

MICROBIOLOGY TODAY

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Putting microbes to work

Boiling muds and scalding soils

Micro-organisms that make and break minerals

A sticky business – microbial polysaccharides

Defusing the environment

A quiet revolution in the bacterial cell factory

A new weapon against waste

The MMR controversy

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SGM Headquarters

Marlborough House,
Basingstoke Road, Spencers
Wood, Reading RG7 1AG
Tel. 0118 988 1800
Fax 0118 988 5656
email mtday@sgm.ac.uk

SGM Website

http://www.sgm.ac.uk

Editor

Dr Meriel Jones

Editorial Board

Professor Dave Kelly
Dr Lynne Macaskie

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Production Editor

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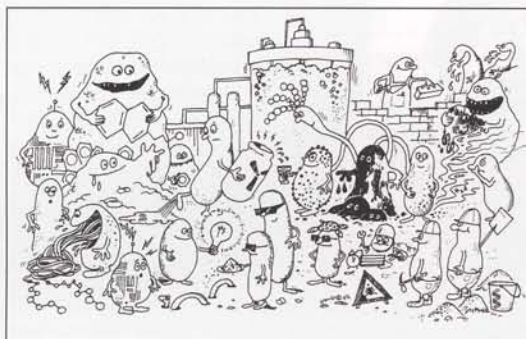
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Above: Microbes at work!

Cartoon by Geoff Gadd
(email g.m.gadd@
dundee.ac.uk).

Vol. 29, Part 2, May 2002

The great diversity and
adaptability of microbes can
be exploited to our benefit
by scientists. Kristien
Mortelmans summarizes
the ways in which micro-
organisms can be put to
work in her introduction to
this issue on applied
microbiology (p. 63).

Extremophiles have
adapted to live in harsh
environments, such as hot
springs, polar zones and
salt lakes. David Lloyd
describes some of these
fascinating microbes and
the metabolism which
allows them to survive,
before exploring the
potential applications of
the enzymes they produce
(pp. 64–66).

Bacterial cells can be
used as protein 'factories'
and David Summers
(pp. 76–78) reports on his
group's development of
a novel cell expression
system with commercial
potential. Industry is
already using microbial
polysaccharides in a wide
range of products, such as
foods and cosmetics, as
Ian Sutherland describes
on pp. 70–71.

Microbes can be
harnessed to clean up
pollution. One application is
to remove explosives from
contaminated land, as shown
by Elaine Boyd and Neil
Bruce (pp. 72–74).
Other microbiologists
are using bacteria in the
bioremediation of metals in
different ways as described
by Jonathan Lloyd
(pp. 67–69) and Victoria
Baxter-Plant and co-authors
(pp. 80–81).

The controversy about
the triple MMR vaccine
continues to dominate the
headlines. We take a look at
the background to this issue
in Comment on p. 116.

Other subjects featured
include science promotion
activities (pp. 90–91) and
reports on overseas
initiatives carried out by SGM
members (pp. 98–100).

These articles appear in
addition to all the regular
features and reports of
Society activities.

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The Semmelweis fate

I was surprised at the remarks by Dr M. Wainwright in the November 2001 issue of *Microbiology Today* (28, 173) that Semmelweis made no major contribution in combating puerperal fever. It has long been known – even in his country, Hungary – that Oliver Wendell Holmes wrote an essay entitled *The Contagiousness of Puerperal Fever* in 1829 which was published 5 years before the work of Semmelweis. Holmes was bitterly attacked by the medical community and he republished his work in 1855. Semmelweis published first in 1849, then he summarized and published his previous works in *The Cause, Concept, and Prophylaxis of Childbed Fever* in German in 1861. Like Holmes, he was also ridiculed and rejected by colleagues. Because the contemporary medical community ignored him and even opposed his firmly held ideas, he started to fight criticism desperately and fanatically, responding with vitriolic letters and sending these to academics worldwide. He did not respect any dogma, great names, authorities or restrictions to save the life of mothers and newborns and so his contemporaries regarded his activities as scandalous and him as mad. He was practically beaten to death in the madhouse in Vienna, and after he died aged 47 in 1865, his family even changed their name because they were ashamed of his 'obsession'. After 1880, Professor Alfred Hegar in Germany recognized the importance of his ideas, because by that time Lister had established aseptic surgery (1865) and Billroth, Professor of Surgery in Vienna had identified streptococci (1874), soon after they had been seen in the blood of a mother with puerperal fever by Pasteur. Hegar produced a small monograph on the career and work of Semmelweis and his collected works were published in German in 1905. Semmelweis is included in the life-sized statues of the 12 greatest physicians and discoverers of all time in the Museum of the International Academy of Surgery in Chicago.

Semmelweis has also been commemorated in late 20th century drama with plays in French and Norwegian; one work has been translated into English and published. Interestingly, until recently the plays have been unknown in both Austria (where Semmelweis made his first observations in Vienna) and Hungary (where he tried to disseminate his ideas and where the biggest medical school in Budapest was named after him on its bicentenary in 1969). In the last sentence of Bjorneboe's drama, he summarizes the life work of Semmelweis: 'Semmelweis eliminated child-bed fever, but he did more. He crushed authorities who, in reality, were themselves the disease.'

● **Dr Joseph Ongradi, Research Fellow, Cancer Research Center, Johns Hopkins University, Baltimore, MD 21231, USA**
Tel. +1 410 955 0650; Fax +1 410 955 0840
email ongrjos@hotmail.com

Dr Wainwright replies ...

I was also surprised to hear that, in my recent article, I suggested that 'Semmelweis made no major contribution in combating puerperal fever'. I hoped that I had made it clear that, while Semmelweis made an important contribution to the study of childbed fever, he was clearly not the first person to recognize that the disease is (a) spread by

bad hygiene and (b) that this spread is prevented by hand washing, with or without antiseptics. Nor is it true, as stated in Dr Ongradi's letter, that 'Semmelweis eliminated childbed fever'. Puerperal fever remained a major problem until the mid-1930s when it at last became treatable, first with the sulphonamides and then penicillin. Even now, this disease remains a major killer in undeveloped countries and so is far from defeated.

The fact that Semmelweis' life and work has been portrayed in the arts comes as no surprise. As I mentioned in my article, 'all human life is there' in the Semmelweis story. The fact is that many scientists, notably Charles White, came to the same conclusions long before Semmelweis. Some, like Oliver Wendell Holmes, also suffered ridicule for publishing ideas that have been almost universally, and wrongly, credited to Semmelweis. Unfortunately, much of the history of the early development of microbiology and germ theory is similarly based on heroic, illustrative stories, which often neglect those who should rightfully have priority on their discoveries.

Reaction to anthrax 'Comment' article

I enjoyed reading Professor Rick Titball's recent 'Comment' article (*Microbiology Today* 29, 60). I agree with everything he says about the need for continuing research into protection against the disease induced by *Bacillus anthracis*. I hope that the importance of his message is recognized by those that fund research in this country.

I feel, though, that I need to point out some inaccuracies in the article. The full course of vaccination with the UK vaccine is, in fact, three doses administered over 6 weeks. The subsequent doses are boosters and one does not need to wait 6 months before being considered vaccinated. Also, the vaccine does, not may, contain oedema factor (EF) and lethal factor (LF), but there are no data that link the presence of these components to any reported reactions in vaccinees. Key aims of the present CAMR anthrax vaccine research programme, and also of a major study sponsored by the Centers for Disease Control and Prevention, Atlanta, on the US vaccine, are to identify the components of the present licensed vaccines, to understand better their immunogenicity and reactogenicity, and to identify the immune correlates of protection.

It is relevant that several groups have demonstrated that components of *B. anthracis* other than PA can contribute significantly to protection and, indeed, may enhance the protection afforded by PA alone (see references below). Hence, the implication that PA is the only protective component of current vaccines is, perhaps, misleading.

● **Peter Hambleton, Director for Strategic Vaccine Development, CAMR**

Brossier, F. & others (2002). Anthrax spores make an essential contribution to vaccine efficacy. *Infect Immun* 70, 661–664.

Koliber, D. & others (2002). Efficiency of protection of guinea pigs against infection with *Bacillus anthracis* spores by passive immunisation. *Infect Immun* 70, 544–550.

Price, B.M. & others (2001). Protection against anthrax lethal toxin challenge in genetic immunisation with a plasmid encoding for lethal factor protein. *Infect Immun* 69, 4509–4515.

Putting microbes to work

Kristien Mortelmans

This issue of *Microbiology Today* with its special features on 'Putting microbes to work' is a tribute to microbial diversity, the adaptability of microbes and the ingenuity of (micro)biologists.

It is believed that all of planet earth was anaerobic about 3 billion years ago. The first microbial forms of life that emerged at that time must have been anaerobic. They must have relied on anaerobic respiration for energy production with terminal electron acceptors such as nitrate, sulphate, sulphur, carbon dioxide and fumarate. With the emergence of photosynthetic blue-green algae and cyanobacteria (and later plants) molecular oxygen (O_2) gradually accumulated in the environment, O_2 being a by-product of photosynthesis. One can actually consider O_2 to be an early environmental pollutant that changed planet earth's atmosphere from a reduced form to an oxidized form. It is well known that O_2 is highly reactive, which made it a prime candidate for becoming the most efficient terminal electron acceptor. One can therefore speculate that some of the early anaerobic life forms must have eagerly accepted O_2 because of the higher energy yield (ATP) obtained per substrate in aerobic respiration compared with anaerobic respiration.

The different types of respiration must have contributed to the ability of microbes to colonize and populate diverse regions of the globe. In addition, some microbes, referred to as extremophiles, have adapted to live in harsh and extreme environments such as:

- the bottom of the ocean (depth of 10,000 m and pressures up to 1,035 atm)
- hot springs (temperature close to boiling)
- Arctic and Antarctic zones (temperature at or near freezing)
- salt and soda lakes (30 % sodium concentration)

Microbes have also adapted to live in close association with humans; this association is fortunately mostly harmonious. Indeed, more than 300 different microbial species, the majority being anaerobes, populate the human oral cavity and the human gut where they play, amongst other things, a protective role against invading microbes. In addition, our gut flora tirelessly work day in and day out to help digest our food and provide us with much needed nutrients. Unlike in humans, the gut of termites is colonized by cellulase-producing microbes that degrade cellulose to soluble sugars much needed by their host. This is a beautiful illustration of natural symbiosis: the termites, eat wood which they cannot digest (just like humans), but they have found the perfect working partner to do it for them. In return, the host provides a protective environment for the microbes to live in and thrive. This symbiosis between termites and anaerobes is, however, unfortunate for anyone living in houses built of wood!

Considering the diversity of the microbial world and the adaptability of microbes, it should come as no



PHOTO SGM

surprise that, since ancient times, microbes have been put to work by mankind to serve mankind. What comes to mind immediately are consumer products, such as wine, beer, cheese and fermented foods. What is so remarkable is that for a long time empirical means were used to exploit microbial activities. This in itself is a tribute to the experimentalists who made it an 'art', establishing and maintaining the optimum (growth) conditions for these microbes to do their work. It is also a tribute to the microbes in that they behaved as great team players in complete anonymity.

These days (micro)biologists are putting microbes to work usually with knowledge about the genus and species. In addition, it is now possible to genetically engineer desirable traits. The emergence of the '-omics' revolution, i.e. genomics and proteomics, as well as bioinformatics, will offer researchers additional tools to extend the arsenal of microbial products or processes, the listing of which is beyond the scope of any review article or even a book. However, in broad terms microbes today are put to work in fields as diverse as:

- the environment (e.g. bioremediation, horticulture, agriculture, oil drilling)
- medicine (e.g. antibiotics, insulin)
- food (e.g. food flavours and emulsifiers)
- energy production (e.g. ethanol, methane, hydrogen)
- solvent production (e.g. acetone, butanol)

The articles that follow are just a few concrete examples of how microbes are used to our benefit.

As a final note, no matter what tools are available to 'put microbes to work' it would be prudent for any researcher to abide by the following five laws of applied microbiology established by the late Dr D. Perlman:

- the micro-organism is always right, your friend and a sensitive partner
- there are no stupid micro-organisms
- micro-organisms can and will do anything
- micro-organisms are smarter, wiser and more energetic than chemists, engineers, etc.
- if you take care of your (microbial) friends they will take care of your future (and you will live happily ever after!)

● Dr Kristien Mortelmans is Editor-in-Chief of 'SIM News' (Society for Industrial Microbiology) and Senior Microbiologist at SRI International, Menlo Park, CA 94025-3493, USA.
email kristien.mortelmans@sri.com

Microbial activities can be harnessed for our benefit in a huge variety of ways. Kristien Mortelmans provides an overview which serves as an introduction to the theme of this issue of *Microbiology Today*.

Boiling muds and scalding soils: new species and enzymes for the future

David Lloyd



We look to the strangest places on earth to find novelty in microbial form and function.

Where the scalding-hot waters of deep-sea volcanic vents (black smokers) meet the icy-cold abyssal sea; that's where you can meet *Pyrolobus fumarii*, the current record-holder for growth at extremely high temperatures. At a depth of 4,000 m (pressure 360 atm) this ecosystem is based on cycles of sulfur reduction and reoxidation, and is completely independent of solar energy. Sites of volcanic activity on land, hot springs, sulfur-rich springs, boiling mud and deep sub-surface strata are filled with hyperthermophilic organisms that like to grow at temperatures higher than 80 °C. All are prokaryotes, although some fungi are known that can survive up to 62 °C, but they are distinctly different from the bacteria of everyday life.

Types of hyperthermophiles

Well known bacterial hyperthermophiles lie in the deepest branches of bacterial genealogy (*Thermotogales* and *Aquificales*). The genome sequences of species, such as *Thermotoga maritima* and '*Aquifex aeolicus*' look as if they have acquired genes from archaeal species. A quarter of *T. maritima* proteins are more similar to archaeal gene products than bacterial ones.

The archaeal hyperthermophiles are much more diverse and fall into three major sub-lineages. The *Crenarchaeota* include those species able to grow at the highest temperatures of all known organisms; they cluster closely together on the phylogenetic tree and have perhaps evolved only slowly from their earliest ancestors on the primitive earth when the oceans were still boiling as a result of bombardment by comets. The *Euryarchaeota* include the methanogenic *Archaea*, and the extremely halophilic halobacteria. A third group, the *Korarchaeota*, branch very near the root of the archaeal tree and were originally discovered as a result

of analysis of 16S rRNA sequences from an iron- and sulfur-rich hot spring in Yellowstone National Park, Wyoming, USA. Several cultured examples of these unique organisms are now available and will perhaps provide fascinating new light on early evolution.

Life-based coenzymes, such as ATP and NADP, cannot exist above about 140 °C as this is the upper limit for their stabilities in aqueous solution. So how can it be that these organisms cannot only

survive elevated temperatures, but actively carry out the processes for growth? Clearly they must have very special components, and the mechanisms that ensure the stability of their proteins, nucleic acids, lipids and membranes can provide new insights into fundamental questions on the nature of life. More practically, novel fundamental studies frequently provide new applications. Thus, the exploitation of constituents isolated from these robust species may be expected to provide biomolecules in which the exquisitely effective selection processes of at least 3.8 billion years have ensured a remarkable temperature stability. Thus, not only can these hyperthermophile products be exploited directly, but we can use computer-aided molecular modelling to try to improve upon their designs, thereby taking thermal stability into even more impressive domains.

Withstanding the heat

Stability has been built-in by many different strategies. The unique lipids of archaeal membranes are even further modified in the extreme thermophilic methanogen *Methanopyrus kandleri*, providing a good example

ABOVE:

Fig. 1. Boiling mud: New Zealand has a number of geothermal fields with a temperature above 220 °C which are exploited for industrial purposes. Hyperthermophiles thrive in the soils and muds heated by this activity.

RIGHT:

Fig. 2. Steam from Iceland's hydrothermal springs; much of Reykjavik's domestic heating is derived from geothermal activity.

PHOTOS DAVID LLOYD



of where molecular design is radically different from mesophilic organisms. Thus, even the normal ether-linked lipid (dibiphytanyl tetraethyl lipid) common to all *Archaea*, that provides a monolayer rather than a bilayer, contains an unsaturated form of side-chain, geranylgeraniol, so that at the upper temperature limit of 110 °C the membranes can still function. The genome structure of these organisms is protected by possession of a reverse gyrase that introduces positive supercoils (rather than the negative supercoils provided by the normal DNA gyrase). The high ionic strength of the cytosol and the special thermoprotectant potassium cyclic 2,3-diphosphoglycerate prevent chemical degradation that would otherwise occur at high temperatures. The presence of special DNA-binding proteins (Sac7d in crenarchaeotes and basic histone-like proteins in euryarchaeotes) protects at high temperatures.

Intracellular enzymes from hyperthermophiles usually show optimal activities at or near that organism's optimal growth temperature, whereas its extracellular enzymes are optimally active well above this temperature. The efficiencies of these enzymes are similar to those from mesophiles, but their thermotolerance results in their enzyme efficiency matching that of enzymes working at a lower temperature in mesophiles.

Interestingly the primary sequences of the proteins are not profoundly different when comparisons are made between homologous enzymes of mesophiles and hyperthermophiles (typically 40–85 % similar). Their three-dimensional structures are superimposable and their catalytic mechanisms are the same. More than 100 genes from hyperthermophiles have been cloned and expressed in mesophiles during the past 5 years; often strong promoters are necessary because of different codon usage, for example between *Pyrococcus furiosus* and *Escherichia coli*; expression in yeast and complementation of yeast mutations has been demonstrated in some cases.

It is often asserted that thermostability requires extra 'rigidity', but the methods used for measurement (frequency domain fluorimetry, anisotropy decay, hydrogen–deuterium exchange rates, tryptophan phosphorescence) give information on different time-

scales and a protein may be rigid on a nanosecond scale, but flexible over milliseconds. Even femto- and atto-second time scales are now experimentally accessible, and it has been shown recently that some protein functions depend on such ultrafast atomic motions. The principal components of hyperthermophilic stability of proteins as we currently understand them may be listed as follows:

- the hydrophilic effect is believed to be the major driving force of protein folding and hydrophobicity is a major force required for stability
- charged-neutral H bonding (i.e. between a side-chain atom of a charged residue and either a main-chain atom of any residue or a side-chain atom of a neutral residue) is especially favourable
- ion pairing, though not an important factor in protein folding, may also be a strong stabilizing mechanism for hyperthermophilic proteins
- intersubunit interactions are also likely to be important in multimeric enzymes and many hyperthermophilic enzymes have a higher oligomerization state than their mesophilic homologues

Other factors include:

- release of conformational strain
- anchoring of N- and C-terminal ends
- metal binding, especially Ca^{2+} , Mg^{2+} and Mn^{2+}
- stabilization by salts, substrates or by post-translational modifications, especially glycosylation

● Commercial applications

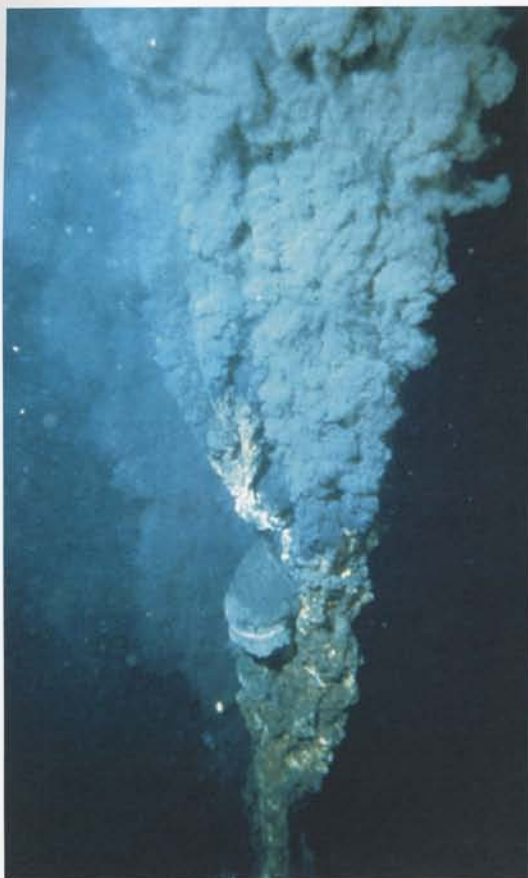
There are already several examples of thermophilic and hyperthermophilic enzymes of commercial importance. In the fermentation industry, starch processing represents an enormously important starting point for the production of fermentation syrups prior to their conversion to ethanol, organic acids or amino acids. Thermostable amylases (from *Bacillus licheniformis* or *Bacillus stearothermophilus*), followed by pullulanase and glucoamylase in combination, are used to produce glucose syrups. Xylose isomerases, the first large-scale immobilized enzymes used for an industrial process, convert glucose into fructose. Several hyperthermophilic enzymes show promise for applications in this process. Protein engineering (e.g. by site-directed mutagenesis and directed evolution) is already being employed in attempts to modify their already thermostable properties to match the exacting conditions traditionally in use.

The widespread use of *Thermus aquaticus* (Taq) DNA polymerase cloned in *E. coli* provides the basis of PCR technology where it survives exposure to 95 °C and functions repeatedly above 65 °C. Other polymerases with proof-reading 3'–5' exonuclease capability, such as Vent DNA polymerase (from *Thermococcus litoralis*) or Deep Vent DNA polymerase (from *Pyrococcus furiosus*), have been developed and marketed for use where high fidelity is necessary. Molecular biology now uses a variety



RIGHT:

Fig. 3. A black smoker; hydrothermal vents harbour unique ecosystems which include hyperthermophilic bacteria. PHOTO PROFESSOR D. RICHARDS



Further reading

Burton, S.G., Cowan, D.A. & Woodley, J.M. (2002). The search for the ideal biocatalyst. *Nat Biotechnol* 20, 37–45.

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Vieille, C. & Zeikus, G.J. (2001). Hyperthermophilic enzymes: sources, uses and molecular mechanisms for thermostability. *Microbiol Mol Biol Rev* 65, 1–43.

of thermostable DNA ligases, aminopeptidases and carboxypeptidases, alkaline phosphatase and restriction endonucleases. Cyclodextrins are used to encapsulate hydrophilic molecules in pharmaceutical, cosmetic and food products; cyclomaltodextrin glycosyltransferases are used to produce these compounds, and are now available from a *Thermococcus* species.

Thermostable enzymes may also be used (sometimes in organic solvents) at low water activity to catalyse key biotransformation steps in difficult organic syntheses. There are many laboratory projects to develop processes that can produce specific stereoisomers by exploitation of enzyme-catalysed syntheses. The only industrial synthetic process currently using a thermophilic enzyme is the synthesis of the artificial sweetener aspartame (L-aspartyl-L-phenylalanine methyl ester) with thermolysin. Lignocellulose degradation to ethanol or other bacterial fermentation products represents a huge, and so far only moderately successful, achievement. The economically widespread utilization of the most abundant non-fossil carbon source on the planet may await the further development of this line of enquiry and its practical applications. Perhaps one day hydrogen, the fuel of the future, will be commercially manufactured using the ingenuity of a hyperthermophile!

● **David Lloyd is Professor of Microbiology at Microbiology (BIOS11), Main Building, Cardiff University, PO Box 915, Cardiff, CF10 3TL, Wales, UK.**
Tel. 029 20874772; Fax 029 20874305
email lloyd@cardiff.ac.uk

SGM 150th meeting in the news

Not only was this the biggest meeting the Society has had in recent years in terms of the number of delegates, but slowly and surely we are beginning to see increased media coverage of our meetings as we work hard to raise our profile.

A full two-page conference report appeared in *New Scientist* (13 April 2002, pp 12–13). This resulted in Michael Hudson from CAMR being interviewed on the TV programme *South Today* (22 April) about his team's work on a possible new vaccine against group B meningitis. [In addition, Alan Parsons and Richard Heal from QinetiQ featured in an article in *The Guardian* (29 April 2002) about the possibility of air-borne signalling mechanisms.] *New Scientist* also ran two stories the following week (20 April 2002, pp 5 & 14) featuring an article on the possible link between cot death and the presence of bacteria on soiled mattresses, and another on the similarities between camelpox and smallpox.

Several stories appeared on *BBC On-line* over the course of the week, and the website *BioMedNet news* featured five papers. We also had interest from further afield. One researcher appeared on Radio Singapore, and another on the South African Broadcasting Corporation!

Microbiology remains constantly in the headlines, mainly as a consequence of large disease outbreaks such as foot-and-mouth or BSE. Many people in the scientific community are concerned that such stories can be hyped up or portrayed inaccurately. But this is all the more reason why scientists need to be more responsive to media enquiries to get a balanced message across. One way that you can help the SGM to do this is to include your details on the Society's media relations database. If you are an expert in a particular research field and would be willing to respond to media enquiries, please email Tracey Duncombe at pa@sgm.ac.uk

Microbiology

Helping the aged gut regulate good bacteria may reduce cancer risk

Strong evidence that the number of bacteria in the gut is linked to the risk of colorectal cancer, suggests that the gut may be a key site for the prevention of this disease.

The study, led by Professor Sir Peter D. Smith, of the University of Edinburgh, is the first to show that the number of bacteria in the gut is linked to the risk of colorectal cancer.

The study, published in the *Journal of Clinical Investigation*, shows that the number of bacteria in the gut is linked to the risk of colorectal cancer.

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Microbiology

Dead and dying: vaccines for meningitis evaluated

The safety of meningitis vaccines has been evaluated in a large trial.

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Bioremediation of metals; the application of micro-organisms that make and break minerals

Jonathan R. Lloyd

Metals have played a pivotal role in the development of human civilizations. As early as 15000 BC gold and copper, which both occur as native metals, were worked into useful and desirable objects. By 4000 BC primitive smelting techniques were developed to extract copper from ores, and within a further 1,000 years other metals, including silver, tin, lead and zinc, were also being extracted, leading the way to the manufacture of alloys such as bronze (a blend of copper and tin). Iron was harder to obtain from rocks and was not worked successfully until about 1300 BC in Asia Minor. The development of the blast furnace many centuries later led to the large-scale production of iron and steel and ushered in the Industrial Revolution. Metals are not just part of our long industrial heritage, however, but are finding increasing use in areas as diverse as medicine, electronics, catalysis and the generation of nuclear power. Given our long and intimate association with metals, and our continued reliance on these important natural resources, it is not surprising that their use (and abuse) can lead to significant environmental problems that need to be addressed.

To put these environmental issues into perspective, the UK brownfield land area is estimated to cover about 360,000 hectares, half of which is expected to be contaminated with toxic metals (for an example, see Fig. 1). Estimates of the global market for the clean-up and prevention of metal contamination vary, but conservative calculations suggest that the current market for metal bioremediation may be about £20 billion per year, rising to £200 billion in the US alone by 2005. The emerging market for the clean-up of radioactive contamination may already be worth as much as £140 billion. Unfortunately, existing chemical

techniques are not cost-effective for the removal of metals from large areas of contaminated land. Current strategies rely on 'dig and dump' approaches that only move the problem to another site, and these are expensive and impractical for large volumes of soil or sediment. Likewise, soil washing, which removes the smallest particles that bind most of the metals, is useful but can be prohibitively expensive for most sites. 'Pump and treat' technologies rely on the removal of metals from the site in an aqueous phase which is treated *ex situ* (e.g. above land). These approaches can cut down on excavation costs but are still expensive, and metal removal can be inefficient. What is needed is a suite of low-cost techniques that can be used in the sediment or soil (*in situ*) to either extract the metals or stabilize them in forms that are immobile or non-toxic. There is also considerable interest in more effective techniques that can be used to treat metal-contaminated water from a range of industrial processes. Problems inherent in currently used chemical approaches include a lack of specificity associated with some ion exchange resins, or the generation of large quantities of sludge through treatment with alkali or flocculating agents. Biotechnological approaches that harness microbial activities may offer practical solutions to these problems, offering highly specific, potentially cost-effective alternatives that can be used at large scale in a range of settings, both *in situ* and *ex situ*. This article gives a very short overview of metal-microbe interactions, and describes how they could be harnessed to clean up metal-contaminated water and land.

● Metal-microbe interactions

Although micro-organisms cannot destroy metals (they are not alchemists!) they can alter their chemical properties via a surprising array of mechanisms (see Fig. 2), some of which can be used to treat metal contamination. In some cases these processes involve highly specific biochemical pathways that have evolved to protect the microbial cell from toxic heavy metals. A good example here is the microbial reduction of mercury, a subject that is discussed in more detail below. Because these detoxification mechanisms are very specific, the biochemical components that recognize and detoxify the target metals may also prove useful for the design of biosensors for 'bioavailable' concentrations of toxic metals. In other examples, microbes can produce new mineral phases via non-specific mechanisms that result in the entrapment of toxic metals within soils or sediments. Other mechanisms of potential commercial importance rely on the production of biogenic ligands that can complex metals, resulting in their mobilization from contaminated soils. The mobilized metals can then be pumped out of the soil or sediment and trapped in a bioreactor on the surface.

Environmental pollution by metals is a serious problem. Jonathan Lloyd describes some ways in which microbes can be used in the clean-up process.

CAUTION

THIS LAND IS A FORMER INDUSTRIAL SITE AND LANDFILL.

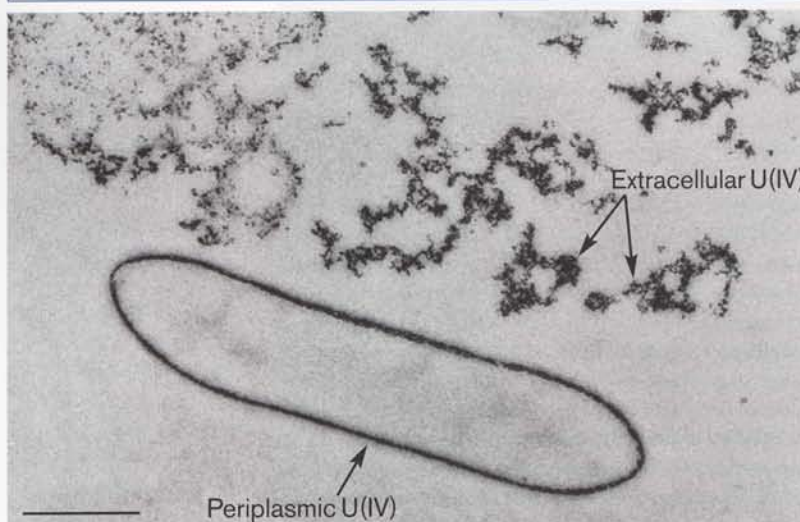
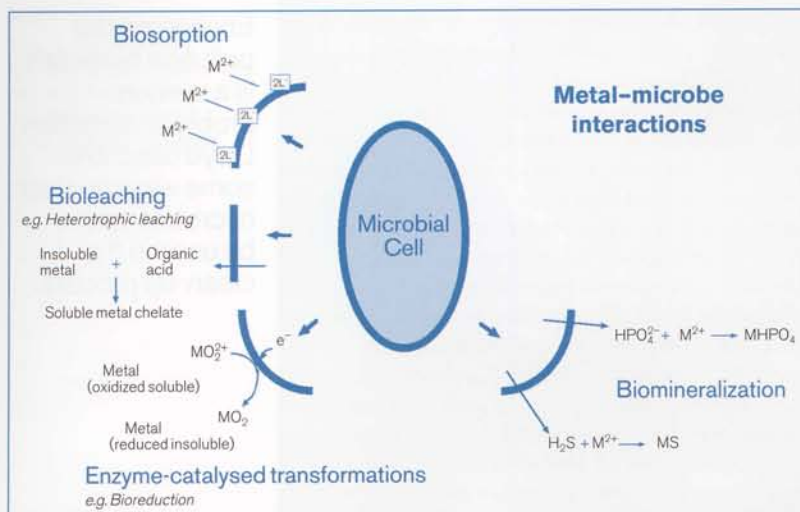
WATER ON THE SITE CAN BE CONTAMINATED WITH CHROMIUM.

CONTACT WITH CONTAMINATED WATER CAN CAUSE SKIN IRRITATION.
DRINKING WATER FROM THE SITE COULD ALSO CAUSE SERIOUS ILLNESS.

NOT ALL WATER ON THE SITE WILL BE CONTAMINATED WITH CHROMIUM BUT THE FOLLOWING ARE SENSIBLE PRECAUTIONS:

- > AVOID SKIN CONTACT WITH WATER IN PONDS, DITCHES OR PUDDLES.
- > DO NOT ALLOW CHILDREN TO PLAY IN OR DRINK FROM ANY WATERS ON THE SITE.
- > PET OWNERS SHOULD ENSURE THAT ANIMALS DO NOT DRINK FROM ANY WATERS ON THE SITE.

LEFT:
Fig. 1. Contamination of land with metals such as chromate is a significant problem in both the developed and developing world. This site is in the North West of England.
COURTESY GREATER MANCHESTER GEOLOGICAL UNIT



ABOVE TOP:
Fig. 2. Mechanisms of metal-microbe interactions that can be harnessed for bioremediation applications.

ABOVE BOTTOM:
Fig. 3. Transmission electron micrograph showing the reduction of soluble U(VI) to insoluble U(IV) by a subsurface metal-reducing bacterium *Geobacter sulfurreducens*. Insoluble U(IV), visible as an electron-dense mineral uraninite, is precipitated outside the cell and also in the periplasm. Bar, 0.5 μ m. COURTESY JONATHAN LLOYD

● Metal-mobilizing micro-organisms

Metals can be extracted from contaminated environments by two potentially useful mechanisms. First, some heterotrophic micro-organisms are able to mobilize metals via the production of organic acids. Alternatively, highly specialized autotrophic bacteria such as *Thiobacillus* species are able to generate significant quantities of metal-leaching sulfuric acid from the oxidation of elemental sulfur. This mechanism of metal mobilization has been used for many centuries to leach metals from low-grade ores, and currently supports a lucrative global market in mineral extraction. It can also be harnessed to remove metals from contaminated soils and sediments, and can be combined with a second *ex situ* step to remove the metals as insoluble sulfides using sulphate-reducing bacteria, which reverse the metal mobilizing step.

● Using microbes as ion exchange resins

Once metals are in solution, one of the simplest ways to remove them is through 'biosorption', which can be

defined as the metabolism-independent sorption of heavy metals and radionuclides to biomass. The cell surface carries a net negative charge at neutral pH due to the presence of carboxyl, amine, hydroxyl, phosphate and sulfhydryl groups, and can adsorb appreciable quantities of positively charged cationic metals. Advantages of this type of metal-microbe interaction include the potential use of low-cost waste biomass sources (e.g. spent brewery yeast) and very rapid kinetics coupled with high adsorption capacities. Indeed, recent comparisons have suggested that biosorbents may be cheaper to implement than other commercially available ion exchange resins. Despite the apparent promise of this type of technology, industry has been slow to take up this approach. Disadvantages include the perceived variation between batches of the biological product, a lack of specificity and sensitivity to changes in pH. Recent studies have suggested that it may be possible to increase uptake and specificity of biosorbents using the tools of molecular biology, for example by targeting engineered metal-binding proteins to the cell surface.

● Enzyme-catalysed transformations

Micro-organisms are ubiquitous and offer a potentially enormous gene pool to select from when looking for enzymes that can help treat metal contamination. Indeed, micro-organisms have evolved a wide range of biochemical tricks to protect themselves from potentially toxic metals and these activities can be useful for bioremediation applications. Many microbial detoxification processes involve efflux or exclusion of metal ions from the cell, which in some cases can result in high local concentrations of metals at the cell surface where they may react with biogenic ligands and precipitate. Alternative mechanisms involve redox transformations, for example the enzyme-catalysed reduction of the toxic mercuric ion (Hg^{2+}) to non-toxic elemental mercury [$Hg(0)$]. This approach has been used recently to treat chloralkali wastewaters contaminated with Hg^{2+} ions. Microbially reduced elemental mercury was trapped in a bioreactor containing a biofilm of mercury-resistant bacteria (pseudomonads).

In addition to the highly specific mercury reduction/detoxification pathway, some specialist subsurface bacteria are able to use high valence metals as electron acceptors for anaerobic growth. Metals that are reduced in this manner include Fe(III), Mn(IV), U(VI), Cr(VI), Se(VI) and As(V). In some cases the biological reduction of these metals can result in dramatic changes in solubility. For example, U(VI) is highly soluble and mobile, but U(IV), formed through enzymic reduction by a range of specialist anaerobic bacteria, is highly insoluble (see Fig. 3). This transformation, catalysed by a class of enzymes known as *c*-type cytochromes, can be used to stabilize uranium in contaminated groundwater. Although uranium is the priority contaminant in

nuclear waste, there are other less familiar isotopes that also cause considerable concern. These include technetium and neptunium, both of which normally exist as oxidized, soluble forms; Tc(VII) and Np(V), respectively. Thankfully, subsurface bacteria are also able to reduce these to less soluble forms [in these cases Tc(IV) and Np(IV)] and may therefore play a role in preventing their migration in contaminated soils and sediments. Another redox-active metal that can cause concern in the UK (see the sign in Fig. 1 from a site in the north west) and abroad is chromate. Film-goers will be familiar with health problems associated with chromate contamination raised in the recent Hollywood film *Erin Brockovich*. Metal-reducing bacteria are able, however, to reduce very toxic soluble chromate [Cr(VI)] to less toxic, less soluble Cr(III). These organisms may prove useful in the bioremediation of sediments contaminated by Cr(VI), or in the treatment of Cr(VI)-contaminated process waters.

● Indirect mechanisms that build novel biominerals

In addition to reducing metals directly using 'metal reductases', anaerobic bacteria are also able to reduce and precipitate a range of metals via indirect mechanisms. For example, Fe(III)-respiring bacteria catalyse the formation of Fe(II)-bearing minerals that can in turn reduce and precipitate high valence metals abiotically. In many cases reduction is extremely efficient, driven by the very large surface area of biologically produced minerals. Examples here include Fe(II)-catalysed reduction of Cr(VI) and Tc(VII), with subsequent precipitation of Cr(III) and Tc(IV) respectively. Sulfate-reducing bacteria are also able to remove metals via indirect mechanisms. Here precipitation, sometimes with concomitant reduction, is driven via sulfide that is produced from respiration using sulfate as the terminal electron acceptor. A wide range of metals react to form insoluble sulfide minerals and this approach has been used successfully in several metal-treatment applications, including the bioremediation of water from a metal sulfide refining site in the Netherlands. Sulfate-reducing bacteria have also been used successfully to treat metal leachates generated by sulfuric-acid-producing *Thiobacillus* species as mentioned previously.

Metal phosphates, like the corresponding sulfides, are sparingly soluble and bacteria are also able to remove toxic metals as insoluble phosphate biominerals. A well studied model system here is a *Citrobacter* species that generates free inorganic phosphate from the degradation of glycerol 2-phosphate via a 'phosphatase' enzyme. This results in high local concentrations of metals and phosphate at the surface of the bacterial cell, driving the formation of an insoluble metal phosphate coat that can entrap significant quantities of toxic metals and radionuclides. Finally, both the sulfide and phosphate

biominerals described are able to remove a range of toxic metals via intercalation into the host mineral.

● Conclusions

From this very brief overview it is clear that there are many microbial activities that may prove potentially useful for the bioremediation of metal-contaminated soils, sediments and waters. The challenge is now to implement these novel approaches in the field. This will require multidisciplinary studies encompassing a diverse scientific and technical community, including engineers, hydrologists and geochemists, as well as microbiologists. Although the application of biological approaches to treat metal contamination has been slow, tighter environmental legislation in combination with the inherent limitations of existing chemical approaches will surely mean that micro-organisms will play a very significant role in controlling metal contamination in the 21st century.

● Dr Jonathan R. Lloyd is a Senior Lecturer in Geomicrobiology at the Williamson Research Centre for Molecular Environmental Science and The Department of Earth Sciences, University of Manchester, Manchester M13 9PL, UK. Tel. 0161 275 7155; Fax 0161 275 3947 email jrlloyd@fs.1.ge.man.ac.uk

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A sticky business. Microbial polysaccharides: current products and future trends

Ian Sutherland

The ingredients list of many foodstuffs includes microbial polysaccharides. Ian Sutherland reveals the potential and applications of these polymers.

Many bacteria, yeasts and fungi can produce polysaccharides. Although much interest in these polymers is due to their role in infection or adhesion, some of them have proved to be useful industrial products which compete with plant and algal polysaccharides as well as synthetic products. While dextran was the first microbial polysaccharide to be commercialized and to receive approval for food use, several such polymers now have a variety of commercial uses. Surprisingly, some of the polysaccharides fetch relatively high prices. Only two, both bacterial polysaccharides, are currently employed in the food industry, except in Japan where all such polymers are regarded as natural products. If you read the labels on many manufactured foods on supermarket shelves or on the sachets of dressings you receive in planes, you will find many contain xanthan, a bacterial polysaccharide. This product is now very widely used by the food industries of Europe and North America and is produced in the US, UK and France as well as other countries.

● Commercial production

Production of most microbial polysaccharides involves growth in stirred tank fermenters using media with glucose or sucrose as the carbon and energy source. Synthesis is often favoured by high C:N ratios. Because of the high viscosity of the fermentation broths, efficient mixing and aeration are required together with considerable energy input. Fed-batch fermentations may be preferable to the use of high initial sugar concentrations. After pasteurization of the broth, recovery by precipitation with iso-propanol is followed by drying and grinding to yield a fine powder. Filtration or centrifugation and other downstream processing add to the final cost.

● Xanthan

Xanthan is a product from the plant pathogen *Xanthomonas campestris*. It has a cellulosic backbone on every second glucose residue of which a trisaccharide side chain is attached. This unusual structure confers physical properties to the polymer which are utilized in food and other industries. Xanthan is stable at both acid and alkaline pH and forms pseudoplastic dispersion in water. Relatively low polysaccharide concentrations produce highly viscous solutions and the viscosity does not change greatly on raising the temperature. The solutions are compatible with many other ingredients in food and give good flavour release. Xanthan is also a good suspending and stabilizing agent for oil/water emulsions such as salad dressings. Because of all these features and its inherent safety, xanthan received GRAS listing (Generally Regarded As Safe) for food use in the US after its initial discovery in the USDA laboratories in Peoria and its development by KELCO. Subsequently, the polysaccharide received approval in the EU.

Xanthan is also widely used in 'drilling muds' for lubricating the drill in oil exploration and development, playing an essential role in keeping us supplied with petrochemical products. The xanthan provides an excellent suspending agent for removing the rock cuttings released on drilling; it is also compatible with barites, used to counteract the high pressures of reservoirs. Xanthan solutions have also been proposed for enhanced oil recovery from depleted reservoirs in which fall in the initial pressure is compensated by pumping down solutions containing viscosifiers. Low oil prices preclude this usage at present.

Xanthan does, however, have a range of other industrial applications making use of its viscosifying and suspending capacity. Currently about 20,000 tonnes are produced annually for food and non-food uses in the US, UK and elsewhere in the EU and in other countries.

● Two are better than one!

Xanthan does not form gels unless trivalent salts such as chromium or aluminium are added. However, if solutions are mixed with locust bean gum (another widely used food polysaccharide from seeds of the Mediterranean leguminous tree *Ceratonia siliqua*), heated to yield disordered solutes and then allowed to cool, gels can be formed with very low concentrations of total polysaccharide. Such mixtures are widely used in the preparation of manufactured foods and in the pet food industry. See how many of the products you buy contain both these polysaccharides listed on the label!

● Gellan

The only other bacterial polysaccharide currently GRAS-listed is gellan, a product from *Sphingomonas paucimobilis*. It is an excellent gelling agent providing clear, brittle gels at a much lower concentration than agar. However, in its native state the polysaccharide carries various esters attached to the sugars and does not gel. These groups must be removed before it is commercially valuable and of course such a process increases the cost of production. As well as food use, gellan has been widely employed as a gelling agent in plant biotechnology under the trade name of gellrite or phytogel; it can also be used in place of agar in bacterial culture media. Other *Sphingomonas* isolates have yielded a family of polysaccharides which are closely related structurally. Although none of the others forms gels, they do yield highly viscous aqueous solutions and have been proposed for various industrial, non-food uses. Time will tell whether they prove to be commercially successful.

● Costly and sticky!

Surprisingly, bacterial cellulose from *Gluconacetobacter xylinus* is a high-value product of biotechnology. Because of its purity and the orientation of its fibres, it can be formed into high quality audio membranes.



Maybe your audio system relies on bacteria for its sound quality! A Brazilian company has also found that bacterial cellulose in wound dressings promoted healing, reduced plasma loss and also appeared to maintain sterility. It suggested that such dressings, marketed under the name 'Biopol', were especially useful for burns victims and for those with extensive skin damage. Despite the apparent success of the procedure, this application does not yet appear to have been widely adopted.

The most expensive bacterial polysaccharide product is hyaluronic acid (HA). This polymer from '*Streptococcus epizooticus*' or related species is mainly employed for ethical products. It is identical to HA from the human and animal body and can substitute for animal HA previously used in eye or joint operations to replace the material lost during surgical manipulations. For this role, HA has to be of the correct mass and is much more costly to manufacture than products such as xanthan or gellan. HA is also an excellent hydrating agent which is incorporated into moisturizers for the cosmetics industry (look at the labels listing the ingredients), but whether the polysaccharide for this usage is currently of animal or bacterial origin is unclear.

● Polysaccharides in health and disease

Some polysaccharides form integral components of vaccines, usually when coupled to a suitable protein. Thus, meningitis vaccines have been prepared in this way and multivalent polysaccharide vaccines have been formulated against *Streptococcus pneumoniae* and *Klebsiella* spp. However, these are expensive to prepare and only use very small amounts of material. Possibly of much greater significance is the role of certain microbial polysaccharides in tumour suppression and immune stimulation. A homopolymer named 'Scleroglucan' or schizophyllan, from several fungal species, appears to be very effective against some cancers when it is applied in the ordered, triple helical form. These β -linked glucans are therefore the subject of much current study and have already been tested clinically in Japan, proving effective against certain types of tumour. Dextran, although no longer used as a food ingredient, is the base from which the 'Sephadex' range of biochemical adsorbents is prepared.

Dextran solutions can also be used as a plasma substitute, being very poorly antigenic and having the correct physical properties.

● What's new?

Although many researchers purport to have found polysaccharides 'of superior viscosity to xanthan', in

reality few match the robustness of the *Xanthomonas* polysaccharide and few can maintain their physical properties in the presence of salts, at higher temperatures or extremes of pH. Most are unlikely ever to find a niche in the polysaccharide market place. Instead, several labs in the milk product sector are looking for new or improved polysaccharide production in Lactic Acid Bacteria (LAB). As these bacteria are already widely used in the production of fermented dairy products, the bacteria are already acceptable for food use. However, most only produce small amounts of polysaccharides. In Belgium, the Netherlands and Switzerland, as well as in the University of Huddersfield in the UK, researchers have recently published structures for many of these polymers, as well as determining the physiological conditions needed to enhance polysaccharide production. Currently, less is known about their physical properties and the ways in which they contribute to the texture and physical characteristics of fermented milk products. If research is successful, these products might well be used to extend or adjust the textures of many fermented milk products and would have the presumed advantage of being acceptable food ingredients. Some of these polysaccharides, as well as levans, are of interest because of their prebiotic or probiotic properties. Many of the most recent studies in the LAB area were reported at a very successful meeting held last year in Brussels.

Current interest in glycobiology and the application of new analytical methods has also stimulated academic research on microbial polysaccharides. However, there is a gap between our knowledge of the structure of polysaccharides and the ability to predict their physical properties, and thus their potential applications. Perhaps, given more time, that will come and we may see further developments in the applications field. For the moment, use of the biological properties and the potential food use of polymers from LAB appear to lead the race.

● Ian Sutherland is Emeritus Professor of Microbial Physiology at Edinburgh University in the Institute of Cell and Molecular Biology, Darwin Building, Mayfield Road, Edinburgh EH9 3JR, UK. email i.w.sutherland@ed.ac.uk

ABOVE:

A culture of *Xanthomonas campestris* producing xanthan on a medium with a high carbon:nitrogen ratio.

PHOTO IAN SUTHERLAND

Further reading

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Defusing the environment

Elaine Boyd & Neil Bruce

Environmental contamination by explosives presents a serious problem. Bacteria and plants may provide the solution, as Elaine Boyd and Neil Bruce describe.

Major international concern is growing over the wide-scale contamination of soil and ground waters with high explosives. For example, in the US an estimated 0.82 million cubic metres of soil at former ordnance sites and military proving grounds are contaminated with the explosive 2,4,6-trinitrotoluene (TNT). The manufacture, use and disposal of high explosives over the last hundred years have resulted in serious widespread contamination of the environment. The presence of these compounds not only presents the risk of detonation and a serious hazard to human health, but many explosives are also highly toxic and recalcitrant, persisting indefinitely in the environment. In addition to TNT, compounds of concern include nitroaromatic 2,4,6-trinitrotoluene (Picric acid), the nitroamines [hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX; Royal Demolition Explosive) and octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX; High Melting Explosive) are also widely used explosives as are the nitrate esters]; pentaerythritol tetranitrate (PETN) and glycerol trinitrate (nitroglycerin) (see Fig. 1).

Current remediation technologies

Effective treatment of the solid and liquid wastes emanating from production and decommissioning explosive processes is of paramount importance. Present and historical methods for the disposal of munitions include open burning, open detonation (Fig. 2), burial and incineration. These methods, however, are becoming increasingly unpopular due to environmental concerns. For example, current incineration of TNT-contaminated soil results in the production of thousands of tonnes of unusable ash. This raises concerns regarding further disposal and also presents a threat to the quality of the atmosphere through the release of fine particulate matter.

Furthermore, the open detonation disposal option can result in the release of further contaminants, including dioxins and polychlorinated biphenyls. Open detonation can also result in major habitat destruction, ecosystem disturbance and extensive structural damage to any property in the vicinity. Alternative technologies must be developed to minimize air, water and soil pollution and to comply with present and anticipated environmental legislation.

Addressing the problem

At the Institute of Biotechnology, University of Cambridge, we have been focussing on both the potential of bacteria to bioremediate explosive-contaminated land and upon phytoremediation, the use of plants for explosives remediation. Such approaches can provide environmentally friendly and aesthetically pleasing alternatives to the harsher and more expensive methods of physical and chemical degradation approaches.

Bacteria – bioremediation potential

It was once thought that micro-organisms were infallible! It was generally considered that they were capable of oxidizing any organic molecule in the environment, providing conditions were favourable. This theory, however, began to be disproved when it was found that anthropogenic compounds (those synthesized by man) were in-fact persistent in the environment. These compounds were often foreign to biological systems and their structures were not easily recognized immediately by the microbial biomass. As a result, they accumulated in the environment and, through processes of bio-concentration and bio-magnification, began migrating to higher levels in the food chain.

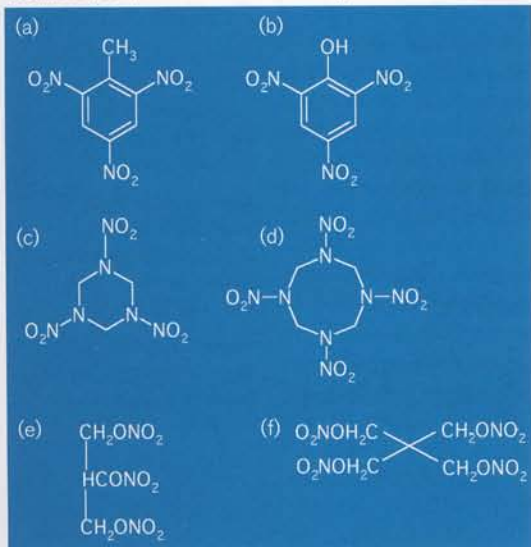
Bacteria possess the natural ability to adapt and evolve degradative pathways to break down anthropogenic compounds, but to achieve this they need to be exposed to the contaminant for a considerable time. Our group was granted access to undisturbed soil samples contaminated with high explosives for over 60 years. This has provided us with the unique opportunity to isolate soil micro-organisms that have evolved the capacity to degrade or transform problem high explosives.

RDX degraders. Novel species have been isolated that can utilize RDX as a sole nitrogen source. Dispersion plates show 'zones of clearance' where RDX has been mineralized by *Rhodococcus rhodochrous* 11Y, a Gram-positive soil bacterium (Fig. 3). Detailed characterization of the primary metabolites has shown that RDX is broken down to simple carbon and nitrogen substrates such as formate, formaldehyde, nitrite and ammonia. All these compounds can then be further metabolized by the general soil microbial biomass.

PETN and nitroglycerin. *Enterobacter cloacae* PB2 was isolated from explosives-contaminated soil in the laboratory on the basis of its ability to grow with nitrate ester explosives, such as PETN and nitroglycerin, as the sole nitrogen source. Characterization of the enzyme

BELOW:

Fig. 1. Structures of important explosives. (a) 2,4,6-trinitrotoluene (TNT); (b) 2,4,6-trinitrophenol (picric acid); (c) Royal Demolition Explosive (RDX); (d) High Melting Explosive (HMX); (e) glycerol trinitrate (nitroglycerin); (f) pentaerythritol tetranitrate (PETN).





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responsible for the ability to transform PETN and nitroglycerin showed that the pathway was mediated by an NADPH-dependent reductase, designated PETN reductase, which reductively liberated nitrite from these compounds. The structural gene encoding PETN reductase was subsequently cloned and over expressed in *Escherichia coli* and the same reduction of PETN and nitroglycerin was observed. PETN reductase has now been characterized in considerable detail and the crystallographic structure of the enzyme was published in 2001. The ability of the innate bacterium and the recombinant species expressing PETN reductase was identified as having considerable potential for assisting in the bioremediation of explosives contaminated soils and groundwaters.

TNT. TNT has been found to be extremely resistant to breakdown by soil microorganisms. This in part is due to the physicochemical characteristics of the molecule that differ significantly from those of other explosives. The π electrons of the aromatic ring system are withdrawn by the nitro groups, making the nucleus electron-deficient and resistant to electrophilic attack. This has a profound effect on the mechanisms by which TNT can be transformed in the environment. The electron-deficient nature of the molecule makes it resistant to attack by oxygenases, the primary mode of attack by bacteria on organic pollutants. The electronic nature of TNT also means that it is readily bound in the soil to humic materials and its mobility and bioavailability (availability to the soil degrading community) within soil systems is thus drastically reduced. Reduction in bioavailability can result in the biomass never becoming exposed long enough in the environment; as a result catabolic pathways for the degradation of TNT may never actually evolve.

Nevertheless, some progress has been made to identify primary modes of attack on TNT. It is well established that TNT can be reductively transformed into Meisenheimer complexes, azoxydimers and diamino-nitrotoluenes, but these compounds have been shown to be resistant and persistent in the environment, being unsurprisingly termed dead-end metabolites. No aerobic bacteria had been isolated that could transform TNT beyond these products; we were surprised to find that PETN reductase could reduce TNT to a hydride-Meisenheimer complex, which was further reduced to dihydride-Meisenheimer complexes, which were yet further reduced to unknown products. Both purified and recombinant *E. coli* expressing PETN reductase were able to liberate nitrogen as nitrite from TNT, showing that, despite its recalcitrant nature, TNT could be degraded under reductive conditions.

LEFT:
Fig. 2. Open detonation.
COURTESY DR DAVID J. WOOD, QINETIQ

BELOW:
Fig. 3. Zones of clearing.
COURTESY DR AMRIK BASRAN,
UNIVERSITY OF CAMBRIDGE



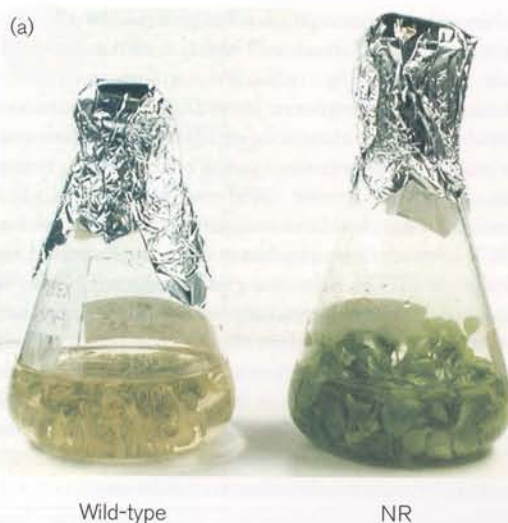
● Plants – phytoremediation potential

Recent attention in the group has focussed on phytoremediation as an approach to cleaning up high-explosive-contaminated environments. Plants possess the ability to extract compounds from the surrounding environment and their root systems are generally extensive, subsequently promoting increased microbial numbers and activity in the rhizosphere. It has been shown, for example, that this unique interaction between plants and bacteria can produce an increase in microbial biomass of an order of magnitude comparable with that of microbial populations in bulk soils. Plants sustain large microbial populations in the rhizosphere by secreting carbohydrates and amino acids through root epidermal cells and by the sloughing of root epidermal cells. The actual composition of the microbial community is a function of root type, plant species, soil

RIGHT:

Fig. 4. (a) Nitroreductase (NR) seedlings grow well compared to wild-type seedlings in TNT-spiked liquid medium. (b) Stunted seedling root growth of wild-type compared to the NR transgenic line when grown on TNT-spiked agarose.

COURTESY NERISSA HANNINK, UNIVERSITY OF CAMBRIDGE



Further reading

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growth of the resultant seedlings was severely stunted in the wild-type, although growth of the transgenic plant lines was prolific (Fig. 4b). Importantly, hydroponic studies showed that these transgenic plant lines could remove and sequester TNT from the medium. This suggests that transgenic plants expressing microbial degradative genes could be used for the bioremediation of explosive contaminated land. By harnessing the unique co-operative interaction between plant and bacterium the field of explosives remediation has been driven forward. Further investigations are currently underway to determine the ability of transgenic plants to remove TNT from soil aged under laboratory conditions.

● Dr Elaine Boyd is a Postdoctoral Research Associate at the Institute of Biotechnology, University of Cambridge, Tennis Court Road, Cambridge CB2 1QT, UK.
Tel. 01223 334171; Fax 01223 334162
email e.boyd@cam.ac.uk

● Dr Neil Bruce is a Reader in Biotechnology at the same Institute.
Tel. 01223 334168; Fax 01223 334162
email n.bruce@biotech.cam.ac.uk

Acknowledgements

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type and exposure history. This interaction between plants and microbial communities in the rhizosphere is complex and has evolved to the mutual benefit of both organisms.

Despite this unique synergistic interaction, previous research has shown that innate biodegradative abilities of plants are less effective than those of adapted or recombinant bacteria alone. However, it was considered that since plants can cover a vast surface area and require low maintenance, then their incorporation into a remediation facility should be encouraged. This raised the interesting question therefore, of whether the biodegradative abilities of bacteria could be combined with the high biomass and stability of plants to yield an optimal system for *in situ* bioremediation of explosives. Seeds from transgenic tobacco plants expressing either PETN reductase or an aromatic reductase were able to germinate and grow in the presence of normally toxic levels of TNT. These concentrations inhibited germination and growth of wild-type (non-recombinant) seeds (Fig. 4a). Root

A quiet revolution in the bacterial cell factory

David Summers

David Summers describes the development of a novel Quiescent Cell Expression System which has commercial potential for the production of proteins.

● The bacterial cell factory

Some recombinant proteins are very easy to produce in *Escherichia coli*. With the gene expressed from a strong promoter one could virtually culture the cells in a bucket, stir them with a stick and still obtain a good yield. This isn't always true, however, and problems can be associated with poor yield, mis-folding of the polypeptide backbone, precipitation of protein into inclusion bodies and poor biological activity. As genomics gives way to proteomics and the number of proteins requiring expression grows rapidly, the number of problem proteins is increasing too. Sometimes the solution is familiar from economics: export production to another Kingdom where it is cheaper or more efficient. There is no question that non-bacterial cell factories, such as the yeast *Pichia* or insect cells, have their staunch supporters. Mammalian cell culture also provides an attractive alternative to bacteria for human protein expression, especially when post-translational modification such as glycosylation is required. Nevertheless, recombinant protein expression in bacteria remains the most desirable option, not least because of the cheapness and ease of bacterial culture compared to any of its eukaryotic competitors.

Three decades of protein expression in *E. coli* have produced many improvements over the 'bucket and stick' approach. Important advances include the development of promoters such as P_{BAD} and the T7 polymerase-specific promoter which can be effectively regulated. Often it is more important to turn off the promoter tightly than to have a high maximum expression level. Effective repression allows product expression to be delayed to a later stage in the culture, which is particularly important where it harms the bacterial host. Product yield can also be increased by modifying the ribosome-binding site and, where the

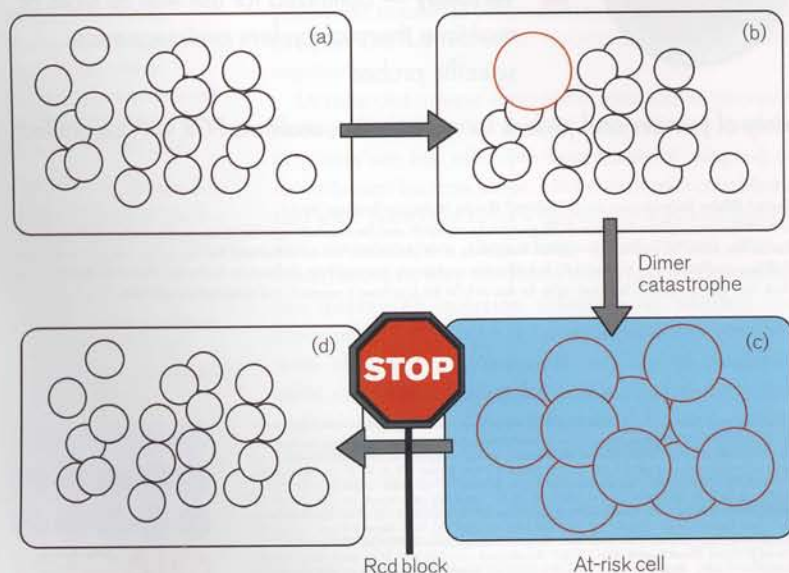
genetic code is redundant, replacing codons which are rare in bacteria with more common alternatives. Improvements in protein folding have been achieved by expressing the product slowly at a lower temperature, and sometimes by simultaneously over-expressing chaperones which reduce mis-folding and precipitation of the recombinant protein. Ingenious and effective though these modifications are, they are all add-ons to the basic bacterial cell factory. In recent years my research group has tried to take a more radical approach, investigating the possibility of rebuilding the cell factory from the ground up.

● A novel approach to the cell factory

What would be some of the features of an ideal bacterial cell factory? Since in all Kingdoms reproduction is a serious distraction from other activities, it would surely make sense to produce recombinant protein in non-growing cells. In the case of bacteria this would allow the channelling of nutritional resources into product rather than into unwanted biomass. This is not a new idea but it is difficult to stop bacteria growing without limiting resources, and starving your workforce is hardly the way to get the best out of them. Another desirable objective would be to focus cellular resources on product gene expression. It is hardly efficient for the product gene to be one of hundreds all clamouring for the attentions of the transcriptional and translational machinery, and the complex apparatus required for protein folding and export. Ideally, we should give priority to product gene expression. To the microbiologist stopping growth without resource limitation and persuading the cell to concentrate on the expression of a single gene may seem like a tall order. However, in the eukaryotic world this is not at all a radical idea. After all, in the human body the expression of specialist proteins is the province of cells which have ceased division and entered the quiescent G_0 state. This allows them to limit gene expression and concentrate their resources on specialized products. In the development of the *E. coli* Quiescent Cell Protein Expression System (Q-Cells) we have tried to apply the 'best practice' learned from eukaryotes to the bacterial cell factory.

The Q-Cells system has its roots in the early 1990s. Michaela Sharpe, a graduate student in the laboratory, was looking at aspects of plasmid inheritance. She became interested in a 70 nucleotide RNA (known as Rcd) encoded by the multicopy plasmid ColE1. This molecule was expressed when the formation of plasmid multimers threatened to disrupt the proper transmission of the plasmid to daughter cells (Fig. 1). Her work suggested that under normal circumstances Rcd expression delays cell division, but she also found that at higher concentrations it could trap cells permanently in the pre-divisive state.

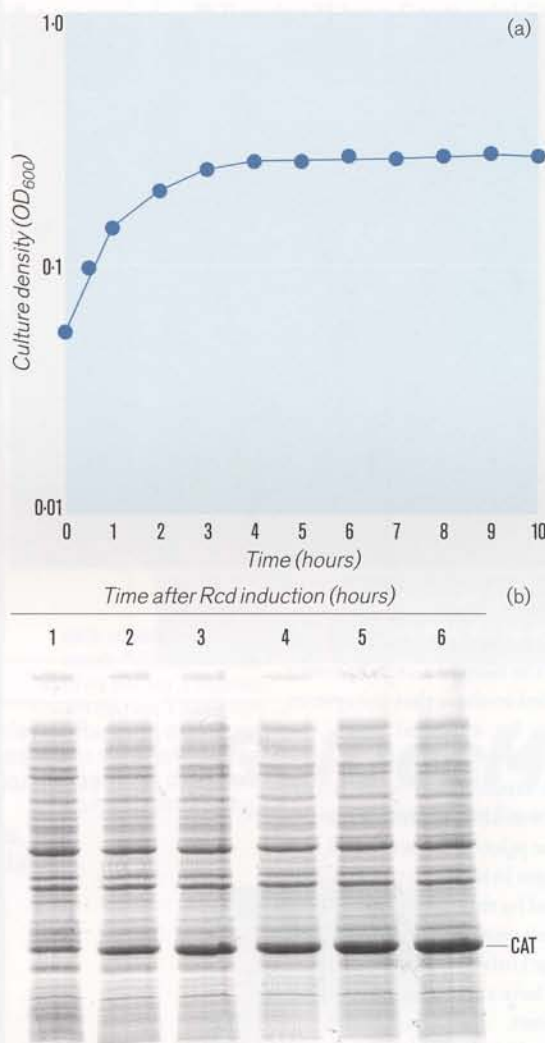
BELOW:
Fig. 1. How ColE1 survives the dimer catastrophe. The majority of *E. coli* cells carrying plasmid ColE1 contain only plasmid monomers (a). Occasionally a dimer forms by homologous recombination (b) and this dimer out-replicates its monomeric cell-mates. The resulting 'dimer catastrophe' means that some descendants of the cell in which the first dimer formed contain only plasmid dimers (c). The Rcd transcript which is expressed in these at-risk cells prevents their division. Resolution of the dimers to monomers by site-specific recombination at the plasmid *cer* site (d) leads to lifting of the Rcd-imposed block and the restoration of normal growth. COURTESY DAVID SUMMERS



Cells trapped in the pre-divisional stage by Rcd over-expression are not resource-limited, and we hoped they might be useful as cell factories. Michaela Sharpe's work had been carried out with cells grown on solid medium, so before we could go any further we needed to reproduce the effects of Rcd over-expression in broth. This seemed a trivial matter but, to our dismay, Rcd over-expression in broth culture merely reduced the growth rate and the cells eventually struggled into stationary phase. These unhappy bacteria were very poor prospects as cell factories. We wondered why the physical structure of the growth medium should affect the response of the cells to Rcd and began to think about physiological differences between cells grown on different media. If it were possible to modify the physiology of broth-grown cells to resemble that of cells grown on a solid medium, it might be possible to achieve growth-arrest in response to Rcd over-expression. Around this time there was considerable interest in growth-phase-related changes in concentration of global regulators of gene expression such as H-NS, IHF and Fis. It seemed possible that if their concentrations also varied between broth and solid medium, this might be responsible for the different effects of Rcd. Finding that altering the level of Fis in broth-grown cells had no effect on their response to Rcd, we turned our attention to H-NS. It had been reported that the H-NS concentration was higher in slow-growing or stationary-phase cells, so it seemed plausible that increasing H-NS in broth-grown cells might mimic the effect of growth on solid medium. Unfortunately H-NS over-expression makes cells difficult to culture, so Duncan Rowe, who had come to the laboratory as a post-doc to work on protein expression, decided to do a control experiment first and looked at the effect of reducing the H-NS concentration. To our surprise over-expression of Rcd in an *hns205* mutant strain led to a complete cessation of growth within 2 to 3 hours and the cells entered a quiescent state (Fig. 2a). Subsequently we discovered that we had been extremely lucky to use the *hns205* allele, which produces an N-terminal fragment of H-NS. Several other mutations which were tested subsequently, including a null allele, failed to enter quiescence in response to Rcd expression.

● Development of the Quiescent Cell Expression System

In our early experiments with cells in broth culture, Rcd was expressed from a plasmid which also carried a chloramphenicol resistance gene. When we analysed the protein composition of cells made quiescent by over-expression of Rcd (called Q-Cells for convenience) we discovered that the CAT protein (the resistance gene product) accumulated to very high levels (Fig. 2b), sometimes as much as 40% of total cell protein. In



LEFT: **Fig. 2.** The establishment of quiescence. (a) A culture of *E. coli hns-205* grows normally in the absence of Rcd expression. However, over-expression of the transcript (at $t=0$) leads to an immediate reduction in growth rate and entry into the quiescent state in 3–4 hours. (b) Expression of plasmid genes continues in quiescent cells. In this case plasmid-encoded CAT protein increases against a background of chromosome-encoded proteins. COURTESY DAVID SUMMERS

contrast there was little evidence of chromosomal gene expression in these cells. It seemed that Q-Cells were concentrating on plasmid gene expression. The reason for this odd but useful reallocation of resources became apparent when we examined Q-Cells by DAPI fluorescence microscopy (Fig. 3). DAPI stains DNA and we discovered that the bacterial nucleoid (i.e. the chromosome and associated protein) was highly condensed in Q-Cells. Presumably, condensation of the nucleoid severely inhibits expression of chromosomal genes, in much the same way that heterochromatin formation in eukaryotes results in global repression of transcription. The observation also provided a clue about how the *hns205* allele makes broth-grown cells sensitive to Rcd. H-NS is nucleoid-associated and is likely to be involved in changes in nucleoid structure during chromosome partition. If the N-terminal fragment produced by *hns205* is still nucleoid-associated but functions inappropriately, this could lead to irreversible condensation of the nucleoid.

A model revolution
Cell factory
David Summers

SGM Symposium Vol. 61 review

Signals, Switches, Regulons and Cascades: Control of Bacterial Gene Expression

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● Taking Q-Cells to market

Q-Cells fulfilled many of our criteria for the ideal cell factory, but could they form the basis of a useful protein expression system? We needed to show that the system was sufficiently robust to be exported from the laboratory to the commercial environment. During her tenure of a BBSRC CASE studentship with Astra-Zeneca, Elisabeth Watson was able to show that the system functioned well at the pilot-plant scale, and was not unduly sensitive to changes in medium composition or culture density. Encouraged by this Drs Duncan Rowe and K.-J. Mukherjee have been working in collaboration with AEA and the Cambridge University Department of Chemical Engineering, and have successfully scaled-up the system into small fermenters.

The Q-Cell system has been protected by international patents, and in 1999 a university spin-off company, Cambridge Microbial Technologies, was set up to finance its technical and commercial development. In collaboration with BTG International we have established relationships with several biotechnology companies with whom we are exploring the potential of Q-Cells to express a variety of recombinant proteins, including antibody fragments and cytokines. Basic research in the Cambridge University Department of Genetics into the physiology of Q-Cells and the development of customized vector and promoter systems is currently supported by the BBSRC.

● Dr David Summers is a Senior Lecturer in the Department of Genetics at Cambridge University, Downing Street, Cambridge CB2 3EH, UK, and a Fellow of Gonville and Caius College.
Tel. 01223 333991; Fax 01223 333992
email dks11@cam.ac.uk

ABOVE:
Fig. 3. The anatomy of the quiescent cell. DAPI-stained quiescent *E. coli* cells are longer than normal *E. coli* cells and contain highly condensed nucleoids which appear as brightly staining spots within the cells.
COURTESY DAVID SUMMERS

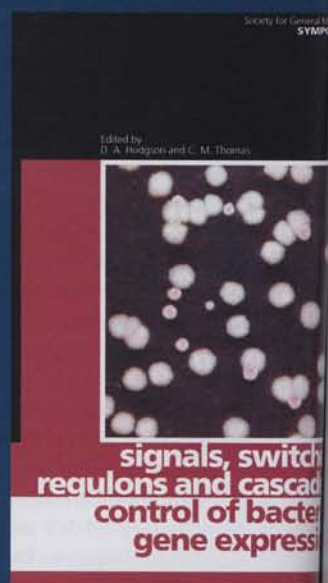
It is a pleasure to welcome another valuable and well edited SGM symposium book. Several topics are common to the last such SGM volume 16 years back: classical metabolic regulators such as LacI, AraC and CRP/FNR, a diversity of sigma factors, nitrogen regulation (here in relation to nitrogenase), modulated transcription termination, supercoiling; but with new depths of new molecular and structural information. Topics absent from that earlier book include switches via DNA rearrangements, cascades such as the phosphorelay for the initiation of *Bacillus* sporulation, quorum sensing both with homoserine lactone (HML) and peptide autoinducers, antisense RNA's and the control of pathogenicity genes. The contributions tend to focus on details of specific systems, but usually with a preamble, provided with useful references, that sketches the general picture – one suspects this to have been a helpful policy of the Editors.

Gaps? (reviewers, tiresomely, always have to finger a few). Phages only figure in transcription termination and there is little mention of the implications of microarray technology. More important omissions, not just from this volume but perhaps in people's thinking include the possible need for, and problems in attempting, large-scale modelling (alluded to in Neidhardt's introduction) and the adaptive biological roles (or maybe lack thereof – accident/drift?) of the intricate mechanisms so lovingly described here.

Still, a really useful book for everyone.

■ Simon Baumberg, University of Leeds

An order form for Symposium Vol. 61 (and earlier volumes in the series) appears on p. 113.



Bacteria, their precious metal armour, and a new weapon against waste

Victoria S. Baxter-Plant, Amanda N. Mabbett & Lynne E. Macaskie

Sulfate-reducing bacteria have exciting applications in the biorecovery of precious metals and in the bioremediation of toxic wastes.

The words 'bacteria' and 'palladium' rarely spring to mind together, but in fact they combine to produce a powerful way of dealing with toxic waste chemicals. Many types of wastes can be treated using sulfate-reducing bacteria (SRB) that as part of their normal cellular respiration process reduce sulfate to hydrogen sulfide, analogous to the way that mitochondria reduce oxygen to water. However, the SRBs are versatile bacteria, and some can use metallic ions or even chlorinated aromatic compounds in place of sulfate.

● Palladium

The price of palladium remains high, with the current annual demand exceeding production. The major palladium sources are Russia and South Africa, accounting for 90 % of the world's platinum group metal (PGM) production. The largest current consumer of palladium worldwide is the automotive industry, where it is used with other PGMs in catalytic converters to control vehicle emission pollution. Palladium is also used in the electronic, chemical and dental industries. Due to the high demand for palladium and the increasing price, its recovery from scrap is becoming increasingly important. Techniques for recovery include pyrometallurgy, chemical treatment, electrochemical recovery and solvent extraction, but these are costly, time-consuming and not environmentally friendly. This means that a 'clean', effective, economical and simple method is needed.

Biorecovery of palladium from waste. Work at Birmingham University has shown that resting cells (growth-decoupled cells) of the SRB *Desulfovibrio desulfuricans* ATCC 29577 can recover palladium from solution, industrial waste and automotive catalyst waste leachates. The technique first uses biosorption of Pd(II) ions onto the biomass, followed by its reduction to minute crystals of metallic palladium [Pd(0)] using an appropriate electron donor. Thus, palladium can be recovered as a base metal 'overcoat' surrounding the biomass ['Bio-Pd(0)'] (see Fig. 1).

'Bio-Pd(0)'. Palladium metal has many uses as an industrial catalyst. 'Bio-Pd(0)', similarly, has catalytic properties which are thought to be dependent upon the distribution and size of the nanocrystalline palladium metal deposits on the biomass surface. The cells can be loaded with palladium in different ways, varying from heavily loaded to almost bare (Fig. 2). The preparation of 'Bio-Pd(0)' using hydrogen as the electron donor can be seen in Fig. 3. The cells loaded with palladium form a black powder which is ground prior to its use as a catalyst.

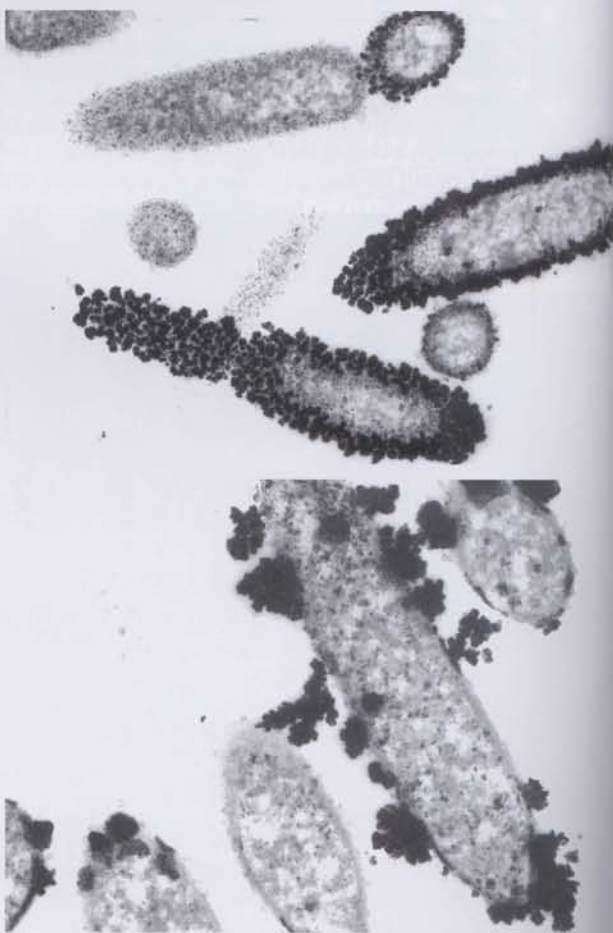
Remediation of toxic wastes. One possible use of the 'Bio-Pd(0)' catalyst is in the remediation of toxic waste.

Two examples have been highlighted below: chromium and polychlorinated biphenyls (PCBs).

● Chromium

Chromium is one of the most widely used metals in industry. In the form of Cr(VI) it is a known mutagen and carcinogen. Cr(VI) exists in solution as CrO_4^{2-} and, due to its structural similarity to SO_4^{2-} , it can overcome the cellular permeability barrier, entering via the transport pathway(s) for SO_4^{2-} . Once inside the cell it can oxidatively damage DNA via the production of the more oxidizing and reactive transient Cr(V) and Cr(IV) species that produce RS^\cdot and OH^\cdot simultaneously. The more inert Cr(III) cannot readily enter the cell and this reduced form, applied exocellularly, is not known to be carcinogenic and can precipitate as $\text{Cr}(\text{OH})_3$. Hence, the reduction of Cr(VI) to Cr(III) is an important step in the removal of Cr(VI) from solution.

Reduction of Cr(VI) using resting cells alone can be fairly slow. Furthermore, the cells have a low tolerance to Cr(VI), limiting the application to the 'polishing' of Cr(VI) wastes. Finely ground palladium metal on its own ['Chemical-Pd(0)'] cannot reduce Cr(VI). However 'Bio-



TOP RIGHT:
Fig. 1. Palladium-coated biomass 'Bio-Pd(0)'
COURTESY V.S. BAXTER-PLANT

BOTTOM RIGHT:
Fig. 2. Cells loaded with varying amounts of palladium.
COURTESY V.S. BAXTER-PLANT

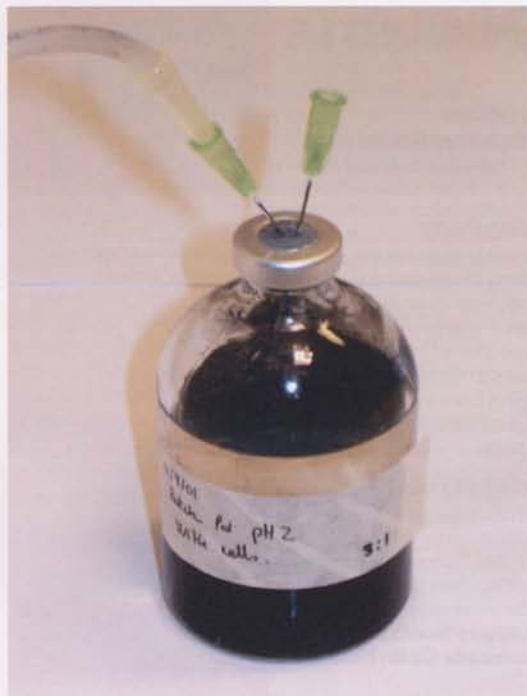
Pd(0)' can rapidly reduce high concentrations of Cr(VI). The solution changes from its characteristic yellow colour to colourless at neutral pH as Cr(VI) is removed, but without producing a precipitate. No residual chromium is left in solution either, and this indicates that the surface of the 'Bio-Pd(0)' is the 'resting place' for the Cr(III). Many industrial wastes are acidic and 'Bio-Pd(0)', held within a flow-through column, completely reduces Cr(VI) to Cr(III) at pH 3 over several weeks. The acid-soluble Cr(III) can easily be precipitated as Cr(OH)₃ downstream by adding a strong alkali like NaOH.

● PCBs

Chlorinated aromatic compounds are another toxic waste and environmental pollutant that are difficult to treat. The polychlorinated biphenyls (PCBs) are composed of two linked benzene rings that can have multiple substitutions by chlorine (or other halogen groups) in a great variety of combinations. PCBs have been used extensively in industry due to their excellent physical and chemical properties, including low water solubility, relative inertness, flame resistance and superb dielectric properties. Approximately one-third of the total USA production of PCBs has been released into the environment via deliberate or accidental discharge. The production and release of PCBs in the USA has been banned since 1978, although contamination still occurs and the accumulation in the environment and potential toxicity to humans and wildlife is of great current concern. PCBs accumulate mainly in fish, meat and dairy produce, affecting the health of the individuals who consume these contaminated products. Skin irritations, respiratory tract symptoms, gastrointestinal effects and even possible liver cancer can result.

'Bio-Pd(0)' has been tested as a bioinorganic reductant for these wastes because of the ability of an iron surface coated in palladium to act as a chemical reductant for PCBs. The reductive dehalogenation of PCBs has proved to be possible using 'Bio-Pd(0)', as measured by the release of chloride ions. Significantly lower rates of reductive dehalogenation were obtained with the 'Chemical-Pd(0)' alone, and in the case of 2,2',4,4',6,6'-hexachlorobiphenyl, a compound which is not water-soluble, this was only attacked (from a hexane in water suspension) by the biologically derived material. The mechanism is thought to involve the Pd(0) loaded on the bacteria, which effects the homolytic fission of H₂ within the crystal matrix for delivery of H[•] to the target PCB.

Industrial Pd-based catalysts are usually supported on, for example, a carbon matrix and it is thought that the biomass acts as a template and support for the 'Bio-Pd(0)', enhancing the catalytic activity. Finally,



LEFT:
Fig. 3. The preparation of 'Bio-Pd(0)' using hydrogen as the electron donor.
COURTESY V.S. BAXTER-PLANT

evaluation of the biomaterial against a commercial supported Pd-catalyst using a test reaction involving hydrogen addition across a C=C double bond showed that it performed comparably.

Thus, in addition to their potential as biorecovery agents for precious metals, SRBs can effect a one-pot conversion of waste to a valuable product, which cannot be achieved by the chemical industry alone, providing a new weapon in the armoury against waste.

● Dr V.S. Baxter-Plant and Dr A.N. Mabbett are Research Fellows and Dr L.E. Macaskie is a Reader in Biotechnology in the School of Biosciences, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK. Tel. 0121 414 5434; Fax 0121 414 5925 email v.s.baxterplant@bham.ac.uk a.n.mabbett@bham.ac.uk l.e.macaskie@bham.ac.uk

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February Council Meeting

New Professional Affairs Officer

● The President welcomed **Dr Geoffrey Schild** to his first Council meeting as the new Professional Affairs Officer.

The 'Broad Church' Working Party

● The Working Party, whose remit is to examine the effectiveness of SGM in addressing the needs of all microbiologists within the UK, met recently under the chairmanship of **Dr Keith Jones** and presented its first report to Council. One recommendation of the group was to offer sponsorship for technicians to attend an SGM meeting, with a view to encouraging them to join the Society. This was approved by Council and details of the new scheme appear on this page.

Council Members and Areas of Focus

● Council approved a proposal that certain areas of interest might be recognized as the responsibility of specific elected members, who might then act to promote and act as communicators for Society members' views on Council. The first two areas so identified were postgraduate matters (**Professors Hilary Lappin-Scott** and **Dave Kelly**) and industrial liaison (**Professor Colin Howard** and **Dr Pauline Handley**).

Schools Membership

● Council was delighted to hear that its new membership category for Schools had encouraged a great deal of interest with some 244 schools, including several from overseas, becoming members to date. They also welcomed news of the launch of the SGM's dedicated website for teachers and pupils: www.microbiologyonline.org.uk

FIS Management Ltd

Council has approved the purchase of a shareholding in FIS (Management) Ltd and the provision of a £5,000 loan to it to support the continuation of the annual meeting organized by the Federation of Infection Societies in the field of clinical microbiology. This forms part of the Society's commitment to welcoming microbiologist members of the Pathological Society into SGM membership.

Kathleen Barton-Wright Memorial Lecture

The bequest which funded this prize lecture has now been exhausted and Council decided that in view of this situation, the lecture should be discontinued. Discussions are underway to see if it might be replaced by another prize and members with any good suggestions are invited to contact the General Secretary.

'Getting Ahead of the Curve'

Council welcomed this very timely report from the Government's Chief Medical Officer, which recognizes the enormous impact of existing and newly emerging diseases, the constant threat and the robust approaches to control and prevention required. Council feels that this is an area where the Society and its members have much to offer and **Dr Geoffrey Schild** will be leading our response in this area.

● Alan Vivian, General Secretary

Annual General Meeting 2002

The Annual General Meeting of the Society will be held on **Tuesday, 17 September 2002** at the Society Meeting at the University of Loughborough. Agenda papers, including reports from Officers and Group Conveners, and the Accounts of the Society for 2001 will be circulated with the August issue of *Microbiology Today*.

Address Book 2002

A new edition of the Society's *Address Book* for members will be produced this year. Any member whose current address (as it appears on his/her mailing label) needs amendment or whose telephone, fax or email details have changed since the last edition should inform the Membership Office at Marlborough House (email members@sgm.ac.uk) by **2 August**.

News of Members

The Society notes with regret the death of **Dr W.H. (Harry) Holms** (member since 1954) and **Dr David D. Wynn-Williams** (member since 1988).

New Grant Scheme Technician Meetings Taster Grants

- Are you a microbiology technician or an NHS MLSO?
- Would you like to attend an SGM scientific conference?
- Is lack of funding stopping you attending?

If so, this SGM Meeting Taster scheme could be of interest.

The Society wishes to offer support to technical staff working in microbiology laboratories in universities, colleges, hospitals/PHLS, research institutes, etc., who are interested in joining the SGM and attending its meetings, but consider the costs to be prohibitive. For a short period we are offering an opportunity for eligible technicians to sample an SGM meeting with expenses of up to £200 being met by the Society. The grant will cover travel, bed and breakfast for an agreed number of nights in university accommodation and a daily subsistence allowance. Non-member registration fees will be waived. Priority will be given to those who have not attended a scientific meeting in the last 5 years.

In return, funded delegates will give their opinion of the meeting and make suggestions for benefits and membership services that SGM might offer to technical staff through a brief meeting with the SGM Education Officer at the event and completion of a detailed questionnaire.

Rules

1. The scheme is open to technical staff working in microbiology laboratories whose salaries are supported by central university funds or by the NHS, or where alternative sources of conference funding are not available, but excluding commercial bodies. Applications are invited from those on a salary no higher than £20,000 per annum (gross), on scales up to and including Medical School Technicians MST2/Grade 2, University Technicians UTSS Grade E and MLSO 1s. Evidence of salary at date of application must be supplied, e.g. copy of monthly pay slip.
2. Applications from technicians who work part-time or with other circumstances that affect the ability to afford meeting attendance will also be considered. *Please give details of such circumstances on the back of the application form.*
3. Applicants may claim for:
 - Second class return rail fare from their laboratory to the meeting venue or car mileage at 25p per mile.
 - Total cost of standard bed and breakfast accommodation for the number of nights necessary for attendance at the sessions specified. This must be booked in university accommodation through the SGM meetings office.
 - Subsistence allowance of £10 per day at the meeting.
4. The maximum grant is £200.
5. Grants are limited to attendance at ONE only of the meetings listed on the application form.
6. Applicants must register separately for the meeting through the SGM meetings office by completing the standard booking form (available on the SGM website: www.sgm.ac.uk/meetings). Payment must accompany registration and so it is advisable to submit the grant application well in advance of the booking being made.
7. Applications received after the meeting cannot be considered.
8. Applicants must comply with the feedback requirements of the grant and return a completed questionnaire within 4 weeks of the meeting start date.

Completed forms should be sent to the Grants Office at SGM HQ.

SGM Prize Lectures and Awards 2002

Fleming Award

The Fleming Lecture is awarded annually for outstanding research in any branch of microbiology by a young microbiologist in the early stages of his/her career. The award is £1,000.

1. Nominees should normally have been engaged in research for not more than 10 years after doctoral qualification or equivalent. Years may be added to this total in respect of career breaks, for parenthood or other substantive reasons.
2. There should normally have been a connection with the scientific activity of the Society, either by means of past and continuing membership of the Society (a minimum of 3 years' membership of the Society would normally be expected), or past presentation(s) at a Society meeting or publication(s) in a Society journal, or an organizational or administrative contribution to the scientific work of the Society.
3. Candidates, who need not be members of the Society, should submit an outline CV including details of qualifications, scholarships, research grants obtained, etc., a list of publications, an outline of their career progression (posts held in postdoctoral research) and the names of two members who are familiar with their work, who will be asked to provide a statement detailing the candidate's contribution to microbiology and merit for the award. Alternatively members who wish to make a nomination should provide such a statement and should arrange for a second member willing to support the nomination to provide a statement, and should ask the candidate to provide the CV and publications list.
4. The recipient will be expected to give a lecture based on his/her work to a meeting of the Society, which will usually not be that which takes place in the Spring. He or she may be asked by the Council of the Society to repeat the lecture at another centre in this country or in Europe. Expenses of the lecturer will be paid by the Society. Requests for such a second lecture should be made to the General Secretary and will be considered by Council. The text of the lecture will be published in either *Microbiology* or in the *Journal of General Virology*, whichever is the more suitable. The choice will be at the discretion of the Editors of the two journals.
5. In the event of there being no successful nominee in any particular year, the Award money will be returned to the funds of the Society. Any given nominee may be chosen once only.

Colworth Prize Lecture

Awarded biennially for an outstanding contribution in an area of applied microbiology. It is sponsored by the Colworth Laboratory of Unilever Research. The prize is £1,000 and the winner gives a lecture on his/her work. The lecture is usually published in a Society journal.

1. Nominations shall be made by any two members of the Society: the nominee need not be a member of the Society. Nominations should be accompanied by a

statement of the contribution to applied microbiology made by the nominee, supported by reprints or other appropriate documentation. A brief CV of the nominee and a full bibliography of his/her work should also be included. Alternatively, candidates may submit all of the information listed above, together with the names of two members who are familiar with their work, who will be asked to supply the appropriate statement with regard to candidate's contribution to applied microbiology.

2. There will be no restriction by reason of age or nationality of those eligible for nomination for the Colworth Prize Lecture. Recipients of the Lectureship may not be nominated on a subsequent occasion.
3. The recipient of the Colworth Prize Lectureship will be expected to give a lecture based on the work for which the Prize Lectureship has been awarded to a meeting of the Society, normally the Spring meeting following the announcement of the award, and to repeat the lecture at the Colworth Laboratory. The recipient will be strongly encouraged to publish the lecture in either *Microbiology* or *Journal of General Virology*, whichever is the more suitable. The choice will be at the discretion of the Editors of the two journals.

Peter Wildy Prize for Microbiology Education

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

1. The Peter Wildy Prize of £500 shall be awarded annually for an outstanding contribution to microbiology education, without restriction on the area of microbiology in which the award is made. Microbiology education for the purpose of the award need not be confined to university teaching. It may also include education of the general public, school pupils or professional groups.
2. Nominations for the Peter Wildy Prize shall be made by any two members of the Society; the nominee need not be a member of the Society. Alternatively, candidates may submit all of the information listed above, together with the names of two members who are familiar with their work, who will be asked to supply the appropriate statement with regard to candidate's contribution to applied microbiology.

Nominations should be accompanied by a statement of the contribution to microbiology education made by the nominee, supported by appropriate documentation if available. A brief CV of the nominee should also be included.

3. There shall be no restriction by means of age or nationality of those eligible for the Prize. Recipients of the Prize may not be nominated on a subsequent occasion.
4. The recipient of the Prize will be expected to give a presentation based on an aspect of educational work for which the Prize has been awarded to a meeting of the Society, normally within a year of the announcement of the award. The presentation may take the form of a lecture, workshop, audio/visual display or any other appropriate activity. The recipient will be strongly encouraged to publish an article based on the presentation in *Microbiology Today*.

Fred Griffith Review Lecture

Held biennially and commemorates the pioneering contributions of Fred Griffith to bacterial genetics. It is awarded in recognition of long and distinguished service to microbiology. The winner receives £500 and gives a personal overview of an area of microbiology. The lecture is usually published in a Society journal.

Procedure for nominations

A range of prestigious awards is made by the Society in recognition of distinguished contributions to microbiology. To facilitate nominations, the rules for each prize lecture due to be awarded in 2003 are provided on this page and a form is available overleaf. It is now also possible for self-nominations to be made for all awards. The award panel will consider the submissions in the autumn and their recommendations will be taken to November Council for approval. The outcome will be announced in the February 2003 issue of *Microbiology Today*.

Nominations are now sought for the 2003 prize lectures. Please complete the form overleaf and send it to Professor Alan Vivian, Centre for Research in Plant Science, Faculty of Applied Sciences, University of the West of England, Coldharbour Lane, Bristol BS16 1QY. Professor Vivian will be pleased to discuss the criteria for nominations, should any queries arise.

The closing date for all nominations is **30 September 2002**.

Grants

International Research Fellowships

This scheme has been established to allow scientists to travel to or from the UK and Republic of Ireland to carry out a defined piece of research in any field of microbiology. Applicants must be of postdoctoral level or above. The visits may be of up to 3 months duration. The awards cover the costs of return travel, a subsistence allowance and a contribution towards the costs of consumables in the host laboratory. There are three rounds of applications during each calendar year. Completion of the appropriate form is necessary. The closing dates for 2002 are **30 March**, **30 July** and **30 November**.

Education Development Fund 2002

Members are invited to apply for small grants to fund either (a) initiatives to promote the public understanding of microbiology or (b) 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. There are different application forms for the PUS awards and the teaching aids. There is no closing date for applications; these will be considered on a first come, first served basis during the calendar year 2002.

International Development Fund

Council aims to assist microbiologists in developing countries in the Far East, Africa, South and Central America, the Indian sub-continent and Eastern and Central Europe through the International Development Fund. Awards are made by competition to SGM members and support may be available for the following.

- Running short lecture courses and laboratory training in subjects designed to meet the needs of countries where microbiology is inadequately developed. Host laboratories are usually expected to provide some evidence of local support for the courses. Grants may cover travel and accommodation and allow the purchase of basic equipment essential for the needs of such training courses.
- Provision of Society journals, symposia and special publications to established libraries for a limited period of time at reduced or zero cost, where these are not readily available.
- Assistance of national microbiological facilities, e.g. culture collections (which underpin microbiology), where these run into temporary difficulties.
- Any other small project to assist in technology transfer from Western Europe to the areas mentioned above for which other sources of funding do not exist.

Applications to the Fund are now invited. Four copies, including full supporting documents, should be sent to the Grants Office at SGM HQ.

The closing date for applications is **25 October 2002**.

The full rules of all Society grant schemes are available on the SGM website at www.sgm.ac.uk. Please consult these before applying for an award. You can download the application forms for schemes where these are required. Click on the 'Grants & Funding' button for details.

Any enquiries should be made to the Grants Office, SGM, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (Tel: +44 (0)118 988 1821; Fax: +44 (0)118 988 5656; email: grants@sgm.ac.uk).

Retired Member Conference Grants

The scheme enables retired members to attend one SGM meeting per year. The grant covers en-suite accommodation and the Society Dinner. The maximum award is £250. It is hoped that the scheme will enable retired microbiologists both to keep up with their science and to share their knowledge with other members. Completed application forms must be submitted to the Grants Office before the meeting. Applications are now invited for grants to attend the Society's meeting at the University of Loughborough, 16–20 September 2002.

Seminar Speakers Fund 2002

The Fund aims to promote talks on microbiological topics in departmental seminar programmes. Applications are invited from higher education institutions where microbiology is taught for total grants of up to £200 towards the travel, and if necessary, accommodation, expenses of up to two invited speakers. Applications will be dealt with on a first come, first served basis during the academic year. Written submissions should be sent to the Grants Office at SGM Headquarters for consideration.

Watanabe Book Fund

Members who are permanently resident in a developing country are reminded that they may apply for funding to acquire for their libraries books, or possibly journals, relating to microbiology. These annual awards are available as a result of a generous donation from Professor T. Watanabe of Japan. The closing date for the receipt of applications, which should be made to the Grants Office at SGM HQ, is **4 October 2002**.

PUS Awards

The following PUS grants have been made recently:

Chris Grainger & Lucy Breakwell, University of Nottingham, have been awarded up to £1,000 towards their participation in a project aimed at understanding how microbial infection spreads in spacecraft (see report in *Microbiology Today* 29, pp. 42–43).

Dr Helen B. Smalley, Liverpool John Moores University, has been awarded up to £673 towards the expenses of running a practical microbiology course for A-level students on Merseyside (see report on pp. 91).

Dr Joy Perkins, University of Huddersfield, has been awarded up to £876 towards the expenses of running a microbiology taster day for Year 11 students in National Science Week 2002: 'Bugs: Bad, Ugly and Good'.

Undergraduate Microbiology Prizes

The prizes are intended to encourage excellence in the study of microbiology by undergraduate students and to promote scholarship in, and awareness of, microbiology in universities. The prizes are awarded annually to the undergraduate student in each qualifying institution who performs best in microbiology in their penultimate year of study for a Bachelor's degree. Each winning student will be awarded £50, a certificate and a free year's undergraduate membership of the SGM.

One prize is available to each university in the UK and Republic of Ireland offering an appropriate microbiology course. The university chooses the assessed microbiological work for which the prize is awarded. The submission should be supported by formal marks, not an informal assessment. Winning students should have attained at least 2(1) overall in their degree examinations at the stage at which the award is made.

Eligible students may be registered for any degree with a significant microbiology content (e.g. Biotechnology, Applied Biology, etc.) not just a BSc Microbiology. Universities are now invited to nominate a student for a 2002 SGM Undergraduate Microbiology Prize. Submissions can only be accepted on the form which has been sent to all institutions. The full rules and further copies of the form may be downloaded from the SGM website or obtained from the Grants Office at Marlborough House. The closing date for nominations is **31 August 2002**.

Meetings

Meetings on the web

Up-to-date information on future Society meetings is available on the website: www.sgm.ac.uk

On-line booking

On-line booking forms are now available on the SGM website.

Meetings organization

The SGM meetings programmes are organized by the committees of the special interest groups, co-ordinated by the Scientific Meetings Officer, Professor Howard Jenkinson. Suggestions for topics for future symposia are always welcome. See p. 108 for contact details of Group Conveners.

Administration of meetings is carried out by Mrs Josiane Dunn at SGM, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (Tel. 0118 988 1805; Fax 0118 988 5656; email meetings@sgm.ac.uk).

Warwick meeting

April 2002

Signals, Switches, Regulons & Cascades: Control of Bacterial Gene Expression

Symposium volume

This is now available from CUP at a special discount price for members. A review of the book appears on p. 78 and an order form is included in this issue.

Abstracts book

The full text of the abstracts book is now available as a PDF file on the SGM website.

Offered Posters

Offered posters are welcome but each one should be associated with a Group. General Offered Posters will no longer be accepted. Titles and abstracts should be emailed to the Events Administrator, Mrs Josiane Dunn, at SGM HQ. The subject content should be relevant to the remit of the Group (see website for details); it does not have to relate to the topic of the Group Symposium taking place at the particular meeting. Abstracts are required in a standard format – see website for details or contact the Events Administrator.

Regional Meetings

Proposals are welcome for one-day regional meetings. These will usually be for postgraduates and first postdocs, with a keynote speaker and offered papers or workshop sessions. The objective is to provide a useful forum, particularly for younger microbiologists, outside SGM Ordinary Meetings. Funding is available to hold up to two of these regional meetings each year. Please submit proposals to the Scientific Meetings Officer, Howard Jenkinson.

Promega Prize

- Are you
- a member of the SGM?
- a postgraduate or first postdoc in your first two years?
- thinking of presenting an offered paper or poster at an SGM meeting?

Why not enter for the Promega Prize Competition? You could win £200 in the SGM section of the competition and go on to compete for a further £2,000 in the *Young Life Scientist of the Year* event. Contact the Meetings Office or see website for details.

Future Meetings

AUTUMN 2002 – 151st Ordinary Meeting

University of Loughborough
16–20 September 2002

● Main Symposium *Staphylococcus*

16–17 September
Organizers: S. Foster, C. Gemmell, D. Hodgson, H. Jenkinson & S. Patrick

● Speakers

- S. ARVIDSON (Stockholm)
Regulation of toxin production
- N. NORVICK (New York)
Quorum sensing and interference
- M. HOOK (Houston)
Surface proteins
- A. COCKAYNE (Nottingham)
Iron acquisition
- S. FOSTER (Sheffield)
Stress resistance
- B. BERGER-BACHI (Zurich)
Components involved in high-level methicillin resistance
- K. HIRAMATSU (Tokyo)
Vancomycin resistance
- Y. JI (Pennsylvania)
Identification of new drug targets
- M. HERMANN (Hamburg)
Staphylococcal biofilms
- F. GOTZ (Tübingen)
Staphylococcus epidermidis virulence and pathogenesis
- J. VAN STRIJP (Utrecht)
Proinflammatory molecules
- K. BAYLES (Idaho)
Interaction with host cells
- C. GEMMELL (Glasgow)
Lessons to be learned from models of staphylococcal infection
- N. DAY (Oxford)
Epidemiology
- J. PATTI (Georgia)
MSCRAMM protein-based therapeutics for staphylococci
- J. IANDOLO (Oklahoma)
Staphylococcal genomics

● Other symposia workshops & events

● Bacterial interactions with extracellular matrix components

Cells & Cell Surfaces Group

19 September
Organizers: Rod McNab (rmcnab@eastman.ucl.ac.uk) & Anthony Smith (prsaws@bath.ac.uk)

● Controversies in antibiotic susceptibility testing, phenotypic and molecular

Clinical Microbiology Group/
British Society for Antimicrobial Chemotherapy

18 September
Organizers: Peter Hawkey (p.m.hawkey@bham.ac.uk) & P. McCoy (pjmccoy@bsac.org.uk)

● From laboratory notebook to patent to exploitation

Education Group

18 September
Organizer: Ian Davidson (ian.davidson@unilever.com)

● Extremophiles and astrobiology – at the limits of life

Environmental Microbiology Group

18–19 September
Organizers: the late David Wynn-Williams & Andrew Ball (andrew@essex.ac.uk)

● The cytoskeleton as an integrator of cell function

Eukaryotic Microbiology Group

19–20 September
Organizer: Clive Price (c.price1@lancaster.ac.uk)

● Integrated process development: the commercial challenge

Fermentation & Bioprocessing Group/
Biochemical Engineering Subject Group

17 September
Organizers: C. Hewitt (c.j.hewitt@bham.ac.uk) & C. Davis (chris.davis@bplpharma.com)

● *E. coli* throughout the food chain

Food & Beverages Group

17 September
Organizers: Mike Peck (mike.peck@bbsrc.ac.uk) & Glenn Gibson (g.r.gibson@reading.ac.uk)

● Genetic susceptibility to infection

Microbial Infection and Clinical Microbiology Groups

18–19 September
Organizers: Paul Langford (p.langford@ic.ac.uk), Peter Andrew (sam20@le.ac.uk) & Tyrone Pitt (tpitt@phls.nhs.uk)

● Protein traffic and secretion in fungi (Symposium 1)

Physiology, Biochemistry & Molecular Genetics Group

18 September
Organizer: David Archer (david.archer@nottingham.ac.uk)

● Low temperature adaptation in bacteria and fungi (Symposium 2)

Physiology, Biochemistry & Molecular Genetics Group

19 September
Organizer: Catherine Rees (cath.rees@nottingham.ac.uk)

● Oral bacteria: diversity and ecology
Systematics & Evolution Group jointly with the British Society for Dental Research, Oral Microbiology Group and Immunology Group

Organizers: M. Curtis (m.a.curtis@mds.qmw.ac.uk), R.A. Whitley (r.a.whitley@mds.qmw.ac.uk) & W. Wade (william.wade@kcl.ac.uk)

● Launch of new Eukaryotic Microbiology Group
19–20 September 2002

Top international speakers will participate in the first symposium of the new Group which will focus on the Cytoskeleton. See website for details of the programme.

● Promega Prize Final 17 September

Promega sponsors this competition to encourage excellence in scientific communication by young scientists. Group Committees have now judged recent oral or poster presentations by members who are postgrads or first postdocs. The finalists from each Group or Branch go forward to compete for Promega Prizes at a special session of short oral presentations on their research. There are two prizes of £200 to be won and in 2003 the winners will go on to compete for the title of *Young Life Scientist of the Year* against finalists from other learned societies.

● Social Events

Monday 16 September
Welcome Reception

Tuesday 17 September
Society Dinner

Wednesday 18 September
Pub Quiz – entrance fee for charity – prizes for the winning team!!

● Offered posters

The deadline for the receipt of titles/abstracts was **17 May 2002**. Contact the Events Administrator if you still wish to submit a paper or poster.

● Meeting flyer – please display

A small poster to advertise the Loughborough meeting is enclosed with this issue of *Microbiology Today*. Please display it on your departmental noticeboard or pass it on to colleagues. If you would like further copies to distribute, these are available from the Meetings Office.

SPRING 2003 – 152nd Ordinary Meeting

University of
Edinburgh
7–11 April 2003

● Main Symposium Microbial subversion of host cells

7–8 April

● Other symposia and workshops

● Type IV secretion systems

Cells & Cell Surfaces Group
Organizer: I. Henderson

● Septicaemia

Clinical Microbiology Group
Organizer: C. Gemmell

● The management of outbreaks

Clinical Virology Group
Organizer: S. Cameron

● Biological control agents

Environmental Microbiology
Group

Organizer: F. de Leij

● Cell culture

Fermentation & Bioprocessing
Group

Organizer: R. Swift

● Endothelial cell–pathogen interactions

Microbial Infection Group

Organizers: P. Langford & P. Dyston

● Molecular aspects of anaerobes

Physiology, Biochemistry &
Molecular Genetics Group

Organizer: N. Minton

● Aeromonads & Vibrios

Systematics & Evolution Group
Organizer: B. Austin

- Vaccines
(Symposium 1)
- Viruses and cancer
(Symposium 2)
- Workshops:

Oncogenic viruses
Virus vectors
Pathogenesis
Virus entry, morphogenesis
and exit
Gene expression
Nucleic acid replication

Virus Group

Contact the Convener

● Offered papers and posters

These are welcome for all Group sessions. Please submit titles and abstracts to the SGM Events Administrator by the deadline of **6 December 2002**.

See notice on p. 86 for general conditions for submitting posters.

Irish Branch

Sensing and signalling in microbial populations

Dublin City University
5–6 September 2002

Organizer: Michael O'Connell
(michael.oconnell@dcu.ie)

Microbial diseases and the immuno- compromised patient

Maynooth
Spring 2003

For details of Irish
Branch activities
contact the Convener,
Catherine O'Reilly
(coreilly@wit.ie)

Other events

● IUMS Congresses

27 July–1 August 2002, Paris, France

The World of Microbes

See www.iums-paris-2002.com for further details.

● SGM IUMS Travel Grants – Second Round of Applications

Applications are now being accepted from SGM members for grants to attend the congresses. The awards provide a contribution towards registration, travel, and accommodation for up to 5 nights. Full details of the rules and an application form are available on the SGM website at www.sgm.ac.uk/PA/gran_fun/g_f.htm#iums

Applications will be processed on a first come, first served basis. The final closing date is **30 June 2002**

● Clinical Microbiology Group

Offered Paper/Poster Competition

Sponsored by
AstraZeneca Academy



The competition aims to encourage clinical scientists and specialist registrars in medical microbiology to communicate their work to a wider audience. The winners of the first round of the competition, held at the Society meeting at Warwick, were as follows.

Oral Presentation Prize (£500) divided equally between:

- K. Reddin (CAMR, Salisbury) – *Neisseria lactamica*: a new approach to vaccines against meningococcal disease
- S.C. Rowe (DSTL, Porton Down) – Evaluation of a cell-free protein production system for the production of *Francisella tularensis* vaccine candidates

Poster Presentation Prize (3 years membership of SGM)

- D. Turner (University Hospital, Nottingham) – AspA. A novel conserved immunogenic and surface-exposed meningococcal autotransporter protein

The next round of the competition will take place at the SGM meeting at Loughborough (18–19 September 2002; topic – *Genetic susceptibility to infection*). Once again there will be a £500 prize for the best offered paper in the Group session and free membership of SGM for the best poster presentation from a junior doctor. The presentations may be on any aspect of clinical microbiology. They will be judged by a panel from the Clinical Microbiology Group and a representative from AstraZeneca.

Abstracts for consideration should be emailed to Professor Stephen Gillespie, the Group Convener (stepheng@rfc.ucl.ac.uk), and copied to meetings@sgm.ac.uk

● One-day symposium to mark the retirement of Dr Ulrich Desselberger

8 July 2002, Homerton College, Cambridge

Topics include rotaviruses, bunyaviruses, viroids, HIV, influenzaviruses. To be followed by reception and gala dinner. Details from Dr Tim Wreghitt, Box 236, Addenbrooke's Hospital, Cambridge CB2 2QW (tim.wreghitt@addenbrookes.nhs.uk).

Projecting microbiology to primary schools

■ Emma Sheppard

When Emma Sheppard's final year undergraduate project involved teaching microbiology to 10-year-olds she didn't know what to expect. Here is her account of what happened when schoolchildren found out that not all micro-organisms are 'gross'...

BELOW:
A poster designed to educate 10-year-olds in some of the roles that good and bad bugs play in our daily lives.
COURTESY EMMA SHEPPARD

What do 10-year-olds know about bacteria, fungi and viruses? I thought their response might be limited to the odd adjective, like 'gross' or 'yucky' and facts, like 'germs make you feel sick'. However, I was surprised to discover that some could draw me pictures of how a virus injects DNA into a cell while others understood vaccination. Who would have thought it?

My project title was *Introducing Microbiology to Schools* and I was to prepare a lesson, school book, poster and teacher's guide to teach this small section of the National Curriculum to Year 6 pupils. Viruses aren't covered in the National Curriculum so I decided to include them as honorary micro-organisms so that the children wouldn't miss out.

To prepare for this daunting task I decided to go into schools and find out what pupils already knew about the subject. The amount different classes had been taught varied from absolutely nothing to full practicals and theory lessons on the subject. One class had undertaken projects on their own, researching prominent microbiologists.

At the first school I sat in on a microbiology lesson and watched how the teacher recapped on the previous lesson and then set tasks for children of all abilities. I wanted to observe how a class was taught so that I could use the techniques when it was my turn. Somehow I was roped into a practical session and got involved in a flour

ways in which microbes could be harmful, but few knew of their advantageous traits. We sat around in a circle and created colourful spider diagrams from everything they knew about microbes. I was very pleased to see that one boy wrote that injections were made from 'bits of the bug', and another knew that 'moulds make a medicine called penicillin'. I came away from my session feeling astounded by the children's awareness, but it was still clear to me that they had remembered more about the bad aspects of microbes than the good. They needed to learn about these to fulfil this part of the National Curriculum, so I decided to cover this in my lesson.

Eventually I had compiled enough information for my school book. My time with the children had made me realize that they were more advanced than I had thought and were able to grasp what I assumed were complicated concepts, like vaccines and antibiotics. I was very lucky that my friend, Bob Rawlinson, was able to create some cartoons to make the book more colourful. I asked him to draw a 'good' microbe character and a 'bad' microbe one, which were used in different sketches. I also decided to show children how microbes influence their daily lives by developing a poster called *Microbes and You*. This illustrated how microbes were with you right from when you ate bread for breakfast (made with the help of yeast) to how you avoided plaque by brushing harmful bacteria off your teeth at night.

It was then time for my lesson – the part I was most dreading! I constructed a PowerPoint presentation with colourful diagrams for a class who had not yet learnt anything about microbiology. The children were enthralled with the laptop and how the projector created an image on the white board, but managed to settle down for my talk. I made the lesson very interactive, starting off with questions to see if the class knew that microbes could be beneficial as well as harmful. I then focused on the use of microbes in food. To make the next 15 minutes more interesting I took in blue cheese, bread, Quorn™, beer and mushrooms to demonstrate how microbes feature in our food and most of the children were very surprised! When I asked if there were any questions, several hands shot up. Most asked very intelligent questions, showing that they had grasped the concept that microbes were good as well as bad. Some children wanted to know more than the short lesson had covered, and asked about mould and decay – the 'gross' factor appealing once more! I left feeling as if I could have covered so much more, if only there had been time. Unfortunately, the National Curriculum only suggests a maximum of 8 hours on the subject, hardly doing justice to the exciting world of microbes.

I enjoyed my final year project so much; it gave me a chance to show the children how exciting micro-organisms can be. It is such a fun subject to bring to children of that age and their responses were amazing; they were genuinely enthralled with the topic and wanted to know more. For me it was an ideal project in science communication. Hopefully the children benefited from it as much as I did. Who knows, maybe I have inspired a new generation of microbiologists! I hope so.

● Emma Sheppard is a Medical Editor and freelance science writer.
email emma.sheppard@science-press.com



Practical microbiology course for post-16 students on Merseyside



Helen Smalley

In the spring of 2000, a high school in Warrington contacted the School of Biomolecular Sciences, Liverpool John Moores University (LJMU), with a plea for help with the microbiology component of A-level Biology. The school had insufficient resources for the suggested practical activities. As a result, we ran a 2-day course in our teaching labs for six pupils, covering much of the microbiology syllabus. A little market research identified a demand for this locally, and in January 2001 we offered a course to schools and FE colleges throughout Merseyside. The response was so great that we ran the course twice, for a total of 90 pupils from nine institutions. To cover costs, we charged pupils a £5 fee. Feedback indicated that the fee, together with travelling expenses, was off-putting for many of the students. This January we ran another course, with the backing of a PUS grant from the SGM, enabling us to waive the £5 fee.

This course was tailored to the AQA A-level Biology specification B, A2 Option Module 7 (Microbes and Disease). This module is studied in the second year of the A-level course and is not compulsory. It includes most of the microbiology content of the specifications. Pupils practised basic microbiological techniques, such as pouring agar plates, streak plating, spread plating, total and viable cell counting and antibiotic sensitivity testing, on their first visit. The uses of selective and indicator media were studied. The pupils made predictions about antibiotic sensitivities of a variety of bacteria and designed their own experiments to test these out. There were opportunities to investigate bacteria present in the environment and several pupils were surprised at what was lurking on their own skin! Pupils returned 2 days later to discover how good their aseptic technique had been and to investigate what had grown using staining techniques.

The course was attended by 92 pupils from 11 schools, accompanied by four teachers. One school sent two laboratory technicians along to see what was involved in practical microbiology, with a view to running its own microbiology classes in school next year for the

first time. Half of the pupils were at AS level and had not encountered microbiology before. One school sent AS students along because the school did not offer the Microbiology option at A2 and it was felt that the course would go some way to remedy this by offering an introduction to the topic. We taught groups of 10 or fewer pupils and kept pupils from individual schools together, so that those with no prior knowledge of microbiology could be introduced to it at a more basic level. Interestingly, several students comment-

ed that they would have liked more interaction between the schools – we will take this into account in any future events.

We ran the event in January. This was a compromise between the best time for us (i.e. during the break between Semesters 1 and 2 when our teaching labs are free) and the best time for schools. AS exams and some other A-level modular exams are held in January and we altered the start times of one session to accommodate this. The timing was unsuitable for some schools, but on the other hand, several schools were embarking on the Microbiology module after the Christmas break, so the timing was ideal for them.

Information about careers in microbiology was available as posters and leaflets during refreshment breaks and academic staff were on hand to answer any specific queries. Quick feedback about the course was gathered by asking pupils what the best and worst aspects of the course were. Generally, comments were very positive and included the opportunity to use equipment not available at school, to design their own experiments and to investigate their own microbial flora. One boy was disappointed that the organism he had isolated already had a name, so he could not call it after himself! Additionally, pupils were asked to fill out a detailed questionnaire giving their opinions, plus information about their proposed career destinations after A-levels. Participation in the questionnaire was voluntary, but encouraged by a prize draw! 98% of pupils said they had enjoyed the course and 74% stated that it had helped to develop an interest in microbiology. Suggestions for improvement included lengthening the course and inclusion of activities more relevant to everyday life.

At the end of the course, all students were given a pack of SGM posters, a certificate of attendance and an LJMU pen.

● Dr Helen B. Smalley, Senior Lecturer in Microbiology, School of Biomolecular Sciences, Liverpool John Moores University, Liverpool, UK. Tel. 0151 231 2098; email h.b.smalley@livjm.ac.uk

SGM Public Understanding of Science Grants of up to £1,000 are available to members wishing to promote microbiology. See www.sgm.ac.uk for details and an application form.

LEFT AND BELOW: A-level students learning about microbiology in practical sessions at LJMU.

PHOTOS CHRIS THEOBALD



SGM student scoops national prize

The finals of the *Promega Young Life Scientist of the Year 2002* took place at the spring meeting of the Genetics Society in York on 21 March. Tracey Duncombe chats to Rut Carballido-López about winning the prize.

The prestigious title of *Promega Young Life Scientist of the Year* and a cash prize of £2,000 were awarded recently to SGM student member Rut Carballido-López, a Spanish student working at Oxford University with Professor Jeff Errington. Rut gave a presentation entitled *Bacterial Cytoskeleton: Cell Shape Determination in Bacillus subtilis*.

Eleven regional finalists, chosen by five different societies, presented talks to a panel of 10 judges, which included microbiologists Professor Colin Harwood and Dr Jim Brannigan. Professor Harwood commented that 'the standard of all of the talks was outstanding but the judges were unanimous in choosing Rut as the *Promega Young Scientist of the Year*'. He added that 'Rut's work provides us with important insights into fundamental issues relating to cell wall architecture and synthesis that have remained a mystery for more than 30 years'.

and dots and it was only after trying many conditions for immunolocalization and analysing many images that we started to realize that the structures could be helical. Then, to try to clarify the 3-D form of these structures, I started focusing up and down the cell, taking optical slices and stacks of images through the z axis of the cell and deconvolving them until the helical structures were resolved. We have very powerful microscopy tools in the lab, and very good software packages for image acquisition and processing so, after many hours "playing" with them, I produced my movie', explained Rut.

The competition

The *Promega Young Life Scientist of the Year* competition has been running for the past 5 years in conjunction with the SGM, the Genetics Society, the Biochemical Society, the British Society for Immunology and the British Society for Histocompatibility and Immunogenetics. The finals of the 2002 round to select the SGM Promega Prizewinners will take place on 17 September at the Society meeting at Loughborough. Competing for the two prizes of £200 and places in the Young Life Scientist finals 2003 will be the following:

Stefanie Gehrig (Dept of Plant Sciences, University of Oxford) *Localization of the protein cluster producing an acetylated cellulose polymer in the plant-colonizing bacterium Pseudomonas fluorescens*

David Turner (Division of Microbiology and Infectious Diseases, University Hospital, Nottingham) *AspA, a novel, conserved, immunogenic and surface-exposed meningococcal autotransporter protein*

Michelle Barr (School of Animal and Microbial Sciences, University of Reading) *Environmentally induced genes of rhizobia*

Olivia Champion (Dept of Infectious & Tropical Diseases, London School of Hygiene & Tropical Medicine) *Construction of a gene-specific composite Campylobacter jejuni DNA microarray*

Douglas West (Centre for Veterinary Science, University of Cambridge) *Characterization of a DhasA allelic replacement mutant of Streptococcus equi subsp. equi*

Natalie Simpson (Dept of Biochemistry, University of Cambridge) *Regulation of carbapenem production in Erwinia spp.*

Andrew Macdonald (School of Biochemistry and Molecular Biology, University of Leeds) *Functional consequences of interactions between HCV NS5A protein and Src family kinases*

David Woodhall (Dept of Medicine, University of Cambridge) *The human cytomegalovirus 72 kDa major immediate early protein interacts physically and functionally with a constituent of ND10 bodies, hDaxx*

Louise Bailey (Dept of Zoology, University College Dublin) *Strain typing of Mycobacterium bovis*

Full details of how to enter the Promega Prize are available on the SGM website.

Practice makes perfect

Mention public speaking to some people and they might run a mile. Other people actually enjoy the experience. As Rut says, 'I haven't given many presentations in the past, but I'm OK when I do them and I actually have fun when I get up there. I do get quite stressed beforehand! It's probably a question of practice.

Up until now my main concern has been the language problem. My English is more or less fine to say what I want to say, but it's not the same being "really fluent" when you lack all those linking words that make the talk smooth. Also, you can't be that spontaneous or make a funny comment, and I am always worried about not understanding the questions that people ask. So I guess I'm not as comfortable as I could be.'

'Strangely though I was fine just before the final (whereas I was panicking before my SGM talk as I found out that I had less time than I had practised for). This time I practised more. My talk was similar, but not the same as the one I gave at the UEA meeting. I kept most of the figures and the 3-D rotational graphic, but I added another time-lapse movie and some new results from recent experiments', said Rut.

Making movies

'The structure of the protein I work on is difficult to represent as a flat image because it is helical, so I opted to make a 3-D reconstruction and a movie. I first made some *B. subtilis* mutants of this protein and the cell-shape phenotype was really interesting, so we thought that the subcellular localization of the protein could provide an insight into its function, which it did! I purified the protein, raised antibodies against it and localized it by immunofluorescence microscopy. But I obtained a very complex pattern of transverse bands



ABOVE: Rut (second from left) receiving her prize from Euan Forbes (second from right) of Promega. The trophy is a reproduction of a lab in blown glass complete with a couple of benches and fine detail such as tubes and flasks, etc.
PHOTO RUT CARBALLIDO-LÓPEZ

SchoolZone

Schools Membership costs only £10 a year. For this, a named teacher representative will receive *Microbiology Today* each quarter, advance notification and copies of new microbiology teaching resources, and discounted fees for attendance on SGM training courses and workshops. Application forms are available at www.sgm.ac.uk

Basic Practical Microbiology Courses for Teachers and Technicians

Bookings are now being taken for:
25 September
University of Leeds
30 September
University of Reading
See website for details.

Website

www.microbiologyonline.org.uk

Enquiries

email education@sgm.ac.uk

ABOVE RIGHT:
Students in a practical microbiology class.
COURTESY JOY PERKINS,
UNIVERSITY OF HUDDERSFIELD

Vocational GCSEs

■ Helen Nankervis

From September this year, 14-year-olds are going to have a choice in the type of education they receive at GCSE level. A suite of pilot 'vocational GCSE' (VGCSE) specifications will be available for any school to teach as an alternative to the ordinary GCSEs, although all students will still have to sit ordinary GCSE English and maths.

These new qualifications replace Part 1 GNVQs and focus on applied aspects of their subject. They are equivalent to two GCSEs and are aimed at students who would like to pursue a more practically based career; they will enable progression to higher or further education, training or employment. Although much of the factual content of the applied science course is the same as for GCSE science, the way the principles will be taught is entirely different.

The pilot specifications for the AQA (www.aqa.org.uk) and OCR (<http://194.73.217.3/schemes/vgcse/science/science.htm>) examining bodies for applied science, health and social care, engineering and manufacturing are available on-line.

VGCSE science – emphasis on microbiology

The specification is still broadly split into biology, chemistry and physics in each of the three units that make up the VGCSE. Every unit also deals with relevant social, ethical, moral and health and safety issues as well as the correct use of equipment and appropriate recording of results. When reading through the specification, it becomes obvious that a large amount of the biology section in each unit is based on microbiology techniques.

Developing scientific skills

The first unit teaches students the skills needed to carry out experiments and work in the laboratory. It includes the hazards and risks associated with the handling and disposal of micro-organisms and the associated health and safety issues. Students learn aseptic technique and use it to culture micro-organisms, for example to produce yoghurt, as well as studying the effect of antimicrobials on micro-organisms. They also cover the use of a light microscope and prepare a temporary slide.

Science for the needs of society

The second unit teaches students about the materials and living organisms that scientists work with. It focuses on the range of different products that living organisms can make. Students learn the differences between plant and animal cells, and go on to recognize that living organisms make pharmaceutical products such as antibiotics and insulin. The basics of genetic engineering are also covered so that students

understand that it involves the transfer of genetic material from one living organism to another to change the characteristics of that organism. The role of micro-organisms in the production of food and drink, such as yoghurt, bread, beer and wine is explained. The students also learn about the micro-organisms responsible for diseases such as tuberculosis, polio, rubella, mumps, measles, foot-and-mouth, athlete's foot and skin infections. The methods of protecting the body from infection, including immunization, sterilization, disinfection and antibiotics, are also covered in some detail.

Science at work

The third unit explores how science may be used to the benefit of industry and society. The unit teaches both information skills and science in the workplace, as well providing direct information on how to monitor the growth, responses and development of living organisms. The students have to complete an investigation where they choose a living organism to monitor and then measure either its growth, development or responses. One of the suggested projects is to attempt to improve the yield of a plant or micro-organism. There is great emphasis on methodology and evaluation of results. The students must produce a plan and record all their results as if they were doing a lab project in any working laboratory and the overall project is then marked as their coursework.

Resources, SGM and beyond...

Support literature is also being produced by educational publishers to go with these new qualifications, although no information on the books is yet available.

As the new VGCSE in applied science places so much emphasis on microbiology, it is fortuitous that the SGM is soon to publish a set of practical exercises in microbiology for secondary schools that will tie in very closely with these new specifications. The booklet will be available from the SGM in September for £5.

However well the VGCSEs in their current pilot form are taken up, it is fairly clear that education of this type is here to stay. This can only be good news both for those wanting a career in science at a technical level and any employers of technicians, especially in microbiology.

● **Helen Nankervis is a research assistant at Nottingham University developing school practicals for the SGM.**



Microbiology Today
Editor Meriel Jones
takes a look at some
papers in current
issues of the
Society's journals
which highlight new
and exciting
developments in
microbiological
research.

AIDS – does HIV-2 hold the key to understanding HIV-1?

The AIDS pandemic continues to spread unchecked in most of the world, with more than 34 million people currently infected with the human immunodeficiency virus (HIV). Most have HIV type 1, but a second closely related virus, HIV type 2 (HIV-2), is responsible for a significant minority of infections. Jacqueline Reeves and Robert Doms from the University of Pennsylvania, USA, have been reviewing the state of knowledge about this second virus, because it is similar but less pathogenic and may give important ideas about how to combat HIV-1. People infected with HIV-2 can live for many years without symptoms, frequently more than a decade, and with few viruses in their blood. It is transmitted much less effectively than HIV-1, and the mortality from HIV-2 is two-thirds lower. However, if the infection does finally progress to AIDS, both the symptoms and outcome are very similar. The reviewers have tried to pick out the differences between the two viruses that make HIV-2 endemic with a stable prevalence rate in most countries, while HIV-1 is pandemic, with increasing prevalence in developing countries.

HIV-2 originated in sooty mangabey monkeys, but on seven independent occasions it was transmitted to humans in West Africa. Guinea-Bissau, The Gambia, Senegal and Guinea are its strongholds, but it is also found in countries with links to the colonial power Portugal,

including southwest India, Angola, Mozambique and Brazil. Even so, it normally only accounts for a few percent of HIV infections.

The reasons for HIV-2's lower pathogenicity are probably related to two factors. First, people infected with this virus maintain an immune response that both limits the amount of new virus that is produced by their cells, and continues to protect against other pathogens. Laboratory tests of cells and fluid taken from people with HIV-2 shows some ability to destroy the HIV-1 virus, although whether this can happen *in vivo* to people who are unfortunate enough to contract a second infection is controversial. The body may be able to detect and counteract some HIV-2 strains more easily because many have errors in a gene that provides a facility to evade the immune system.

The second feature of HIV-2 that is very different from HIV-1 is the way it enters cells. Both viruses have sugar-coated envelope proteins that protrude from their surface

and latch onto human cells. The protein then changes shape and attaches to a second co-receptor to trigger a series of events that end up with the virus and human cell fusing, so that the virus can deliver its lethal genetic package. HIV-1 picks out a particular feature on the cell surface, called the CD4 receptor, and invariably uses one of two co-receptors. HIV-2 also uses the CD4 receptor, but can also enter cells that lack it, and exploits a very large number of co-receptors. The source of these differences in the structure of the viral envelope protein, with the consequence of making the virus more ready to fuse with human cells. CD4-independent strains are more sensitive to the immune system, perhaps due to these slight changes. There may be something in this that can be used to develop a vaccine to HIV-2, and perhaps point out ideas towards a vaccine against HIV-1.

Reeves, J.D. & Doms, R.W. (2002). Human immunodeficiency virus type 2. *J Gen Virol* 83, 1253–1265.



OPPOSITE PAGE:
St Thomas' Church, Brno, Czech Republic, in which Jošt Lucemburský, a 14th century Margrave (see inset), is buried. A new species of *Rhodococcus*, *R. jostii*, has been isolated from his recently excavated grave. COURTESY LYDIE ZUKALOVA, FOREIGN RELATIONS DEPARTMENT, BRNO (WWW.BRNO.CZ)

RIGHT:
A sooty mangabey monkey, the species in which HIV-2 originated. PHOTO MARK MURCHISON, KATHERINE PHILLIPPI-FALKENSTEIN AND RON VEAZEY, TULANE NATIONAL PRIMATE RESEARCH CENTER, LOS ANGELES, USA

Novel *Rhodococcus* species from medieval Czech grave

The Margrave Jošt Lucemburský was an important Czech ruler who reigned over Moravia at the turn of the 14th century. Among other things, in March 1393 he gave the Mayor of Brno and the town councillors and officials the privilege of serving high quality imported wine and mature Schweinditz beer. He was buried in St Thomas' church in Brno, and his grave was opened in 1999 by the Brno City Museum for archaeological and anthropological research. Researchers from the Czech Republic and other countries have been studying the micro-organisms that they found in the grave of this early appreciator of fermentation technology.

These included three colonies of pink-pigmented bacteria from a femur. The bacteria had the typical appearance of members of the genus *Rhodococcus*. When the researchers compared the sequence of the 16S rRNA gene, which is frequently used to characterize bacterial species, with that of representative members of the genus, it turned out to be distinctly different. Together with some physiological characteristics, these were sufficient to indicate that the bacteria belonged to a new species, which was named *R. jostii* in honour of the Margrave on whom it was found.

Takeuchi, M., Hatano, K., Sedlacek, I. & Pacova, Z. (2002). *Rhodococcus jostii* sp. nov., isolated from a medieval grave. *Int J Syst Evol Microbiol* 52, 409–413.



Charcoal keeps coils in culture

Helicobacter pylori is the cause of chronic gastritis and peptic ulcers and is associated with the development of gastric cancer in humans. Members of this genus have also been found causing gastrointestinal disorders in animals as diverse as dogs, mice, poultry and cheetahs. The bacteria have very idiosyncratic requirements for growth outside their host and are probably often missed. In particular, the bacteria sometimes travel to infect the liver and bile tree and are then especially difficult to culture. Yet another problem is that the bacterial cells change shape from spiral to spherical when they are grown in the laboratory. Regardless of the reason for this change, media that maintain the bacteria in their normal spiral shape are preferable.

Researchers at the University of Lund in Sweden, working with colleagues at the National University of Ireland, Galway, have been investigating exactly which medium is best for five *Helicobacter* species, both to permit them to grow at all, and also to keep their spiral morphology. They tested both liquid and solid media, and also the effect of adding compounds like activated charcoal, porcine gastric mucin and β -cyclodextrin. Activated charcoal stimulated growth best, even though it has no nutritional value. Toxic compounds, such as hydrogen peroxide, become adsorbed on the charcoal, so this points firmly at a sensitivity to toxic compounds in *Helicobacter* species.

Activated charcoal and β -cyclodextrin also slowed down the change from a spiral to a spherical shape. One hypothesis for this change is that the bacteria are responding to stress, which matches with the fact that both these compounds can hold toxins away from the bacteria. These experiments indicate that adding charcoal to growth media could help diagnostic laboratories grow *Helicobacter* species, and also maintain them in their normal morphology for longer to aid identification.

Taneera, J., Moran, A.P., Hynes, S.O., Nilsson, H.-O., Al-Soud, W. & Wadström, T. (2002). Influence of activated charcoal, porcine gastric mucin and β -cyclodextrin on the morphology and growth of intestinal and gastric *Helicobacter* spp. *Microbiology* 148, 677–684.

Prion-like proteins in *Saccharomyces* and *Candida*

Prions have changed from one of the most obscure topics in biology to being well known to the public as well as scientists because of BSE. This disease of cattle is the consequence of a single protein changing its shape and then forming clumps within the brain that are ultimately fatal. The way that the disease is transmitted, through contact with the mis-shaped protein, is one of its most surprising aspects, and has made researchers look again at several other conditions that are inherited in strange ways. Some of these have also turned out to be caused by proteins that can act as prions.

One of these is [PSI⁺], characteristic of the yeast *Saccharomyces cerevisiae*. Sup35p is the name of the protein that causes the problem. After changing shape, it becomes deposited within the cell, rather than carrying out its normal function. It is required as part of the essential cellular machinery for synthesizing proteins, and a similar protein is needed by all living cells, including mammalian ones. Researchers at the Universities of Kent in the UK and Lisbon in Portugal have been investigating why the *S. cerevisiae* protein can transform into a prion, while others do not. For example, the Sup35p of another yeast, *Candida albicans*, has never been detected in aggregates like a prion, even when it is mixed with the prion form of Sup35p from *S. cerevisiae*.

The Sup35p protein contains two distinct regions. One of them, the C domain, is essential for its normal function and is

similar in all known Sup35p proteins. The other region, called the N domain, is much more variable, and the conversion into prion aggregates in *S. cerevisiae* cannot happen without it. There are five stretches of repeated amino acids within the N domain, and removing even one of them prevents the prion-like behaviour. When the researchers investigated Sup35p from *C. albicans*, they were surprised that its N domain had many of the same features, including the repeated regions of amino acids. There are a large number of proteins that have runs of one amino acid, glutamine, and several dozen of these polyglutamine tracts have been found in *C. albicans* alone. What is unusual is that the lengths of the tracts, i.e. the numbers of glutamines, vary between different *Candida* strains. It is also known that in human diseases, like Huntington's disease, for which proteins containing polyglutamine tracts have been implicated, the severity of the disease increases as the length of these tracts increases in a particular protein. The question is, therefore, what is the significance of these strain-specific variations in polyglutamine tract lengths to the function of Sup35p and/or to *Candida* itself.

The researchers checked that the *C. albicans* protein really had the same function as the one from *S. cerevisiae* by deliberately disrupting the gene for Sup35p in some *S. cerevisiae* cells, and then providing them with the one from *C. albicans*. The *S. cerevisiae* cells could use this gene to make the essential protein, although

they needed more of it than of their own protein, implying that it did not work as efficiently. It also could not be induced to change into a prion-like form by Sup35p aggregates within the *S. cerevisiae* cell.

The question still remains of why these similar proteins have very different abilities to undergo the shape-change and aggregation that are characteristic of prions. From their experiments, combined with information from other research groups, the researchers think that the subtle control that cells exert over the ways that proteins fold may be important.

Resende, C., Parham, S.N., Tinsley, C., Ferreira, P., Duarte, J.A.B. & Tuite, M.F. (2002). The *Candida albicans* Sup35p protein (CaSup35p): function, prion-like behaviour and an associated polyglutamine length polymorphism. *Microbiology* 148, 1049–1060.

The SGM publishes two monthly journals, **Microbiology** and **Journal of General Virology**.

The **International Journal of Systematic and Evolutionary Microbiology (IUSEM)** is published bimonthly on behalf of the IUMS in conjunction with the ICSP.

The three journals are now available online. For further information visit the journal website: www.sgmjournals.org

Members may purchase SGM journals at concessionary rates. See p. 61 or contact the Membership Office for details. Information on commercial subscriptions is available from the Journals Sales Office.

TOP RIGHT

The badger (*Meles meles*), the animal at the centre of the bovine TB controversy in the UK.

PHOTO ALEX TILL, CORNWALL COLLEGE, CAMBORNE

LOWER RIGHT:

Electron micrograph of badger herpesvirus showing full and empty capsids.

PHOTO EM UNIT, VETERINARY LABORATORIES AGENCY, NEW HAW

OPPOSITE PAGE:

The Grand Canal, Venice, from where *Ilyobacter inseutus* was isolated.

PHOTO JANET HURST, SGM

Something in the air

Amazing things can turn up in the air. Researchers in Germany have found a new species of bacteria floating around a composting facility in Kassel, Niederzwehren. The bacteria were trapped on a filter and then cultivated on conventional microbiological growth media. Some were readily identified, but one was more elusive. Peter Kämpfer and his colleagues pinned it down to the genus *Nocardiopsis*, bacteria where the cells are arranged as easily fragmented filaments. However, working out which of the 10 species of *Nocardiopsis* they had caught was more difficult.

These species are distinguished by the fats found in their cells, the composition of their cell walls and by the sequence of one of their genes, that for 16S rRNA. Compared with the others, this isolate had some distinct differences. It contained different proportions of some fats, was able to make use of a different range of growth substrates and also had differences in the sequence of the 16S rRNA gene. As a consequence, the researchers are confident that they have uncovered a new species. Given its source, *N. compostus* seems an entirely appropriate name.

Kämpfer, P., Busse, H.-J. & Rainey, F.A. (2002). *Nocardiopsis compostus* sp. nov., from the atmosphere of a composting facility. *Int J Syst Evol Microbiol* 52, 621–627.

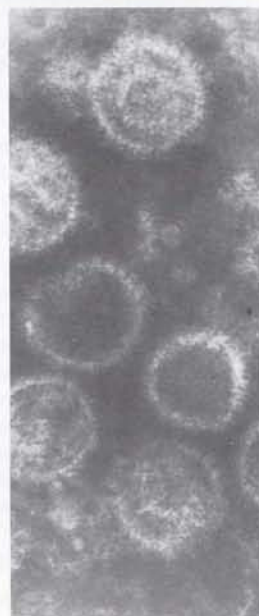


Novel virus may hamper use of a TB vaccine for badgers

The role of badgers in transmitting tuberculosis to cattle in the UK is controversial. One solution that researchers at the Veterinary Laboratories Agency have been working towards is to develop a TB vaccine for badgers, so preventing them from passing on the disease. As part of these experiments, they have recently discovered a new virus which may affect the health of badgers. They were examining the emaciated corpse of a young adult female badger. The researchers managed to grow some of the badger's lung-cells in artificial culture, and were surprised by the presence of dead cells containing small symmetrical particles that looked like herpesviruses. Their analysis of several genes from the virus indicated that it was a new member of the gammaherpesviruses. This type of virus had never been found in a badger before. Closely related viruses can sometimes cause cancer or suppress the immune system, so the researchers wanted to know more about it.

The researchers attempts to get the virus to infect cultures of other animal cells were unsuccessful, except for mink cells. Since mink are closely related to badgers, this indicated that the virus is very specific for its host. One thing that they do not know yet, and are anxious to discover, is how commonly badgers are infected with this virus. It may well not cause any obvious symptoms, but if it reduced the effectiveness of their immune systems, the badger could become more susceptible to other diseases, such as TB. In addition, it can be more difficult to obtain a protective response from a vaccine in animals suffering from problems with their immune responses. Either of these considerations will add new factors to the debate about badgers and TB.

Banks, M., King, D.P., Daniells, C., Stagg, D.A. & Gavier-Widen, D. (2002). Partial characterization of a novel gammaherpesvirus isolated from a European badger (*Meles meles*). *J Gen Virol* 83, 1325–1330.



An extraordinary new species from the canals of Venice

Researchers at the Universities of Munich and Konstanz in Germany have scooped up a truly unusual spherical bacterium from the muddy sediment of the canals of Venice. They have recently named it *Ilyobacter insuetus* (*insuetus* is a Latin adjective meaning extraordinary or unusual) in recognition of the extraordinary fact that the only two compounds that it will grow on are quinic and shikimic acids. Despite their strange names, there are large amounts of these materials in plants because they are used to synthesize wood. The researchers tested over 30 other substrates, including sugars such as glucose that can be used by very many bacteria, but *I. insuetus* left them untouched. In addition, this species is killed by oxygen from the atmosphere and uses a novel strategy for disassembling its sole food source to obtain carbon and energy.

Its taxonomic position was not obvious because when the researchers did the appropriate tests, its nearest relatives were members of both the genera *Ilyobacter* and *Propionigenium*. Although they were all similar, based on the sequence of several genes, there were such significant differences in their cell physiology that the researchers think that once more information is available it will be clear that these bacteria are actually members of several currently unrecognized genera.

Brune, A., Evers, S., Kaim, G., Ludwig, W. & Schink, B. (2002). *Ilyobacter insuetus* sp. nov., a fermentative bacterium specialized in the degradation of hydroaromatic compounds. *Int J Syst Evol Microbiol* 52, 429–432.



Friendly gut bug produces killer protein

Probiotics have been defined as living micro-organisms which when eaten in adequate numbers exert positive health benefits beyond inherent basic nutrition. A probiotic microflora is believed to act through its metabolic activities and its physical presence, with benefits such as the competitive exclusion of medically significant pathogens, stimulation of the immune system and treatment or neutralization of the side effects of antibiotic therapy. Many probiotics have the desirable property of producing antimicrobial substances called bacteriocins. These small proteins are secreted by the bacteria to kill or inhibit other bacteria. Bacteriocin-producers contain genes that give them immunity to their own bacteriocins. A very large number of bacteriocins have been identified, and researchers know about their synthesis and secretion, at least in general terms.

Now, researchers from University College Cork in Ireland, in collaboration with Norwegian scientists, have for the first time isolated the genes responsible for bacteriocin production by a probiotic isolated from the gut of a human, along with the bacteriocin itself. The probiotic bacterium was *Lactobacillus salivarius* UCC118, a member of the lactic acid bacteria that are generally considered to be a beneficial component of the intestinal flora. This strain can synthesize a bacteriocin called ABP-118 that inhibits a number of food-borne and medically significant pathogens, including species of *Bacillus*, *Listeria*,

Enterococcus and *Staphylococcus*, without apparently affecting other lactic acid bacteria. This is fortuitous, since bacteriocins often inhibit bacteria related to the producer.

After isolating the bacteriocin from the growth medium of an *L. salivarius* UCC118 culture, the researchers could sequence the protein and from that deduce the type of gene that should encode it. With this information, they analysed a region of the genome of the bacterium which turned out to have 16 genes with all the instructions for synthesizing and secreting the bacteriocin ABP-118, along with protection from its effects. The bacteriocin turns out to be made of two proteins, only one of which is active against other bacteria. The other protein enhances this toxicity, but is harmless on its own. Both of the proteins are a little longer when they are first synthesized within the cell, than after they are secreted into the environment. The extra region instructs the cell to secrete the proteins and it is then chopped off. The two genes for the secretion system were among the ones found by the researchers, as was the gene that confers immunity on the cells to their own bacteriocin, and a further three that provide the system to detect and transmit signals to initiate synthesis of the toxic proteins. The researchers initially identified the genes only by their similarity to ones in other bacteria, but were later able to carry out a series of experiments to confirm their identification. In one of these, they added the gene they thought

conferred immunity to ABP-118 to a strain of bacteria that was usually killed by it. These bacteria became immune to the bacteriocin, indicating that this was indeed the function of the gene product.

Among the other eight genes, the researchers think that some may be instructions for more types of bacteriocins, but none of their experiments indicated that these genes worked. This is something that they are continuing to investigate, along with the regulation of the production of ABP-118. Although the health-contributing effects of this bacterium may be difficult to assess within the intestine, its ability to inhibit or kill pathogenic bacteria can only benefit its host.

Flynn, S., van Sinderen, D., Thornton, G.M., Holo, H., Nes, I.F. & Collins, J.K. (2002). Characterization of the genetic locus responsible for the production of ABP-118, a novel bacteriocin produced by the probiotic bacterium *Lactobacillus salivarius* subsp. *salivarius* UCC118. *Microbiology* 148, 973–984.

International Development Fund reports



Fifth International Symposium on Typhoid Fever and other Salmonellosis and Workshop on Molecular Methods in the Epidemiology and Diagnosis of Typhoid

Karachi, Pakistan, 4–7 February 2002

■ Gordon Dougan

Typhoid is still a very common disease in many poorer countries of the world. The World Health Organization estimates that globally there are still more than 17 million cases annually and that these infections are associated with around 600,000 deaths. These figures are almost certainly an underestimate as the disease is difficult to confirm clinically or immunologically. The gold standard for typhoid diagnosis is still a positive blood culture and in the absence of good microbiological facilities the disease can be missed. A major factor affecting the treatment of typhoid is the emergence of multiple-antibiotic-resistant bacteria in many regions of the world, again illustrating the importance of good microbiological practice in handling the disease and associated outbreaks. Perhaps surprisingly, the level of research activity on *Salmonella enterica* subsp. *enterica* serovar Typhi (*Salmonella* Typhi) is comparatively low. In most Western laboratories researchers prefer to work on the convenient murine model of the disease (caused by other *S. enterica* serovars such as Typhimurium). Although the murine disease superficially resembles typhoid, it is not the human disease. This point is emphasized by examining the recently published genome sequences of Typhi versus Typhimurium, where up to 10% of the genes are different.

Against this background an international meeting on typhoid has been organized on a bi-annual basis. The meetings are normally held in a country where the disease is endemic and this year it was the turn of Pakistan. The task of pulling the meeting together was given to Professor Zulfiqar Bhutta of the Aga Khan University in Karachi and a small organizing committee. International events were going to make the task extremely difficult. The outbreak of war in neighbouring

Afghanistan immediately put a cloud over the meeting as political pressure built up in Pakistan, a near neighbour. Also, a week before the meeting was due to take place the US journalist Daniel Pearl was kidnapped in Karachi. All of these events meant that there was considerable uncertainty surrounding the meeting up until the last minute.

A team of SGM-sponsored scientists, Professor Gordon Dougan, Dr John Wain and Dr Tahir Ali (all from Imperial College) and Dr Nick Thomson (Sanger Centre), set out for Karachi on 2 February, uncertain of how events would unfold. Arrival in Karachi was uneventful and we settled in by gorging on a delicious curry smorgasbord in the hotel. The next morning we met in the hotel lobby and were thrilled to be greeted by an enthusiastic gathering of dedicated typhoid scientists who had all made it to Pakistan in spite of the problems. We climbed into a bus to head off to the workshop on molecular methods (organized by Dr Rumina Hassan of the Aga Khan University, supported by John Wain, Nick Thomson and Tahir Ali). Armed soldiers simultaneously boarded the bus and took up their protective posts with rifles pointing out of the windows as we set off through the rush hour traffic. On arrival at the Aga Khan University we went straight into the first session on PCR assays for typhoid and never looked back. The audience/participants were a mixture of international academics and clinicians along with many local (Pakistani) scientists and students. Topics covered ranged from PCR methodologies, ELISA, pathogenicity islands, diagnostics and culture methods. A special treat was provided by Nick Thomson (introduced mistakenly as Nick Sanger at the meeting), who set up a real-time demonstration of the genome browsing tool Artemis and handed out free CDs containing the full program. The participants alternated between laboratory and seminar sessions and we were all enthralled by the enthusiasm of the participants and their desire to learn.

The workshop was followed by the international meeting. The programme had been depleted as several people failed to turn up, but substitutes were quickly found and the full sessions went ahead. Many excellent



ABOVE:
Participants in the Symposium and
Workshop held in Karachi, Pakistan.

RIGHT:
Workshop participants learning new
laboratory techniques.

PHOTOS GORDON DOUGAN

presentations were made. Of note was the effort made by Myron Levine of the University of Maryland who against all political odds and time constraints made it to the meeting and provided a superb overview of vaccinology (a testament to his dedication). Exciting data were presented by the Chinese on the impact of Vi vaccination in China and the threatened emergence of *Salmonella* Paratyphi A to take its place. Professor Dougan summarized the meeting and chaired a discussion on future prospects.

The meeting was complemented by several dinners held in different locations and excellent food was served at all times. The SGM contingent focused their attention on sampling as many curries as possible. Eventually, the time to leave arrived and we boarded the plane to Dubai, regretfully leaving a superb meeting. In Dubai we just had sufficient time to down a pint of Guinness in the Irish Pub before taking the plane to London. We all agreed that this was one of the most stimulating scientific meetings we had attended. This was in the face of so many compounding factors in the region. Much of the credit must go to Zulfiqar Bhutta who kept his nerve where others lost theirs and still managed to be the perfect scientific host.

● **Professor Gordon Dougan, Centre for Molecular Microbiology and Infection, Department of Biological Sciences, Imperial College of Science Technology & Medicine, London SW7 2AY, UK. email g.dougan@ic.ac.uk**



Respiratory bacteriology training in Tanzania

■ **Stephen Gillespie, Tim McHugh & Bambos Charalambous**

The Department of Medical Microbiology at the Royal Free and University College Medical School, University College London has been collaborating with a hospital in Northern Tanzania, the Kilimanjaro Christian Medical Centre, for more than 13 years. A new medical school and health sciences faculty has been established there since 1997 and provides training for undergraduate, postgraduate medical and many paramedical and nursing students. This is part of the Tumaini University of Tanzania ('tumaini' is the Swahili word for 'hope'). There is a need to develop the teaching and research infrastructure. We were awarded a grant from the SGM International Development Fund to develop the respiratory bacteriology reference and training facilities.

Lower respiratory tract infections exact an enormous toll of death in sub-Saharan Africa, caused by *Streptococcus pneumoniae* in children and *Mycobacterium tuberculosis* in people of all ages. Yet little is known about the epidemiology, population genetics and antibiotic resistance patterns of these organisms on the continent. This is of particular importance for the formulation of vaccines and antibiotic regimens which usually depend on information obtained from studies performed in Europe and North America.

The SGM grant was used to support the development of facilities for the molecular epidemiology of respiratory bacteria. A PCR machine, gel rigs, power packs and materials to archive strains, were sent out to the clinical laboratory of Kilimanjaro Christian Medical College.

The equipment has already been put to good use in a cross-sectional and longitudinal study of *S. pneumoniae* carriage that in addition to serological and antibiotic susceptibility tests will identify the molecular basis of the changing prevalence of different serotypes and resistant clones. Related studies currently underway include the collection of invasive pneumococcal isolates to identify the nature of the link between carriage and invasive disease. These will include genotyping the organisms by multilocus sequence typing to understand the processes of natural capsule switching and multiple colonization.

Also underway is a study of the genetic heterogeneity of wild-type *M. tuberculosis* in patients on treatment. A visiting UCL research fellow has established PCR assays for a range of genes associated with resistance and used this as an opportunity for

training in molecular methodology. A Tanzanian fellow is now visiting the UK to have further training in molecular respiratory bacteriology and will return to Tanzania to start a project that links the molecular lineage of *M. tuberculosis* strains to clinical outcome.

Research is not the only objective of our collaboration and there will be increasing training of local university staff in molecular methods of diagnosis. We also anticipate local courses on diagnosis of respiratory infections and testing for antibiotic resistance in the future. Thus, the grant has already contributed to the development of research and teaching capacity of the Kilimanjaro Christian Medical College, Tumaini University, and provides a foundation for further initiatives.

● **Professor Stephen H. Gillespie, Dr Timothy D. McHugh and Dr Bambos M. Charalambous, Department of Medical Microbiology, Royal Free and University College Medical School, Rowland Hill Street, London NW3 2PF, UK. email stepheng@rfc.ucl.ac.uk; tmchugh@rfc.ucl.ac.uk**



TOP LEFT: View of the rear of Kilimanjaro Christian Medical College showing some of the paramedical training schools in the shadow of Kilimanjaro.

ABOVE: Staff training in PCR.

PHOTOS ROLY GOSLING

International Research Fellowship report

■ Tsitsi Ndowora

THIS PAGE:

Fig. 1. *N. benthamiana* infected with the TBTV-A2 isolate (left) and a healthy plant (right).

OPPOSITE PAGE:

Fig. 2. dsRNA isolated from *N. benthamiana* plants (thick lane) that were mechanically inoculated with the TBTV-A2 isolate showing four prominent dsRNA bands of about 4.6 (TBTV genome), 1.6, 1.3 and 0.75 (sat-RNA) kbp. A Promega 1 kb DNA ladder was used as a molecular mass standard (thin lane).

PHOTOS COURTESY TSITSI NDOWORA

Tobacco bushy-top virus (TBTv) is a tentative member of the Umbravirus genus. This unique genus consists of plant viruses that have ssRNA genomes that do not encode a coat protein, and thus do not form conventional virus particles in infected plants. In naturally infected plants, an umbravirus occurs in association with a helper luteovirus that facilitates the transmission of the umbravirus by aphids in a persistent manner.

Definitive members of this virus genus include carrot mottle (CMoV), carrot mottle mimic (CMoMV), groundnut rosette (GRV), lettuce speckles mottle (LSMV), pea enation mosaic virus-2 (PEMV-2) and tobacco mottle (ToMV) viruses. Tentative members include sunflower crinkle, sunflower yellow blotch and tobacco yellow vein viruses, as well as TBTv.

There are two diseases of economic importance caused by umbraviruses in sub-Saharan Africa (SSA). One is the groundnut rosette disease, caused by GRV and its helper virus, groundnut rosette assistant virus (GRAV), which was first recorded on the African continent in 1907 in Tanzania and occurs throughout the SSA region. The other, tobacco bushy-top disease, was first described in Zimbabwe in 1958–59 and since then has been reported in South Africa, Malawi and Zambia. An apparently similar disease is now known to occur in China. Although it is a disease of tobacco in nature, in greenhouse studies the virus complex has been transmitted to important solanaceous crops such as tomato, pepper and paprika. Another umbravirus, TMoV, in association with its helper, tobacco vein distorting virus, causes tobacco rosette disease, first reported in Zimbabwe in 1938.

In the Plant Pathology department, at the Kutsaga Research Station, we are studying the ecology and epidemiology of TBTv with the aim of devising an effective disease control strategy. To detect the virus in infected plants and viruliferous aphids requires the development of primers for RT-PCR and this in turn requires the cloning and sequencing of the TBTv genome. To speed up the process, we requested collaboration with Dr D.J. Robinson and his team at the Scottish Crop Research Institute (SCRI) in Invergowrie, Scotland, who have cloned and sequenced the GRV genome, determined the respective functions of some of the GRV ORFs, and recently cloned and sequenced portions of the TMoV genome.

The SGM International Research Fellowship funded



our work on the cloning and sequencing of the TBTv genome at the SCRI. I arrived in Scotland on a date etched in everyone's memory, 11 September 2001, and despite the shock waves work began the following day with the mechanical inoculation of a TBTv isolate (TBTv-A2) into *Nicotiana benthamiana* seedlings maintained in a glasshouse. Symptoms were visible about 5 days after inoculation. Infected plants were generally paler than healthy plants and there was a mottle of dark green upon a light green leaf. Affected plants soon developed a bushy appearance as shoots proliferated from the axillary buds (Fig. 1).

dsRNA was isolated from the affected plants 2 weeks after inoculation, bands were separated on an agarose gel (Fig. 2), and the 4.6 kbp dsRNA corresponding to the TBTv genome was electroeluted from the gel. dsRNA was denatured using methylmercuric hydroxide, transcribed into cDNA and cloned using standard methods. Of the clones obtained, six contained candidate TBTv cDNA sequences, and the sequences of these inserts were determined. Analysis of the sequence data is continuing to identify motifs characteristic of umbravirus genomes. Meanwhile, primers were designed using the sequence of one of the clones. However, these primers amplified the expected size product by both PCR and RT-PCR, suggesting that the insert in this clone is a fragment of host-plant DNA.

This work has set the foundation for and started the ball rolling on the cloning and sequencing of TBTv. We intend to do hybridization studies using the cloned fragments to determine if these clones originated from the TBTv genome. Sequences of TBTv will be compared to those of other umbraviruses, especially GRV which causes an important disease of groundnuts in SSA. The technique of cDNA synthesis from dsRNA for virus cloning learned at the SCRI will

Further reading

Mo, X.H. & others (2002). First report of tobacco bushy-top disease in China. *Plant Dis* 86, 74.

Murant, A.F. & others (2000). Genus Umbravirus. In *Virus Taxonomy. Classification and Nomenclature of Viruses*, pp. 785–790. London: Academic Press.

Smith, K.M. (1946). Tobacco Rosette: a complex virus disease. *Parasitology* 37, 21–24.

Taliansky, M.E., Robinson, D.J. & Murant, A.F. (1996). Complete nucleotide sequence and organization of the RNA genome of groundnut rosette umbravirus. *J Gen Virol* 77, 2335–2345.

Wickens, G.M. (1938). A new and serious disease of tobacco in S. Rhodesia. *Rhod Agric J* 35, 181–184.

MicroShorts

The Microbiology of Drinking Water 2002

The Standing Committee of Analysts has announced the publication of *The Microbiology of Drinking Water 2002* in the series *Methods for the Examination of Waters and Associated Materials*. This is a revision of *The Microbiology of Water 1994 - Part 1 - Drinking Water*, commonly referred to as *Report 71*. *The Microbiology of Drinking Water 2002* comprises 10 parts covering water quality and public health, sampling, laboratory procedures and analytical methods for a range of indicator and pathogenic bacteria. The revised document addresses issues arising from European and UK legislation and includes details of significant changes over recent years with respect to laboratory procedures and practices, and the use of new methods. The 10 parts are:

- Part 1** Water quality and public health
- Part 2** Practices and procedures for sampling
- Part 3** Practices and procedures for laboratories
- Part 4** Methods for the isolation and enumeration of coliform bacteria and *Escherichia coli* (including *E. coli* O157)
- Part 5** Isolation and enumeration of enterococci by membrane filtration
- Part 6** Methods for the isolation and enumeration of sulphite-reducing clostridia and *Clostridium perfringens* by membrane filtration
- Part 7** The enumeration of heterotrophic bacteria by pour and spread plate techniques
- Part 8** Methods for the isolation and enumeration of *Aeromonas* and *Pseudomonas aeruginosa* by membrane filtration
- Part 9** Methods for the isolation and enumeration of *Salmonella* and *Shigella* by selective enrichment, membrane filtration and multiple tube most probable number technique
- Part 10** Methods for the isolation of *Yersinia*, *Vibrio* and *Campylobacter* by selective enrichment

The Microbiology of Drinking Water (2002) is available in electronic format from the Environment Agency via Dr David Westwood [Tel. +44 (0)115 921 3705; Fax +44 (0)115 921 3760; email david.westwood@environment-agency.gov.uk]. In due course it is anticipated that all parts will be available from the Agency's internet website.

Food Standards Agency research programme

The FSA has announced the names of 12 eminent scientists and academics who will make up its independent Advisory Committee on Research. The Committee will guide a £30.8 million research programme, ensuring that the FSA's research is clearly focused on providing the evidence the Agency needs to develop its policy aims and is relevant to the needs of consumers. The Committee has three experts to represent life sciences, of whom two are members of the SGM:

Professor Duncan Maskell, the Marks and Spencer Professor of Farm Animal Health, Food Science and Food Safety at Cambridge University, and **Professor William Donachie**, Deputy Director of Moredun Research Institute.

The Royal Society Summer Science Exhibition

2-4 July 2002

The annual exhibition is a showcase for scientific innovation and provides a unique opportunity to meet leading researchers from around the UK. It is particularly suitable for post-16 students with an interest in science, or who may be considering a scientific career. One of the exhibits this year, *Surfing the woodwide web*, which aims to raise the public awareness of fungi as soil microbes, has received sponsorship from the SGM PUS Fund. The exhibition takes place at 6-9 Carlton House Terrace, London, and entry is free. See www.royalsoc.ac.uk for details of opening times and other exhibits.

The BA Festival of Science

9-13 September 2002, University of Leicester

Europe's largest science extravaganza expects to attract 3,000 visitors and 400 scientists to its packed programme of talks, exhibitions, debates, visits and social events. The theme this year is *Science and the quality of life*. Full details of the programme and booking are on the web at www.the-ba.net

Women in Science

New Athena Award Scheme

The Athena Project, which supports the advancement of women in academic science, engineering and technology (SET), is co-funding a new scheme with the Royal Society. Bids are now invited for awards which will celebrate higher education institutions that can demonstrate that they have increased the number of women working in SET, improved their career development, raised their profile or heightened awareness and understanding of the career barriers they face. A department, faculty, centre, network or whole institution can apply. The submission deadline is **19 August 2002**.

Email athena@ecu.ac.uk for details.

Life Science Careers 2002

SGM is once again participating in the one-day careers conferences for undergraduate and postgraduate students of the life sciences. These include a packed programme of talks about a wide range of work options, further training opportunities, job finding and interviews, plus a CV clinic and exhibition by employers, professional bodies and universities. Attendance costs only £10 to include all refreshments and a delegate pack. This year's events are:

- 2 November University of Sheffield
- 16 November University of Glasgow
- 30 November Kings College London

A booking form will be published in the next issue of *Microbiology Today*. Details of the events are available on the web at

www.uklsc.org/careers2002.htm

be invaluable in our work at Kutsaga Research Station. We shall continue to collaborate with Dr Robinson and his team on this, and hopefully other projects. This project also allowed me to interact with several virologists of whom I knew, but had never met, and provided excellent networking opportunities.

I wish to thank the SGM for awarding me the International Research Fellowship, Dr Robinson for welcoming me into his laboratory, all the scientists (and top-notch technical staff) at the SCRI who assisted me, and the management and plant pathologists at the Kutsaga Research Station for their support and encouragement.

● **Dr Tsitsi Ndowora**, Kutsaga Research Station, PO Box 1909, Harare, Zimbabwe. email tsitsi_ndowora@kutsaga.co.zw

Reviews

If you would like your name to be added to our database of book reviewers, please complete the book reviewer interests form now available on the SGM website.

A classified compendium of book reviews from 1996 to the present is also available on the website.

The Way of the Cell: Molecules, Organisms and the Order of Life

By F.M. Harold
Published by Oxford University Press (2001)
£19.95, pp. 305
ISBN: 0-19-513512-1

What is life? This book is a thought-provoking bedtime read for a microbiologist. Franklin Harold pulls together ideas from across the decades and disciplines of biology and ponders how a cell is different from its parts. The challenge is not to recount the minutiae that make up living cells, but rather the less tangible concept of what we mean by saying that they are alive. This very readable book has a distinctly microbial bias, and emphasizes concepts rather than cataloguing facts. The origin of cells and discussion of current ideas on the evolution of prokaryotes and eukaryotes occupies the latter half of the book, following his thoughts on the structure of mainly microbial cells. Topics are described in succinct terms, enlivened with thoughtful comments and questions, and with an extensive reference list to satisfy readers who want to know more.

■ **Meriel Jones**
University of Liverpool

The Fungi. Second Edition

By M.J. Carlile, S.C. Watkinson & G.W. Gooday
Published by Academic Press (2001)
P/B US\$45.00, pp. 588
ISBN: 0-12-738446-4
H/B US\$75.00, pp. 588
ISBN: 0-12-738445-6

This undergraduate textbook gives an overview of the whole of mycology. The authors use examples throughout the fungi, without over-emphasizing taxonomy. The tension between describing a topic in depth, while maintaining the breadth required for undergraduate teaching means that no textbook would

satisfy everyone. However, this one may also be useful for graduate students meeting fungi for the first time, since it fills a gap between many textbooks of microbiology, biochemistry, genetics and ecology through covering topics specific to mycology that they often omit. For example, fungal cells and the unique aspects of their growth strategies gets 100 pages, without including features common to all eukaryotes. Some of the expanding insights from the application of molecular biology are indicated in this second edition, although details are outside its scope. This book is certainly a library purchase, and at £30 for the paperback edition is affordable for students studying a mycology course.

■ **Meriel Jones**
University of Liverpool

Recent Advances in the Biochemistry of Plant Lipids

Edited by J.L. Harwood & P.J. Quinn
Published by Portland Press (2001)
£75.00, pp. 480
ISBN: 1-85578-146-8

This book is a collection of 159 short papers, mostly two pages long, covering the biosynthesis and breakdown of plant fatty acids and complex lipids, signalling and lipids, environmental effects and biotechnological applications. They are the papers presented at the 14th International Symposium on Plant Lipids held in July 2000. However, one has to question the need for a separate, hard-bound set of the papers in book form since they have already been published in *Biochemical Society Transactions*.

It is perhaps surprising that there is so little coverage of the lipids of lower plants and photosynthetic micro-organisms; even yeasts and fungi, so often used as model plants, are only represented by three papers. Therefore, it might be assumed that SGM Members would not even bother to look at this book, but plant scientists play a leading role in many aspects of lipid biochemistry, and

microbiologists working on lipids or membranes will find much to stimulate their research, from methodology to function and current theories. However, whether such interest will be enough to provoke private purchase is doubtful and libraries are likely to have the journal publication already.

■ **Nick Russell**
Imperial College at Wye, Ashford

Meningococcal Vaccines: Methods and Protocols. Methods in Molecular Medicine, Vol. 66

Edited by A.J. Pollard & M.C.J. Maiden
Published by Humana Press (2001)
US\$120.00, pp. 416
ISBN: 0-89603-801-7

This volume is devoted to studies on vaccines against disease caused by *Neisseria meningitidis*. It contains excellent and up-to-date reviews and many working protocols, for example, detailing precise state-of-the-art methods for purifying subcellular fractions as components for formulating vaccines. It has a broad scope, ranging from novel scientific approaches to overcoming the technically perplexing problem of developing a vaccine against disease caused by serogroup B meningococci, to a very informative account of the recent successful UK vaccination programme against group C meningococci.

The book is an essential purchase for all those working on meningococci, even if not concerned directly with producing vaccines against meningococcal disease. There is much of general interest and utility for any laboratory investigating microbial pathogenesis or vaccine development. It represents a valuable, coherent and timely resource for all microbiologists researching meningitis, vaccines and related areas.

■ **Jon Saunders**
University of Liverpool

Molecular Pathology of the Prions. Methods in Molecular Medicine, Vol. 59

Edited by H.F. Baker
Published by Humana Press (2001)
US\$99.00, pp. 279
ISBN: 0-89603-924-2

While in a 'Methods' series, this is not a recipe book, rather a collection of discussions on the prion protein's role in normal and infected animals. The association between the protein's abnormal conformation and pathology is now widely accepted, but how it 'replicates' and spreads to the brain to kill neurones in strain-specific ways is still largely a mystery. The book presents the protein as a binder of copper, protector of cells, neurotoxin, and agent of precise neuronal targeting. Several chapters explore the use of disease models in normal and transgenic mice, tissue slices and mammalian and yeast cell cultures to examine the role of the prion protein and its mutations in disease. This is no introductory textbook to the prion protein; some knowledge of prions is required to appreciate the relevance of the varied contents and to place them within the context of TSE molecular pathology.

■ **Chris Bostock**
Institute for Animal Health, Compton Laboratory

Human Papillomaviruses: Clinical and Scientific Advances

Edited by J.C. Sterling & S.K. Tyring
Published by Arnold, London (2001)
H/B £65.00, pp. 153
ISBN: 0-340-74215-1

Human papillomaviruses are increasingly drawing attention, not only as the cause of cutaneous and mucosal warts of various kinds and as being intimately associated with the development of cervical dysplasia and cancer, but also due to significant progress in recent years in

elucidating the molecular biology of these viruses, including their various effects on the host cell and in treatment, including immunostimulatory, specific antiviral and vaccine approaches. The Editors have done a very good job in bringing together a multinational team of highly competent contributors, bridging the 'gene to clinic' span, and reviewing the literature, including their own work until 1999/2000. Due to this symposium-like approach the book is of interest to a broad audience of virologists, immunologists, molecular and cell biologists, physicians of a wide range and vaccinologists, and is highly recommended.

■ **Ulrich Desselberger**
Addenbrooke's Hospital,
Cambridge

Nodulation in Legumes

By J.I. Sprent
Published by Royal Botanic
Gardens, Kew (2001)
£27.00, pp. 146
ISBN: 1-84246-013-7

There are about 18,000 species of legumes, and the majority form root nodules containing nitrogen-fixing bacteria called rhizobia. Most nodulation research is devoted to a handful of crop species, but Janet Sprent is interested in the others, and this book distils a lifetime of experience. It provides a comprehensive account of our present knowledge of the taxonomic distribution of nodulation, but it is not just a dry list of species. Sprent is the undisputed expert on the diversity of nodule structures and their development, and has included a chapter on this, as well as chapters on legumes and on rhizobia, covering their taxonomy, physiology and ecology, and on the evolution of the symbiosis. All this material is presented in a highly accessible style that will ensure that this book is essential reading for beginners as well as an inspiration for field studies and an authoritative reference for advanced researchers.

■ **Peter Young**
University of York

Development of Novel Antimicrobial Agents: Emerging Strategies

Edited by K. Lohner
Published by Horizon Scientific
Press (2001)
£84.99/US\$169.99, pp. 284
ISBN: 1-898486-23-9

This book is concerned predominantly with the development of possible strategies aimed at discovering novel approaches to antimicrobials and is a collection of disparate reviews, only loosely linked to the stated theme. The possible value of genomics and combinatorial chemistry is well covered as is the topic of vaccines, including the development of adhesion vaccines and the use of attenuated bacteria as delivery vehicles. There are only two chapters from industry, one of these, the final chapter, being an account of the commercial development of a peptide antibiotic. Although of great interest to some, this seems quite out of place in this book. There is much of interest in this book, but it is difficult to agree with the publisher's claim of it presenting current research on the development of new classes of antibiotics, or of it being 'essential reading for all microbiologists' especially at a price of £84.99.

■ **Pam Hunter**
Horsham

Mycobacterium tuberculosis Protocols. Methods in Molecular Medicine, Vol. 54.

Edited by T. Parish & N.G. Stoker
Published by Humana Press (2001)
US\$135.00, pp. 416
ISBN: 0-89603-776-2

This is a research protocols book for working with *Mycobacterium tuberculosis* and contains information more relevant to this organism than that contained in *Mycobacteria Protocols* by the same Editors. It contains 24 chapters, each written by different authors with practical expertise, covering a range of

topics, including: nucleic acid extraction; methods for mutagenesis; methods for typing; *in vitro* models; functional genomics; proteomics; and strain storage and safety. In addition to containing 'how to' steps, each of the chapters begins with informative paragraphs giving the reader a historical context, otherwise gained by reading reviews. Additionally, the chapters contain notes giving useful tips such as convenient stopping points in the protocol and where to be particularly careful. This book would appeal to a limited audience, i.e. those working with mycobacteria, but I would say it was essential for any lab doing research on *Mycobacterium tuberculosis*.

■ **Sharon Kendall**
London School of
Hygiene and Tropical
Medicine

Epstein-Barr Virus and Human Cancer.

Current Topics in Microbiology and Immunology, Vol. 258

Edited by K. Takada
Published by Springer-Verlag
GmbH & Co. KG (2001)
DM198.91/sFr171.20/£68.50/
US\$99.00, pp. 233
ISBN: 3-540-41506-8

Of all the human viruses implicated as causative agents in cancer, Epstein-Barr Virus (EBV) is the one under the greatest suspicion. It is associated with a high proportion of Burkitt's lymphomas and nasopharyngeal carcinomas and there is growing evidence for its involvement in cases of Hodgkin's disease, gastric carcinoma and breast cancer. This book features articles by specialists (all from the US or Japan) who discuss various aspects of the properties of EBV relevant to these and other diseases. There is also some coverage of the role of the related Human Herpesvirus 8 in AIDS-associated lymphomas. Most of the topics and studies presented are already accessible in the primary literature and there is no strong need for a book of this

type. Nevertheless, it brings together several interesting topics under one cover and may be suitable for purchase by well-funded libraries in medical schools and virology departments.

■ **Mike Clemens**
St George's Hospital
Medical School, London

Xenotransplantation

Edited by J.L. Platt
Published by ASM Press (2001)
US\$89.95, pp. 308
ISBN: 1-55581-167-1

This book contains a series of reviews addressing some of the scientific questions underlying xenotransplantation, a topic that has received considerable attention over the past few years. The fascination of this subject stems in large part from the mixed feelings evoked by the potential good (i.e. therapeutic benefit) and harm (via infection) resulting from application of interspecies transplantation. Individually, many of these chapters are good reading. However, a few have a rather tired, recycled feeling as though the authors have already said everything they have to say on the subject. Collectively, there appears considerable repetition and some omissions. Overall, a stronger editorial hand on the wheel would have been desirable. For example, do we really need to read four descriptions of complement activation? Where are the descriptions of results obtained with the best pre-clinical models?

While reading this book I spent much time wondering about its purpose and the motivation of those involved in putting it together, given the amount of similar material that has already appeared in press. After reading the first chapter I briefly allowed myself to hope that this book might provide a critical view of the current status of the field as well as a grand vision of the future. Unfortunately, this hope was soon

dashed and I am left wondering how the initial momentum of the field can be regained.

■ **Jonathan Stoye**
National Institute for
Medical Research,
London

Aspergillus fumigatus: Biology, Clinical Aspects and Molecular Approaches to Pathogenicity. Contributions to Microbiology, Vol. 2

Edited by A.A. Brakhage, B. Jahn & A. Schmidt
Published by Karger (1999)
CHF198.00/ 131.41/US\$172.25,
pp. 222
ISBN: 3-8055-6714-6

Aspergillus fumigatus, the main causal agent in a range of life-threatening opportunistic infections, continues to provide a challenge in terms of diagnosis, treatment and understanding of its pathogenesis. This timely volume seeks to bring together current understanding on issues ranging from taxonomy, clinical manifestations of disease, antifungal testing and virulence. The chapters, each written by experts in their field, vary from a general chapter on clinical presentation to more detailed chapters on pigment production as a virulence factor. There are some new and interesting images and analyses, such as a comparison of conventional and liposomal amphotericin B treatment. A chapter on the transformation of *A. fumigatus* will prove useful. The chapter by Jean-Paul Latgé perhaps tried to cram in too much and separate chapters on fungal antigens and molecular epidemiology may have been better. This book is to be recommended for anyone working on this fungus.

■ **Glyn Evans**
University of Wales
College of Medicine,
Cardiff

A Dictionary of Virology, Third Edition

By B.W.J. Mahy
Published by Academic Press
(2001)
US\$49.95, pp. 422
ISBN: 0-12-465327-8

Since the majority of vertebrate virus families have been recently renamed and reclassified, virus nomenclature has become a quagmire of uncertainty for many virologists. Thus, this dictionary proves a well-timed reference source, excellent for researching not only virus species and genera, but also the latest techniques used in the laboratory today. Most entries are cross-referenced and synonyms, acronyms and abbreviations are provided to assist the reader at every turn. Helpful citations are also supplied, enticing the virologist into further exploration of the field. It is somewhat disappointing, however, to find that, although by the author's own admission, viruses infecting invertebrates, plants, bacteria and fungi are beyond the scope of this publication. Nevertheless, this does not detract from what is already an informative source of reference material, but paves the way for, perhaps, volume II. In short, this dictionary should most certainly be on the bookshelf of every self-respecting virologist.

■ **Catherine Tarbatt**
SGM Marlborough House

 **Bergey's Manual of Systematic Bacteriology, Second Edition, Vol. 1: The Archaea and the Deeply Branching and Phototrophic Bacteria**
Volume editors: D.R. Boone & R.W. Castenholz.
Editor-in-Chief: G. M. Garrity
Published by Springer-Verlag GmbH & Co. (2001)
£68.50/US\$99.00, pp. 721
ISBN: 0-387-98771-1

The second edition of Bergey's Manual is finally arriving on our bookshelves and promises to be

well worth the wait. It brings two departures from previous incarnations; the arrangement of taxa is now phylogenetic and the introductory chapters have been expanded in scope and number. Indeed, almost the first quarter of this book involves 15 contributions from distinguished taxonomists which provide an authoritative reference work on modern bacterial systematics. The Second Edition continues the high reputation of earlier volumes in the delivery of the descriptions of taxa. Genus descriptions include useful information on culture conditions, enrichment, maintenance and, of course, identification of species. One of the delights of the book is the extensive range of beautiful photomicrographs of obscure and bizarre microbial cells. This book is an essential purchase for the library and, given the reasonable price, well worth considering by the individual microbiologist interested in these groups of bacteria.

■ **Fergus Priest**
Heriot-Watt University,
Edinburgh

 **Fungi as Biocontrol Agents: Progress, Problems and Potential**
Edited by T.M. Butt, C.W. Jackson & N. Magan
Published by CABI Publishing
(2001)
£75.00/US\$140.00, pp. 416
ISBN: 0-85199-356-7

This volume covers fungal biocontrol research comprehensively in 14 chapters, each well referenced. The potential for commercial exploitation in field situations, the problems associated with production and goals for successful marketing are well reviewed, illustrated by a good range of case histories. Safety aspects are a major consideration and current legislation is referred to throughout. Some of the photographic figures are poor quality and not all have scale bars. The reader would have benefited from better labelling of many figures. Some diagrams are

simplicistic and oversized. Tighter editorial control might have balanced the chapters better; one is overlong for what is achieved, and the consistency of style could have been improved. However, the book is essential reading for anyone embarking on biocontrol research, it is a must for those who are already involved and will form a useful addition to the microbiology section of any library.

■ **Susan Isaacs**
University of Liverpool

Fundamental Virology, Fourth Edition

Edited by D.M. Knipe, P.M. Howley, D.E. Griffin, R.A. Lamb, M.A. Martin, B. Roizman & S.E. Straus
Published by Lippincott Williams & Wilkins (2001)
US\$99.95/£75.00, pp. 1,395
ISBN: 0-7817-1833-3

This is the 4th edition of this book that contains a number of chapters from the corresponding edition of *Fields Virology*. These are devoted to basic aspects of the subject as opposed to clinical aspects. A variety of new chapters have been added in the general section of this latest edition. The Editors-in-chief indicate that these additions should help to make this a more useful textbook for molecular and general virology modules. Whilst this is definitely the case, the price might deter senior undergraduates and, possibly, postgraduate students from buying it. These are two of the categories of targeted readers. However, lecturers should certainly recommend that institutional libraries buy it as a reference text for their modules. For other researchers interested in this area of virology it would be an appropriate and useful purchase, especially if they think the fuller unabridged version is too expensive for them.

■ **Liz Hoey**
The Queen's University
of Belfast

Ainsworth & Bisby's Dictionary of the Fungi, Ninth Edition

By P.M. Kirk, P.F. Cannon, J.C. David & J.A. Stalpers
Published by CAB International
(2001)
£49.95/US\$90.00, pp. 624
ISBN: 0-85199-377-X

The ninth edition of this work appears 58 years after the first edition, signifying its staying power and value to the scientific community. At a time when fungal classification is being provided with new, gene-sequence-based data, the dictionary has moved to incorporate the information into revised schemes for the *Ascomycota* and *Basidiomycota* and to integrate the anamorphs into a single classification system, something that many would support. The arcane world of fungal nomenclature is tackled well, but I struggled to find simple explanations of word derivations that might be illuminating; for example, nowhere could I find reference to the aspergillum, a dispenser of holy water that gives its name to *Aspergillus*. Why can you find peroxisome and mitochondrion, but no nucleus or vacuole? The answer is of course that any dictionary has its idiosyncrasies but, in this case, its strengths far outweigh its limitations.

■ **David Archer**
University of Nottingham

Hidden Worlds: Looking Through a Scientist's Microscope

By S. Kramer
Published by Houghton Mifflin
(2001)
H/B US\$16.00, pp. 64
ISBN: 0-618-05546-0

Dennis Kunkel is a familiar name to the SGM External Relations Office staff as a helpful source of beautiful false colour enhanced EMs of micro-organisms. This former research scientist at the University of Hawaii has been fascinated by microscopy since childhood. He captures his explorations of the invisible natural world on film and the

resulting photographs have won many awards. This coffee table size book briefly charts Dennis Kunkel's career before covering in depth some of the topics he has researched with the aid of a microscope. These include such diverse subjects as sand, mosquitoes, muscle cells and mites, as well as microbes. The chapter on microscopes describes how the different types work very clearly and succinctly. The book is copiously illustrated with stunning colour photographs. The quality is fantastic. It is not clear who the book is aimed at. The text is by a children's writer, which is reflected in the style, and the work is probably intended for the burgeoning scientist. However, at only \$16 it is worth buying just to gaze in amazement at the pictures.

■ **Janet Hurst**
SGM External Relations
Office

Free-Living Freshwater Protozoa: A Colour Guide

By D.J. Patterson
Drawings by S. Hedley
Published by Manson Publishing
(1998)
£29.95, pp. 223
ISBN: 1-874545-40-5

The preface states that 'this is a guide on those organisms that are most likely to be encountered in freshwater habitats'. It assumes that most readers, who want basic information, do not have access to specialist staining techniques, but are more likely to observe the organism in a sample and ask 'Wow, what the h*** is that!' (or is that comment only heard in my lab?). This book, with its 430 colour plates of protozoa and several schematics of protozoan communities, allows identification at least to the level of genus. The book contains other gems of information such as the care of microscopes, how to use them and how to actually view a sample. It is not patronizing as this branch of science is becoming a lost art. Coupled with an extensive glossary and bibliography, this book can work at two levels: first,

for those who want to look at the beauty of this morphologically diverse range of organisms; and second, those, who with limited experience, want to look at the communities in finer detail. An excellent book for all, as most of us rarely consider this branch of microbiology.

■ **Roger Pickup**
CEH Windermere

Teaching Biotechnology at School: A European Perspective

By H. Bayrhuber, W. Garvin & J. Grainger
Published by IPN, Kiel, Germany (2000)
DM20.00, pp. 158
ISBN: 3-89088-137-8

Over the past decade a group of teachers, teacher educators and educational researchers have been working together to promote biotechnology education within Europe, under the banner of EIBE (European Initiative for Biotechnology Education). This book, which is an edited selection of talks and papers presented by members of EIBE, provides a summary of that work and a fascinating insight to cultural and educational differences across Europe. The first half of the book, which focuses on practical techniques and the challenges which these can present in the school classroom, would be of particular interest to teachers and teacher educators. The second half of the book, which considers the impact of recent advances in biotechnology on society and the implications of this for biotechnology education, might be of more interest to educational researchers and policy makers. Given the diversity of its content, and hence of its potential readership, this book is better suited to the institutional library than the personal bookshelf.

■ **Jenny Lewis**
University of Leeds

Biofilm Community Interactions: Chance or Necessity?

Edited by P. Gilbert, D. Allison, M. Brading, J. Verran & J. Walker
Published by BioLine (2001)
£35.00 (UK only)/£36.00 (Europe)/£39.00 (ROW), pp. 370
ISBN: 0-9520432-9-7

This is the fifth publication from meetings of the Biofilm Club; it follows the standards of its predecessors in making information in the biofilm area rapidly available. Many of the 35 papers are highly informative, giving details on the methods used and considerable scientific information; others represent very brief reports. Unfortunately a few only provide vague generalizations and even repeat earlier mistakes. Will microbiologists never realize that alginate from *Pseudomonas aeruginosa* does not behave identically to commercial algal alginate and form complexes with calcium ions? Also, evaluation of phage therapy by US workers has already indicated that even when several specific phages acted simultaneously on a single host, it was not eliminated!

As always, however, the volume represents an inexpensive and useful addition to the biofilm literature. It will assist both newcomers and established 'biofilers' in assessing current work in water, dental and other complex biofilm environments.

■ **Ian Sutherland**
University of Edinburgh

Human Polyomaviruses. Molecular and Clinical Perspectives

Edited by K. Khalili & G.L. Stoner
Published by Wiley-Liss (2001)
£115.00, pp. 688
ISBN: 0-471-39009-7

A comprehensive book on polyomaviruses is timely, since there have been some significant advances in the field in the last 10 years. And this book, at over 650 pages, is indeed comprehensive. The first four chapters are devoted to the isolation of JC and

BK viruses from progressive multifocal leukoencephalopathy and are written in the first person by scientists involved in the work at the time, bringing a personal touch to the whole story. Further chapters explore the detailed molecular biology, receptors, mechanisms of latency and persistence, clinical aspects of progressive multifocal leukoencephalopathy and tumorigenicity of polyoma viruses. The final chapters address epidemiology, immunology, and evolutionary aspects. As often happens with multi-author books, there is a good deal of repetition in this book (there are 39 contributors), and it would have been much improved by stricter editing. The authors suggest that the book will be of interest to graduate students, medical students and advanced undergraduates, but in practice, I imagine it will become a useful reference book for interested clinical neurologists, virologists and research scientists.

■ **Dorothy H. Crawford**
University of Edinburgh

Pulsed Electric Fields in Food Processing: Fundamental Aspects and Applications. Food Preservation Technology Series

By G.V. Barbosa-Cánovas, Q.H. Zhang & G. Tabilo-Munizaga
Published by Technomic Publishing Co. Inc. (2001)
£96.00, pp. 268
ISBN: 1-56676-783-0

Current moves towards minimal food processing have revived interest in non-thermal methods, including pulsed electric fields (PEF). This multi-authored book encompasses data accrued over the last 40 years. After a useful introductory overview and a descriptive mathematical model, seven chapters deal with enzyme inactivation (including two on *P. fluorescens* proteases). Four chapters on inactivation of selected microbes comprise the main microbiological interest. Three chapters on organoleptic considerations follow, and an

excellent final chapter on product safety assurance concludes that much research is needed before PEF can be applied effectively. Whilst graphical data presentation is good, the overall presentation is marred by poor quality photographs, three repetitions of the same PEF chamber diagram, some variable block diagrams and lack of reference citations post-1999, despite the publication of a substantial number of papers, including those authored by the book's contributors. Overall, some appeal to food scientists but limited use for microbiologists.

■ **Martin Collins**
The Queen's University of Belfast

Fungal Pathogenesis: Principles and Clinical Applications. Mycology Series, Vol. 14

Edited by R.A. Calderone & R.L. Cihlar
Published by Marcel Dekker (2001)
US\$195.00 (US\$75.00 on orders of five or more copies for classroom use only), pp. 776
ISBN: 0-8247-0568-8

Just as well the old adage tells us not to judge a book by its cover because this one does nothing to flatter the contents covering selected topics on fungal virulence, host immunity, antifungal drugs and clinical diagnostics. What we have is 32 individual chapters, for the most part written by the leading authorities in the field, painting a larger picture through perspectives of their own research areas. The challenge lies in a second adage – whether the whole exceeds the sum of its parts. I think it does, but this book is more likely to be read as an encyclopaedia with the reader dipping into chapter(s) of interest rather than being exposed to a coherent synthesis of ideas. It is perhaps no longer possible to expect a magnum opus in the field and the next best thing is a

comprehensive compendium of well written vignettes, which is exactly what this is.

■ **Neil A.R. Gow**
University of Aberdeen

Mechanisms of DNA Tumor Virus Transformation. Monographs in Virology, Vol. 23

Edited by L.J. Rosenthal
Published by Karger (2001)
CHF148.00/ 98.17/US\$128.75, pp. 164
ISBN: 3-8055-7247-6

This book is a collection of reviews on a number of DNA tumour viruses. Given its nature, the individual chapters vary in content and style: some delve in greater detail on the molecular biology of the virus, while others take a more general overview of the virus' role in cancer. When possible, a welcome comparison is made between cell transformation *in vitro* and tumorigenesis *in vivo*. Unfortunately this is not easily done for some of the viruses (i.e. papillomaviruses), for which there is still relatively scant information on their *in vivo* activity. The chapters are well written (notwithstanding the occasional measurement of gene length in amino acids, and the occasional reference in 'Endnote' format) and clear. The book is directed not so much to seasoned tumour virologists, as to graduate or postgraduate students, or to workers just entering the field. Given the paucity of university students, the book is thus more suitable for institutional purchase! Shortly before I received this book, the journal *Oncogene* published a special issue on oncogenic DNA viruses. Although not completely overlapping, there is inevitably a great degree of similarity between the two publications.

■ **Saveria Campo**
Glasgow University Veterinary School

Nonculturable Microorganisms in the Environment

Edited by R.R. Colwell & D.J. Grimes
Published by ASM Press (2000)
US\$89.95, pp. 360
ISBN: 1-55581-196-5

This compilation concentrates on bacteria in the 'viable but non-culturable' (VBNC) state. Considering the title, I would have preferred if more chapters had discussed the vast majority of 'yet to be cultured' bacteria that dominate natural environments. Many capable authors review the strategies bacteria use to survive, persist and colonize their habitats. Several chapters aptly discuss small cell size and nutritional versatility as adaptations for survival. The term environment is wisely interpreted broadly, including water, soil, rock, animals, humans and food. Important societal issues, such as the significance of VBNC bacteria in epidemiology, public health and genetic modification are dealt with well, despite some inevitable repetition of earlier material. Almost all the contributions have explicit titles and concise, easily identifiable conclusions, making the book easy to navigate. All these factors ensure that this comprehensive volume will be valuable for institutional libraries serving microbiologists or scientists working on VBNC bacteria.

■ **John Fry**
Cardiff University

DNA Viruses: A Practical Approach

Edited by A.J. Cann
Published by Oxford University Press (1999)
£31.95, pp. 312
ISBN: 0-19-963718-0

This book has 10 chapters on methodology to study DNA viruses. Chapters 1-3 consider how viruses can be grown and purified, genomes characterized and sequenced, and mutants isolated and analysed. Chapters 4-6 describe methods to investigate interactions between

viral and cellular proteins and virus gene expression at the transcriptional and post-transcriptional stages. Methods for analysing secreted cytokine-binding proteins, virus proteins involved in neoplastic transformation, and the resistance of some DNA viruses to antiviral drugs are provided in chapters 7-9. Finally, chapter 10 considers herpes and adenovirus vectors with an emphasis on their application for gene therapy. This useful book describes a wide range of protocols for studying DNA viruses. One imperfect feature is protocol repetition in different chapters, such as methods for growing and titrating virus stocks, transfection and RNA analysis. Nevertheless, the book is a useful reference source for research student and postdoctoral scientists working in these areas.

■ **Geoffrey L. Smith**
The Wright-Fleming Institute, Imperial College, London

Marine and Freshwater Products Handbook

Edited by R.E. Martin, E.P. Carter, G.J. Flick, Jr & L.M. Davis
Published by Technomic (2000)
£131.00, pp. 964
ISBN: 1-56676-889-6

This is a comprehensive, but unusual handbook that covers a strange combination of topics ranging from an in-depth section on the biology of mollusc species, including clams, oysters and Pacific snails, to a section on the processing of surimi and surimi seafoods. The book includes chapters on human pathogens in fish and shellfish, seafood allergies and intolerances, and even a chapter on cookery, with recipes for hollandaise and horseradish sauce. It is difficult given the range of topics covered by the publication, to know what market the book has been aimed at. Most readers are likely to be interested in a limited number of the sections and have access to similarly detailed information in other more focused reference books. In Europe the book is likely

to have less appeal as many of the chapters have a distinct US bias. The book is also very expensive at £131.

■ **David Stone**
CEFAS Weymouth Laboratory

Zoonoses and Communicable Diseases Common to Man and Animals, Third Edition, Vol. 1 Bacterioses and Mycoses.

Scientific and Technical Publication No. 580
Edited by P.N. Acha & B. Szyfres
Published by Pan American Health Organization (2001)
US\$36.00, pp. 392
ISBN: 92-75-11580-X

This book provides a very useful and accessible source of reference information on zoonoses and communicable diseases common to man and animals. In particular, it brings together information on diagnosis, epidemiology and control of a wide range of the rarer, generally exotic diseases. This is particularly timely in light of the recent concerns on the use of agents like anthrax and plague for non-peaceful reasons and the continued displacement of animals and man due to, among other things, conflict and climate change. The bibliographies are a little historical and there is scant mention on the emerging importance of molecular tools to assist epidemiological and outbreak investigations in many diseases. Nevertheless, this book does provide a valuable one-stop source of reference for an eclectic group of diseases whose importance and profile has increased in recent times. The book is reasonably priced and will be of interest not only to workers in public health, medicine and veterinary medicine, but to those responsible for developing policies to limit the impact of many of these important emerging and zoonotic diseases. I for one will add this edition to my book cupboard.

■ **Chris Thorns**
Veterinary Laboratories Agency, Addlestone

Pathology and Pathogenesis of Human Viral Disease

By J.E. Craighead
Published by Academic Press (2000)
£86.95, pp. 447
ISBN 0-12-195160-X

This book is a comprehensive review of pathology associated with human viral infection. It covers all the major syndromes and describes the epidemiological, as well as the clinical and pathological aspects. There is very little mention of molecular biology and immunology and as a consequence, despite 'pathogenesis' appearing in the title, there is very little discussion around the mechanisms by which viruses cause disease. The volume lacks a general introduction, but launches straight into chapters dedicated to the different viral groups. As a result, the reader is encouraged to focus on a virus rather than to compare and contrast the pathogenic mechanisms used by different virus groups. The collection of figures showing gross and microscopic pathology is impressive; however, the remainder of the information in the book can be found in other texts. Its price is likely to restrict its purchase to institutions.

■ **Chris Ring**
Glaxo Smithkline R&D, Stevenage

Hepatitis C. Biomedical Research Reports Series

Edited by T.J. Liang & J.H. Hoofnagle
Published by Academic Press (2000)
£66.95, pp. 493
ISBN: 0-12-447870-0

This book provides a very impressive and up-to-date review of all aspects of hepatitis C infection, covering virology, molecular biology, epidemiology, pathology, prevention and treatment. Its chapters are written by well known researchers in the field and is probably the most comprehensive and useful review of the area

presently available. I could not recommend it more highly. The text is very detailed and yet very readable, making it suitable for anyone working in the area of Hepatitis C, both experienced researchers and graduate students alike. In this regard, it is a particular shame that the cover price is beyond the budget of most graduate students – a soft back version would be very welcome and undoubtedly result in greater sales!

■ **Chris Ring**
Glaxo Smithkline R&D, Stevenage

Books received

● **The Invisible Enemy: A Natural History of Viruses**

By D.H. Crawford
Published by Oxford University Press (2002)
P/B £8.99, pp. 275
ISBN: 0-19-856481-3

● **Microbiology, Fifth Edition**

By L.M. Prescott, J.P. Harley & D.A. Klein
Published by McGraw-Hill (2002)
£32.99, pp. 1,156
ISBN: 0-07-112259-1

july 02

INTERNATIONAL CONFERENCE: APPLICATIONS OF BIOMICS (GENOMICS, PROTEOMICS AND BIOINFORMATICS) IN THE RESEARCH AND DIAGNOSTIC LABORATORY

**PHLS Central Public Health Laboratory, London
1-2 July 2002**

CONTACT: Professor H.N. Shah, Conference June 2002, PHLS Central Public Health Laboratory, 61 Colindale Avenue, London NW9 5HT (Tel. 020 8358 3095; Fax 020 8205 7483; email hshah@phls.org.uk)

INTRODUCTION TO BIOINFORMATICS. A TWO-DAY COMPUTER LECTURE/HANDS-ON COURSE

University of Hertfordshire, Hatfield, 2-3 July 2002

CONTACT: Dr Ralph Rapley, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 285097; Fax 01707 286137; email r.rapley@herts.ac.uk; http://herts.ac.uk/natsci/STC)

RNA EXTRACTION AND ANALYSIS. A ONE-DAY LABORATORY/LECTURE COURSE

University of Hertfordshire, Hatfield, 4 July 2002

CONTACT: Dr Ralph Rapley (see above)

PCR METHODS AND APPLICATIONS. A ONE-DAY LABORATORY/LECTURE COURSE

University of Hertfordshire, Hatfield, 5 July 2002

CONTACT: Dr Ralph Rapley (see above)

DESIGN OF VACCINATION PROGRAMMES: FROM SERO-EPIDEMOLOGY TO COST-EFFECTIVENESS

**University of Warwick, Coventry
8-12 July 2002**

CONTACT: Dr Stephen Hicks, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL (Tel. 02476 523540; Fax 02476 523701; email s.j.hicks@warwick.ac.uk)

MICROSCIENCE 2002: WHERE SCIENCE MEETS MICROSCOPY

**ExCel London Docklands
9-11 July 2002**

CONTACT: Royal Microscopical Society, 37/38 St Clements, Oxford OX4 1AJ (Tel. 01865 248768; Fax 01865 791237; email info@rms.org.uk; www.microscience2002.org.uk)

12TH INTERNATIONAL BIODETERIORATION AND BIODEGRADATION SYMPOSIUM (BIOSORPTION AND BIOREMEDIATION II)

**Prague, Czech Republic
14-18 July 2002**

CONTACT: Prof Katerina Demnerova, Dept Biochemistry and Microbiology, Institute of Chemical Technology, Prague, Technicka 3, 166 28 Praha 6, Czech Republic (email: demnerok@vscht.cz; www.ibbs.vsch.cz)

ICRO TRAINING COURSE IN VIRUS ELIMINATION AND DETECTION

**ARC-Roodeplaas, Pretoria, South Africa
15-26 July 2002**

CONTACT: G.C. Bothma, ARC-Roodeplaas, Vegetable and Ornamental Plant Institute, Private Bag X293, Pretoria 0001, South Africa (Tel. +27 12 8419611; Fax +27 12 8081499; email gbothma@vopi.agric.za)

21ST ANNUAL SCIENTIFIC MEETING OF THE AMERICAN SOCIETY FOR VIROLOGY

**Lexington, Kentucky
20-24 July 2002**

CONTACT: Sidney E. Grossberg, Secretary-Treasurer, American Society for Virology, Department of Microbiology and Molecular Genetics, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226-0509, USA (Tel. +414 456 8104; Fax +414 456 6566; email segrossb@mcw.edu; www.mcw.edu/asv)

27TH INTERNATIONAL HERPESVIRUS WORKSHOP - 2002

**Cairns, Australia
20-26 July 2002**

CONTACT: IHV 2002 Workshop Secretariat, GPO Box 128, Sydney NSW 2001, Australia (Tel. +61 2 9262 2277; Fax: +61 2 9262 3135; email: herpesvirus@tourhosts.com.au; www.herpessworkshop.net)

august 02

54TH HARDEN CONFERENCE: ENZYMOLOGY: EMERGING TRENDS AND FUTURE PROSPECTS

**St Martin's College, Ambleside
20-24 August 2002**

CONTACT: The Meetings Office, Biochemical Society, 59 Portland Place, London W1B 1QW (Tel. 020 7580 3481; Fax 020 7637 7626; email meetings@biochemistry.org)

BIOFILMS IN INDUSTRY, MEDICINE AND ENVIRONMENTAL BIOTECHNOLOGY: THE SCIENCE

**Galway, Ireland
24-29 August 2002**

CONTACT: Dr Therese Mahony (email therese.mahony@nuigalway.ie; www.nuigalway.ie/microbiology/mel800/bio-imeb.html)

55TH HARDEN CONFERENCE: DYNAMICS OF MEMBRANE TRAFFIC

**St Martin's College, Ambleside
25-30 August 2002**

CONTACT: The Meetings Office, Biochemical Society (see above)

ESBES-4 LIFE: SCIENCE AND TECHNOLOGY. 4TH EUROPEAN SYMPOSIUM ON BIOCHEMICAL ENGINEERING SCIENCE

**Delft, The Netherlands
28-31 August 2002**

CONTACT: email esbes-4@tnw.tudelft.nl; www.esbes4.tnw.tudelft.nl

aug-sept 02

CELLULAR AND MOLECULAR BASIS OF REGENERATION. EUROCONFERENCE ON THE STEM CELLS INVOLVED IN TISSUE REPAIR AND REGENERATION PROCESSES

**Castelvecchio Pascoli, Italy
31 August-5 September 2002**

CONTACT: Dr J. Hendekovic, European Science Foundation, EURESCO Unit, 1 quai Lezay-Marnésia, 67080 Strasbourg Cedex, France (Tel. +33 388 7671 35; Fax +33 388 36 69 87; email euresco@esf.org; www.esf.org/euresco/02/1c02177)

september 02

PROTEIN TECHNIQUES. A TWO-DAY LABORATORY COURSE

**University of Hertfordshire
Hatfield, 2-3 September 2002**

CONTACT: Prof. John Walker, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284546; Fax 01707 284510; email j.m.walker@herts.ac.uk; http://herts.ac.uk/natsci/STC)

NUCLEIC ACID TECHNIQUES. A THREE-DAY LABORATORY COURSE

**University of Hertfordshire, Hatfield
4-6 or 11-13 September 2002**

CONTACT: Dr Virginia Bugeja, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284590; Fax 01707 286137; email v.bugeja@herts.ac.uk; http://herts.ac.uk/natsci/STC)

EIGHTH EUROPEAN WORKSHOP ON VIRUS EVOLUTION AND MOLECULAR EPIDEMIOLOGY

**Leuven, Belgium
4-11 September 2002**

CONTACT: Prof. Anne-Mieke Vandamme, AIDS Research Unit, Rega Institute & University Hospitals, Minderbroedersstraat 10, B-3000 Leuven, Belgium (email annemie.vandamme@uz.kuleuven.ac.be; www.kuleuven.ac.be/aidslab/veme.htm)

DANGEROUS PATHOGENS 2002

**Center Parcs, Longleat
9-11 September 2002**

CONTACT: Sonya Rowe, Chemical and Biological Sciences, Room A201, Building 7, Dstl Porton Down, Salisbury SP4 0JQ (Fax 01980 614307; email scrowe@dstl.gov.uk)

10TH BIENNIAL AND CENTENARY CONFERENCE OF THE CHALLENGER SOCIETY FOR MARINE SCIENCE

**Plymouth, Devon
9-13 September 2002**

CONTACT: email challenger@mail.pml.ac.uk; www.challenger2002.org.uk

UNDERSTANDING THE USE OF MASS SPECTROMETRY IN PROTEOMICS. A ONE-DAY LECTURE COURSE

University of Hertfordshire, Hatfield, 18 September 2002

CONTACT: Prof. John Walker (see above)

october 02

CHINA HI-TECH FAIR/BIOTECH 2002

**Shenzhen, PR China
12-17 October 2002**

CONTACT: Brenda Yau, Coastal International Exhibition Co. Ltd, Room 3808, China Resources Building, 26 Harbour Road, Wanchai, Hong Kong (Tel. +852 2827 6766; Fax +852 2827 6870; email general@coastal.com.hk)

may 03

ACHEMA 2003: 27TH INTERNATIONAL EXHIBITION-CONGRESS ON CHEMICAL ENGINEERING, ENVIRONMENTAL PROTECTION AND BIOTECHNOLOGY

**Frankfurt am Main, Germany
19-24 May 2003**

CONTACT: DECHEMA e.V., PO Box 1501 04, D-60061 Frankfurt am Main, Germany (Tel. +49 69 7564 0; Fax +49 69 7564 201; email achema@dechema.de; www.achema.de)

Comment

MMR vaccine

There is a serious decline in the vaccination of young children against measles, mumps and rubella due to concerns about safety and possible links between the triple vaccine and bowel disease and autism. Drs Afzal and Minor explore the scientific background to this important issue.

Measles, mumps and rubella (MMR) vaccine was introduced to the UK National Immunization Schedule in October 1988 and now about 600,000 doses are distributed annually. The vaccine is licensed by the government through the Medicines Control Agency (MCA) and contains three live viruses (measles, mumps and rubella). Their ability to cause disease has been reduced by growing each virus in a series of embryonated hen's egg and chicken embryo fibroblast (CEF) cells. Each vial of the finished triplet formulation contains a well defined amount of each component virus that is known to be sufficient to provoke effective immunity in the vaccine recipients. Only batches meeting the required specifications for potency, identity and thermostability after laboratory testing are released for use.

In Britain MMR vaccine is administered under a two-dose vaccination schedule in which the first dose (primary immunization) is given at or around 12 months of age while the second dose (booster immunization) is given between 5 and 7 years. Two doses are needed to raise immunity in the population to 95 %, the level required to break the transmission of measles, mumps or rubella virus circulating in the community. A single immunization, at best, confers immunity in only 80–90 % of vaccine recipients, since about 20 % of the target population either fails to receive the primary dose altogether or fails to respond to the vaccine.

● Adverse events following immunization

MMR vaccine is highly efficacious and has no undesirable effects in most recipients. However, some children following vaccination may have symptoms of fever, skin rash or burning/stinging at the site of injection or other mild local reactions. Other rare reactions include sore throat, malaise, swollen glands, nausea, diarrhoea, low numbers of blood platelets, livid spots, and febrile and afebrile convulsions. Aseptic meningitis following MMR vaccination has been mainly associated with a specific brand of vaccine that contained the Urabe strain as a mumps virus component; this was withdrawn from the UK immunization programme in 1992. MMR vaccines currently licensed in the USA, UK and most other European countries contain the Jeryl Lynn strain as the mumps component which has not been linked to post-vaccinal meningitis.

However, in 1993 Dr Andrew Wakefield's group at the Royal Free Hospital, London, proposed that early measles infection could be linked to the onset of Crohn's disease later in life. Independent attempts to detect any genes of the measles virus in tissues as reported by this group failed and epidemiological studies concluded no link.

Subsequently, it was suggested that measles vaccine given as MMR was also linked with a specific gut syndrome, termed 'Ileal-lymphoid-nodular-hyperplasia' which was associated with Autistic Spectrum Disorder (ASD).

● MMR vaccine safety reviews

The alleged link between MMR vaccination and bowel inflammation leading to autism has raised serious concerns over the clinical safety of MMR vaccine. This has been extensively debated in scientific fora worldwide. In the UK between 1998 and 2001 bodies such as the Medical Research Council (MRC), the Medicine Control Agency (MCA), the Committee on Safety of Medicine (CSM) and the Joint Committee on Vaccination and Immunization (JCVI) conducted scientific reviews of its safety. Experts concluded that there was no evidence to support any association between MMR vaccine and inflammation of the bowel and autism. Following each review it was recommended that vaccination with MMR should be continued in line with the National Immunization Programme. More recently, the UK Department of Health commissioned the MRC to conduct a full review of all aspects of autism research. Although the report failed to identify any causal association between MMR vaccination and autism, it highlighted several key factors, including the environment, genetic predisposition, physiological and dietary aspects and other psychological abnormalities that require further investigation.

The issue of MMR vaccine in relation to juvenile autism has also been extensively discussed in the USA, including in a congressional hearings committee meeting and in expert panels formulated by the Institute of Medicine (IOM) and by the American Academy of Pediatrics. The review panel of the IOM committee rejected the claims of the causal relationship between MMR vaccine and autism. However, it warned that the possibility that MMR vaccine might contribute to ASDs in a subset of recipients could not be ruled out. One of their recommendations was the need to conduct further research on the possible occurrence of ASD in a small number of children following MMR vaccination and that the intestine of children with ASD should be tested for the possible presence of measles vaccine strain. A recent report from Professor John O'Leary's group, in collaboration with Andrew Wakefield's group, of the presence of measles virus fragments in the gut of autistic enterocolitis patients is thus of considerable interest. It is not yet known whether the virus sequences amplified were identical to the sequence of the vaccine strain or to any wild-type measles strain. These findings have not been verified independently, and in our opinion that must be done before any firm conclusion of the possible links between measles, MMR, and bowel inflammation and autism can be drawn.

● **Dr M.A. Afzal is a Principal Scientist and Dr P.D. Minor is Head, of the Division of Virology, NIBSC, South Mimms, Potters Bar EN6 3 QG, UK. email mafzal@nibsc.ac.uk; pminor@nibsc.ac.uk**

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