do the next generation of leading microbiologists any good at all. I think it is our obligation to encourage debate, if nothing else to produce well-rounded, informed microbiologists who can discuss meaningfully issues such as these.

Empirical evidence for early events in the history of the Universe, for the age of the Earth and for the origin of life on our planet is comparatively overwhelming. Instead of muffling opposing views, we should be banging the science drum. As empiricists, we take for granted the theory of evolution and often fail to recognize that its intricacies may not be understood fully by most people.

2009, the year of Charles Darwin's 200th birthday and the 150th anniversary of *On the Origin of Species* should give us the perfect opportunity to highlight this magnificent explanation for the variety of life on Earth.

▲ Adam and Eve, and DNA as the 'Tree of Knowledge. *Jean-François Podevin / Science Photo Library*

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Please note that views expressed in Comment do not necessarily reflect official policy of the SGM Council.