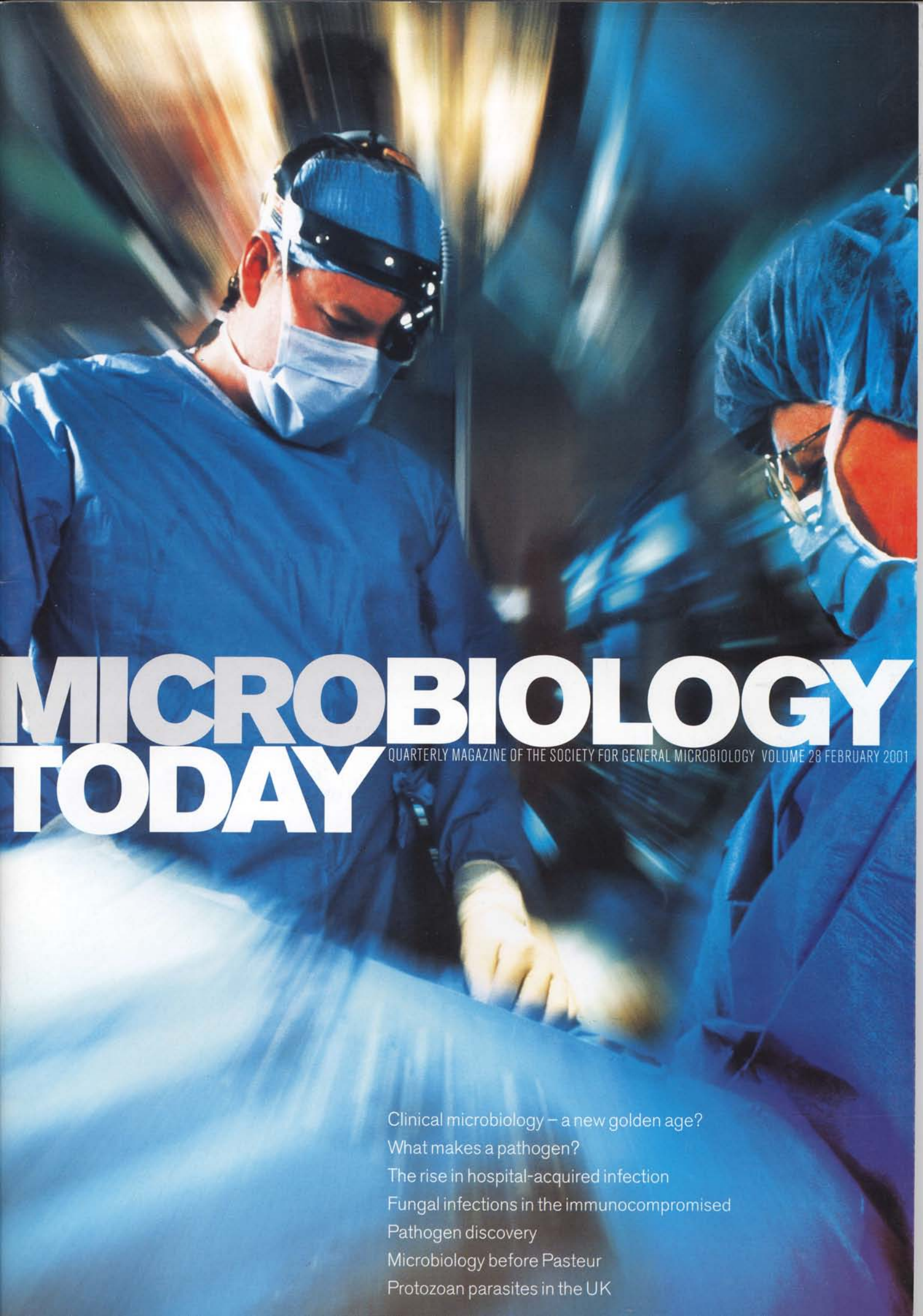

MICROBIOLOGY TODAY

QUARTERLY MAGAZINE OF THE SOCIETY FOR GENERAL MICROBIOLOGY VOLUME 28 FEBRUARY 2001

Clinical microbiology – a new golden age?
What makes a pathogen?
The rise in hospital-acquired infection
Fungal infections in the immunocompromised
Pathogen discovery
Microbiology before Pasteur
Protozoan parasites in the UK

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Above: The rise in hospital-acquired infection. How serious is the threat to our health care? *Courtesy Larry Mulvehill/ Science Photo Library*

Vol. 28, Part 1, February 2001

In this issue we celebrate the birth of the new SGM Clinical Microbiology Group. Convener Stephen Gillespie starts the ball rolling with an overview of the science and what the new group hopes to achieve on p. 3.

The importance of modern molecular techniques in advancing our knowledge of pathogens and how they work is emphasized in several articles. Tony Hart and Craig Winstanley investigate why some microbes are harmful on pp. 4–6, whilst Paul Kellam and Robin Weiss (pp. 16–18) show how new pathogens are being discovered.

Peter Hawkey takes a look at one of the knottiest problems facing clinical microbiologists – antibiotic-resistant bacteria – highlighting infections acquired in hospital (pp. 7–9) and Ad C. Fluit and Franz-Josef Schmitz (pp.14–15) describe how new methods can speed up their detection.

Fungal infections are also a cause for concern, particularly in the immuno-compromised, as Marc Mendelson shows (pp. 10–13) and Tim McHugh covers the risks from protozoan parasites in the UK (pp. 22–23).

Pasteur did not make all the significant discoveries in microbiology. As Milton Wainwright shows (pp. 19–21) many important microbes were known before his fermentation studies were carried out.

Other topics include how to have fun with fungi in the north of England (pp. 28–29), promoting science on the radio (p. 30) and a preview of the main symposium at the Society's spring meeting on the threats from virus infections (p. 33). Last but not least on p. 39 we welcome news of our sister organization in the USA – the Society for Industrial Microbiology.

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

Articles

Regular Features

Other Items

Letters

In praise of Hoyle and Wickramasinghe

Dear Editor

While I enjoyed the article by Don Cowan and Monica Grady (*Microbiology Today* **27**, 174–177) in which they discussed panspermia, I feel that they might have given more emphasis to the role played by Hoyle and Wickramasinghe in making this idea respectable (to their credit they provide a reference to these authors). Although Lord Kelvin is usually considered to have been the first to espouse the scientific view of panspermia (during the late 1880s), it was Hoyle and Wickramasinghe, through their popular books and scientific papers, who have made it a truly credible hypothesis. Unfortunately, these two astronomer-mathematicians have gone the way of many heretics who suffer from being labelled as 'mad' only to find themselves written out of the story when the one-time 'lunacies' are transmuted into orthodox science. Since we talk about the Darwin-Wallace theory of evolution, why not the Hoyle-Wickramasinghe theory of panspermia?

By the way, I am looking forward to the day when their other heresies become acceptable, namely that influenza and other diseases arrive on earth from space and that evolution has been influenced by DNA originating from the same source.

● ***Milton Wainwright, Department of Molecular Biology and Biotechnology, University of Sheffield, Sheffield S10 2TN***

Mycology today

Dear Editor

We are writing, on behalf of the British Society for Medical Mycology, in response to the article by Tony Trinci in the August 2000 issue of your magazine (*Microbiology Today* **27**, 115). We are delighted that he has highlighted the importance of fungi to man, particularly the increasing morbidity and mortality caused by invasive fungal infection. The annual incidence of candidaemia in the UK is now 11·2 per 1000 beds (1), a figure similar to that found in the US where *Candida* species are the fourth commonest isolate from blood cultures (2). Similarly, the incidence of invasive aspergillosis has increased 14-fold over a decade in Europe (3) and in some groups, such as those undergoing allogeneic bone marrow transplantation, the mortality is in excess of 90% (4).

The decline of mycology, which forms the subject of Professor Trinci's article, also concerns us greatly. We have seen the numbers of senior mycologists involved with service work in the UK gradually fall over the last decade, such that there are now fewer than 10 left and three of these are expected to retire in the next eight years (5). Professor Trinci makes the point that departments of microbiology do not feel the need to re-appoint mycologists to their staff once they have gone. However, he feels that medical mycology is an exception, citing Manchester as an example, having three medically qualified individuals with research interests in the field of medical mycology. Manchester is certainly an active medical mycology research centre and indeed there are seven or so such academic foci around the UK, but, regrettably, there are fewer and fewer trained mycologists in the service sector. As the article states, we are seeing increasing numbers of immuno-compromised patients as a consequence of advances in medical care, but this is not being linked with the infrastructure needed to manage their infectious complications.

We welcome Professor Trinci's call to forge stronger links with fellow societies with an interest in mycology (although we would point out that our society was renamed some years ago and is no longer known as the British Society for Mycopathology!) and, for example, we are in active discussions with the British Mycological Society and other organizations with mycological interests. A strong academic base is essential to sustain the speciality, but we need to find a way of encouraging scientists into the service sector by providing adequate training programmes and a suitable career structure. Without these a downward spiral is inevitable, but we aim to prove Professor Trinci wrong in believing that it may be too late to reverse this decline.

● ***Dr C.C. Kibbler MA FRCP FRCPath, Chair British Society for Medical Microbiology Training Working Party***
● ***Professor R.J. Hay DM FRCP FRCPath, President of the British Society for Medical Microbiology***

References

1. **Ainscough, S., Barnes, R., Gant, V., Gransden, W.R., Holliman, R., McCrae, B., Perry, J., Wilson, J., Schelenz, S. & Kibbler, C.C. (2000).** Blood stream infections due to *Candida* species in England and Wales: Data from the ECMM epidemiological survey of candidaemia in Europe. Abstract. European Confederation of Medical Mycology meeting, Barcelona, November 2000.

2. **Fridkin, S.K. & Jarvis, W.R. (1996).** Epidemiology of nosocomial fungal infections. *Clin Microbiol Rev* 9, 499–511.

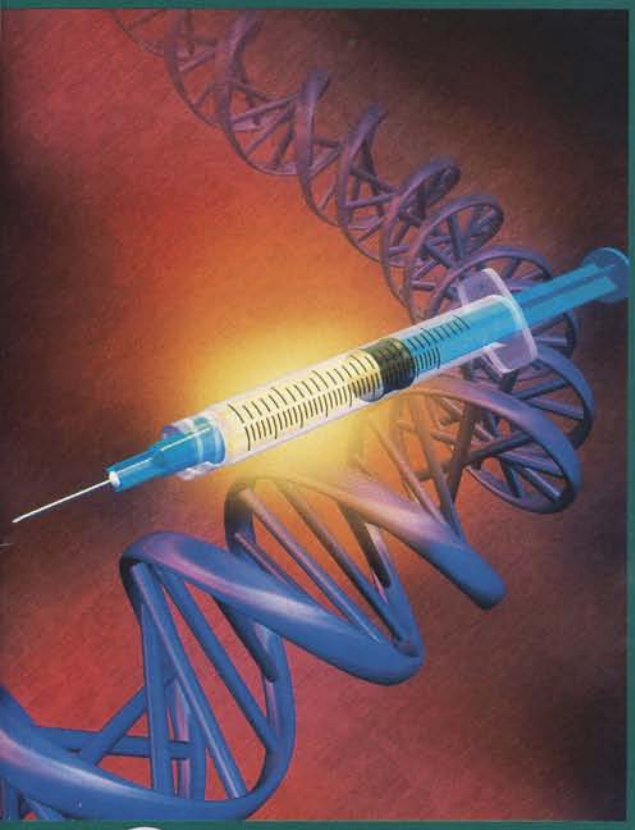
3. **Groll, A.H., Shah, P.M., Mentzei, C., Schneider, M., Just-Nuebling, G. & Huebner, K. (1996).** Trends in the postmortem epidemiology of invasive fungal infections at a university hospital. *J Infect* 33, 23–32.

4. **Denning, D.W. & Stevens, D.A. (1990).** Antifungal and surgical treatment of invasive aspergillosis: review of 2,121 published cases. *Rev Infect Dis* 12, 1147–1201.

5. **Kibbler, C. & Hamilton, A. (2000).** Medical mycology in the United Kingdom: time to stop the dry rot. *Commun Dis Publ Health* 3, 80–81.

Clinical microbiology: a new golden age?

Stephen Gillespie



Clinical microbiology has never been more important and the SGM has formed a new Group to cater for the needs of practitioners and researchers. Stephen Gillespie, Convener of the Group, describes the current state of clinical microbiology in the context of the history of the science. For details of the Group's first symposium, see the enclosed programme booklet.

The Spring 2001 meeting at Heriot-Watt University sees the birth of a new interest group within the Society for General Microbiology: Clinical Microbiology. It is intended to be a focus for microbiologists who are actively involved in clinical practice whether as doctors, clinical scientists, dentists or veterinary practitioners. The interests of the group will be in clinical diagnosis, epidemiology and therapy of microbial infections, and will complement the interests of the Clinical Virology and Microbial Infection Groups with whom joint meetings will be held in the future. The inaugural symposium addresses the important issue of antibiotic resistance and international speakers have been invited to cover the diverse aspects of this complex topic from evolution of antibiotics to rapid diagnosis in clinical practice.

To celebrate the birth of the new group, clinical microbiology is the theme of this issue of *Microbiology Today*. Just over 100 years ago the revolutionary 'germ theory' of disease coupled with the technological leap made by Robert Koch's use of dyes, developments in the microscope and the introduction of agar-based isolation media brought about the first golden age of clinical microbiology. Month by month, new pathogens and disease processes were described. These advances in knowledge were linked to improvements in treatment through aseptic surgery, vaccines and finally antimicrobial chemotherapy. Now, as we stand on the cusp of the third millennium we can look at the possibility of a new 'golden age'. The technological revolutions brought about by genomics, proteomics and structural biology have enhanced our ability to answer the critical scientific questions in infection. As Tony Hart and Craig Winstanley outline in this issue, the views about what makes an organism a pathogen have developed from the days of Koch, whose postulates delineated the scientific evidence to identify an organism as an unequivocal pathogen. Our increasing understanding of the role of host factors and immune defence have made it necessary to revise these ideas. The control of many of the epidemic diseases has shifted attention to the rise of antibiotic-resistant bacteria in our hospitals. Some of these pathogens have developed resistance to all of the main antimicrobials, returning us to the pre-antibiotic era in some cases as Peter Hawkey describes. The nature of hospital patients has also changed with an increase in the proportion who are severely immunocompromised. This permits organisms such as fungi to become important invasive pathogens. Marc Mendelson describes the impact of these agents on clinical practice.

The technological revolution has finally started to produce an impact in clinical microbiology laboratories. Until relatively recently the methodology had remained largely unchanged from the days of Koch, but now new DNA and RNA amplification techniques are playing an increasing role in routine diagnosis. A.C. Fluit and F.-J. Schmitz review some of the approaches that are being introduced into diagnostic laboratories. The first golden age was one of new pathogen discovery and once again new pathogens are being described by the use of DNA- and RNA-based amplification methodology. Paul Kellam and Robin Weiss describe this process and some of the new agents that have been identified by these methods.

We all have a tendency to romanticize the past, peopling it with heroes who saw clearly what the fools around them could not. We forget the uncertainties, difficulties and the conflicts that previous microbiologists suffered to publish and promote their revolutionary ideas. If the last few years of the 19th century were exciting times to be a clinical microbiologist , then we can be sure that the early part of the 21st century will be equally challenging. Armed with our new concepts of pathogenicity and new technological tools we can all expect important discoveries that will result in the new treatment and preventive measures that will benefit mankind in the future.

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PHOTO COURTESY KEN EWARD/ SCIENCE PHOTO LIBRARY

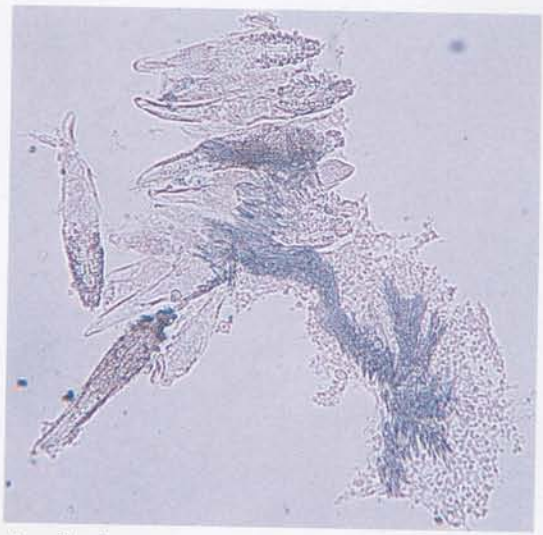
What makes a pathogen?

C. Anthony Hart & Craig Winstanley

Large numbers of micro-organisms inhabit the human body. In most cases our normal flora is beneficial or harmless. Tony Hart and Craig Winstanley explore why some microbes are pathogenic.

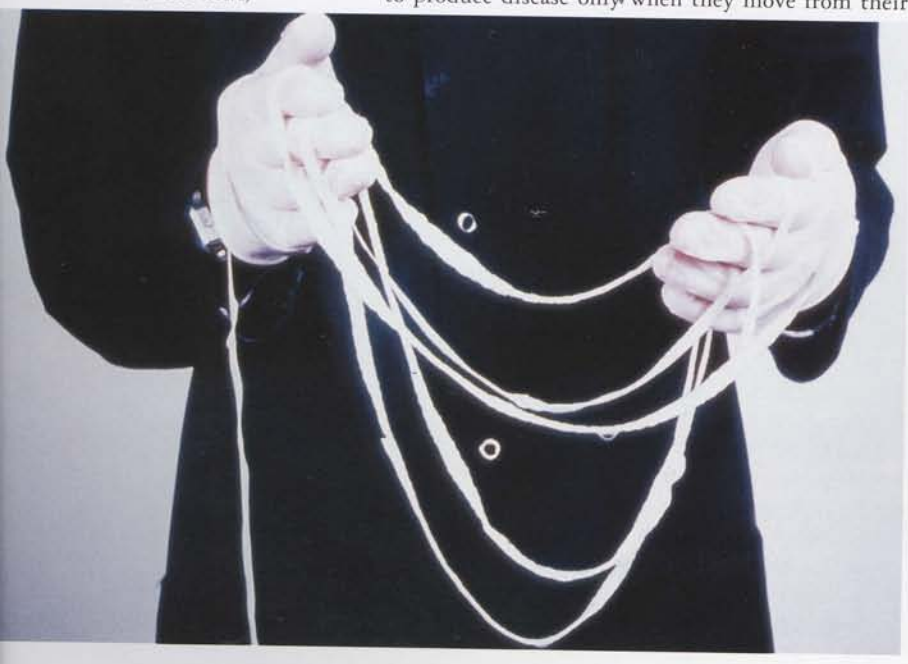
It is estimated that each adult human is made up of approximately 10^{14} cells. However, only 10% of these are human, the remainder make up the normal flora that coat our body surfaces inside and out. Although the majority of the normal flora are bacteria, other kingdoms are present. Viruses, such as most of the herpesviruses, papovaviruses, adenoviruses and even HIV, can be present for long periods without overt disease. Whether they are truly normal flora is a moot point. All of us carry a variety of fungi, including *Candida* and *Malessazia* spp. We can asymptomatically excrete protozoa, including various *Entamoeba* and *Trichomonas* spp. as well as more complex parasites such as *Endolimax nana*, *Taenia saginata* (Fig. 1) or even *Enterobius* spp. We also play host to insects such as the follicle mite, *Demodex follicularis* (Fig. 2). Clearly we are all walking zoos.

In most cases our normal flora is beneficial and absence of, or major changes in normal flora are detrimental. The majority of the intestinal normal flora are anaerobic bacteria and they also contribute greatly to non-specific immunity in producing colonization resistance, by competing for receptors and producing antimicrobial compounds. It is now clear that early intestinal colonization of newborn children by *Bacteroides fragilis* is important in maturation of humoral immunity. Thus these 'normal' bacteria are also essential for the development of one arm of the specific immune system. The intestine is the major reservoir of normal flora and it is no coincidence that 70% of the immune cells in the human body reside here. Although there are competent pathogens such as *B. fragilis* and *Clostridium perfringens* among the normal flora, anaerobes tend to produce disease only when they move from their site of colonization to contiguous areas of normally sterile tissue, often as a result of surgery or intestinal perforation. In contrast, aerobic bacteria such as *Neisseria meningitidis*, *Haemophilus influenzae* and *Streptococcus pneumoniae* which colonize the upper airways, and *Escherichia coli* and *Salmonella enterica* which inhabit the intestine, have a great propensity to turn from harmless commensals into ravening pathogens. Our understanding of what makes a pathogen and the mechanisms used to subvert normal human cellular activities has increased exponentially over the last decade.



RIGHT:
Fig. 2. Follicle mites.
COURTESY T. HART

BELOW:
Fig. 1.
A man demonstrating his own beef tapeworm.
REPRINTED WITH PERMISSION FROM *DIAGNOSIS IN COLOUR: MEDICAL MICROBIOLOGY* (T. HART & P. SHEARS, 1996, MOSBY WOLFE)



E. coli is the major aerobic Gram-negative bacterium in the intestinal normal flora, [we excrete about 10^7 colony forming units (c.f.u.) per gram of faeces]. It is estimated that *E. coli* and *S. enterica* diverged some 100 million years ago, whereas man has been developing for a mere 1·5 million years. The majority of the differences between the two genera result from acquisition of large tracts of DNA termed loops, or genomic islands. Some islands encode metabolic functions, some antibiotic or other resistances and others are involved in pathogenicity (pathogenicity islands, PI). PIs can be found in pathogens (but not their non-pathogenic variants), both Gram-positive and Gram-negative bacteria, and in animals and plants. These islands contain 20–40 open reading frames (ORFs), many of which are similar in PIs in different Gram-negative pathogens. They have G + C mol% ratios different from the rest of the chromosome, are often inserted in proximity to tRNA genes (implying that their acquisition might be mediated by bacteriophages) and can be unstable. In Gram-negative bacteria, some PIs encode a secretion system (type III or IV) that is used to deliver effector molecules directly into or onto host cells (Tables 1 and 2).

The discovery of PIs and their secretion systems has ushered in a new and exciting era in bacteriology and is transforming our understanding of microbial pathogenesis. It is now clear that there is extensive biochemical

cross-talk between the bacteria and their target eukaryotic hosts, encoded by the PIs and delivered by their secretion systems.

Type III secretion systems (TTS)

TTS are assembled and disassembled according to the environmental conditions in which the bacterium is placed. For example, *in vitro*, removal of Ca^{2+} or change in temperature have been known to initiate TTS assembly in *Yersinia* and *Bordetella* spp., respectively. *In vivo*, it is likely that contact with the eukaryotic host cell is the trigger. TTS are made up of over 20 proteins that assemble to make a channel from the bacterial cytoplasm through both cell membranes to the exterior and a surface structure which can be pilus-like [e.g. in enteropathogenic *E. coli* (EPEC) or *Pseudomonas syringae*] or a needle-complex (e.g. in *S. enterica* or *Shigella flexneri*). In each case the surface structures are used to inject effector molecules through the eukaryotic plasma membrane or, in the case of internalized bacteria, through endocytotic vacuoles. The TTS structural proteins are highly conserved between pathogens. For example, we were able to delineate the TTS of *Burkholderia pseudomallei* by using probes from the TTS of the plant pathogen *Ralstonia solanacearum*. However, by using experiments to trans-complement mutations in TTS, at least three families have been delineated, typified by those related to the Ysc (*Yersinia* secretion) TTS and to the *Salmonella* pathogenicity islands 1 and 2 (SPI-1 and 2). Some of the proteins of TTS resemble

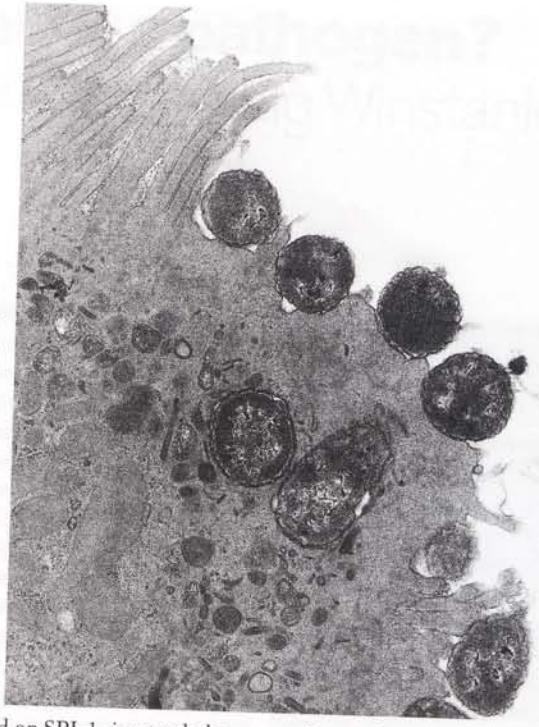
Table 1. Examples of TTS

	Bacterium	Genetic location	Effector(s)	Effect on host cell	Disease
Plant pathogens	*Erwinia amylovora*	Chromosome	HrpN	Hypersensitive response	Soft-rot, Fire blight necrosis
	Pseudomonas syringae	Chromosome	Harpins	Hypersensitive response	Bacterial speck
	Xanthomonas campestris	Chromosome	Harpins	Hypersensitive response	Bacterial spot (tomato, pepper)
	Ralstonia solanacearum	Plasmid	PopA1	Hypersensitive response	Bacterial wilt (potato)
	Rhizobium spp.	Plasmid	Y4xL, NoLX	Nodulation	Symbiont
Animal pathogens	*Bordetella bronchiseptica*	Chromosome	Products of *bopD, bopN* Bsc22	Induction of apoptosis Inactivation of NFκ-B	Kennel cough (dogs and cats) Atrophic rhinitis (pigs)
	Burkholderia pseudomallei	Chromosome	Unknown	Unknown	Melioidosis
	*Chlamydia psittaci**	Chromosome	Unknown	Unknown	Atypical pneumonia
	EHEC, EPEC†	Chromosome	Tir, Esps	Own receptor (Tir) Cytoskeletal rearrangement	Diarrhoea
	Pseudomonas aeruginosa	Chromosome	Exotoxins S,T,U,Y	ADP ribosylation, cytotoxicity	Opportunist pathogen
	Salmonella enterica (SPI-1)	Chromosome	Sops, Sips	Enterocyte invasion Induction of apoptosis	Diarrhoea
	Salmonella enterica (SPI-2)	Chromosome	SpiC	Invasion into tissues	Diarrhoea, Septicaemia
	Shigella spp.	Plasmid	Ipas	Membrane ruffling, apoptosis Phagosome lysis, cell invasion	Dysentery
	Yersinia spp.	Plasmid	Yops	Cytotoxic, F-actin disruption Inhibition of phagocytosis	Plague, Diarrhoea

*See 'Hot off the Press', p. 36. †EHEC, Enterohaemorrhagic *E. coli*; EPEC, enteropathogenic *E. coli*.

Table 2. Examples of TFS

	Bacterium	Secreted structures	Activity in host cell	Disease
Plant pathogens	*Agrobacterium tumefaciens*	T-DNA, VirE2, VirF	Oncogenesis	Crown gall
Animal pathogens	*Bartonella* spp.	Unknown	Intracellular survival	Cat-scratch fever, Oroya fever, Trench fever
	Bordetella pertussis	Pertussis toxin	ADP ribosylation of GTP-binding proteins	Whooping cough
	Brucella suis	Unknown	Intracellular survival	Brucellosis
	Helicobacter pylori	CagA protein	Host cell cytoskeletal rearrangement	Gastritis, Peptic ulcer, Gastric carcinoma
	Legionella pneumophila	Unknown	Survival and growth in macrophages	Pneumonia (Legionnaire's disease)
	Rickettsia prowazekii	Unknown	Intracellular survival	Louse-borne typhus
	Wolbachia spp.	Unknown	Unknown	Obligate endosymbiont of insects and filaria



RIGHT:
Fig. 3. Electron micrograph of jejunal mucosa with closely adherent EPEC that have produced localized effacement of the brush border. Two bacteria have also penetrated inside the enterocyte. COURTESY T. HART

those of flagella assembly systems which may give a clue as to their evolutionary origin.

TTS are used to secrete effector macromolecules powered by ATP. The genes for such effectors can be found on the same PI as the TTS, on different PIs or even in entirely different regions of the bacterial chromosome. Indeed, SopE, which is secreted by the TTS encoded on SPI-1, is encoded on a cryptic P2-like phage. How synthesis and secretion are co-ordinated with the assembly of the TTS is not entirely clear but it is known to involve a new type of small cytosolic chaperone which may also act as a pilot to attach the effector molecule to the cytoplasmic end of the TTS.

In general the effector molecules can be classified as those with enzymic activity, those that affect the cytoskeleton and those that interfere with intracellular signalling. The enzymic activities include phosphotyrosine phosphatases (e.g. YopH in *Yersinia* or SptP in *Salmonella*), serine-threonine kinase (e.g. YopO), inositol phosphate phosphatase (SopB), ADP-ribosyltransferase (ExoT in *P. aeruginosa*) and adenylate cyclase (ExoY). Effects on the cytoskeleton include stimulation leading to pinocytosis (SipA, SopE and IpaA in *Salmonella* and *Shigella*) and disruption leading to cytotoxicity or inhibition of phagocytosis (e.g. YopE, YopH, YopT or ExoS). Those interfering with intracellular signalling include YopP, which inhibits the transcriptional activator NFκ-B and the mitogen-activated protein kinases (MAPK), ERK1/2, p38 and JNK. This leads to a decreased expression of TNF-α and other pro-inflammatory cytokines, thus dampening the inflammatory response. Recently the TTS of *Bordetella bronchiseptica*, which causes atrophic rhinitis has been shown to secrete effectors which both inhibit NFκ-B activation and induce apoptosis. SipB (*Salmonella*) and its homologue IpaB (*Shigella*) bind to caspase I and induce apoptosis. Finally, one of the effectors secreted by the TTS in EPEC is Tir (transferable intimin receptor). This inserts into the host-cell membrane and acts as a receptor for intimin, a protein on the surface of EPEC, thus facilitating intimate attachment that is the hallmark of attaching-effacement induced in enterocytes by EPEC (Fig. 3).

Type IV secretion systems (TFS)

Originally a family of sec-dependent autotransporters, including the IgA1 proteases of pathogenic *Neisseria* spp. and *H. influenzae* were classified as TFS. Nowadays, the term is reserved for secretion systems built from components of conjugation machinery. Interestingly, TFS can export large nucleoprotein complexes (e.g. T-DNA from *Agrobacterium tumefaciens*), A/B subunit toxins (e.g. pertussis toxin from *Bordetella pertussis*) and monomeric proteins (e.g. CagA from *Helicobacter pylori*).

Pertussis toxin has five B (toxophore) subunits and one A unit with ADP ribosylation activity similar to both diphtheria and cholera toxins. The A and B subunits are delivered by a two-step process. They are first transported across the inner membrane and then assemble in the periplasmic space before being transported across the outer membrane.

CagA is a monomeric 145 kDa protein encoded on the *cag* pathogenicity island of *H. pylori*. It is secreted by a TFS and induces signal transduction in gastric cells, resulting in tyrosine phosphorylation of itself and other proteins adjacent to bacterial attachment. It also appears to lead to cytoskeletal rearrangements which might be responsible for the attaching-effacement activity also induced by *H. pylori*.

Conclusions

From the foregoing we hope it is apparent that medical bacteriology has entered a new and exciting era. It poses great challenges to medical microbiologists in that not only do we need to have understanding of microbial disease and molecular microbiology, but also of mammalian cell biology. However, the rewards will be great, perhaps resulting in new antibacterial agents, vaccines and vaccine delivery systems, and new insights into how our own cells work.

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Further reading

Christie, P.J. & Vogel, J.P. (2000). Bacterial type IV secretion: conjugation systems adapted to deliver effector molecules to host cells. *Trends Microbiol* 8, 354–360.

Mecsas, J. & Strauss, E.J. (1996). Molecular mechanisms of bacterial virulence: Type III secretion and pathogenicity islands. *Emerg Infect Dis* 2, 271–288.

Smith, W. & others (2000). The activities of bacterial pathogens *in vivo*. *Philos Trans R Soc* 355, 547–712.

Spratt, B.G. (1998). Resurgent/emergent infectious diseases. *Br Med Bull* 54, 521–765.

Winstanley, C. & Hart, C.A. (2001). Type III secretion systems and pathogenicity islands. *J Med Microbiol* (in press).

The enemy within – hospital-acquired, antibiotic-resistant bacteria

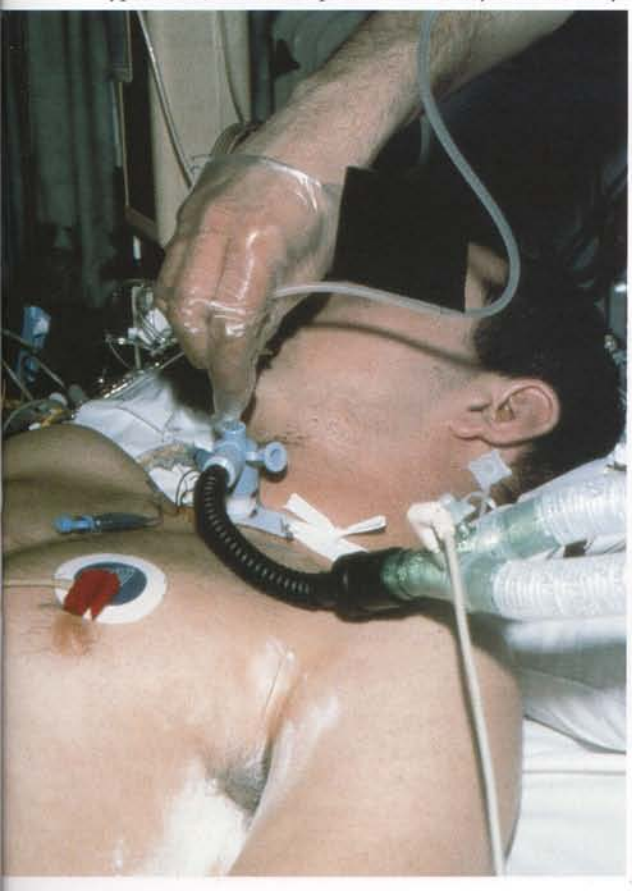
Peter Hawkey

It is perhaps ironic that the recognition of the aetiology of hospital-acquired (nosocomial) infection was by the surgeon and self-taught microbiologist, Joseph Lister. In 1865, at the Edinburgh Royal Infirmary, the mortality following amputation of a limb was 43%, the principal cause of death being bacterial sepsis. Mortality was reduced to single figures by the introduction of the antiseptic phenol spray which bathed the operative site and the use of post-operative dressings of phenol. Such was the impact of this medical breakthrough that he was the first member of the medical profession to be elevated to the Peerage as Lord Lister of Lyme.

Quite quickly, antiseptic surgery passed out of fashion to be replaced by aseptic surgery, championed in the UK by surgeons such as Lawson Tait. The subsequent introduction of effective antimicrobial therapy further dramatically reduced the incidence and importance of nosocomial infection.

The rise of nosocomial infections

The emergence in the late 1950s of strains of *Staphylococcus aureus* resistant to penicillin, erythromycin, tetracycline and chloramphenicol, which also were good at surviving and spreading in hospitals, such as phage type 80/81, led to a sharp rise in morbidity and mortality.



This was effectively terminated when the isoxyl penicillins, resistant to penicillinase, such as cloxacillin, were introduced. The subsequent development of both intensive care and treatment for cancers in the 1960s and 1970s created a new group of vulnerable patients prone to infection caused by Gram-negative bacteria such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Serratia marcesens* (Fig. 1). The heavy use of gentamicin in turn drove the emergence of resistance mediated by amino-glycoside-inactivating enzymes, which by virtue of being located on transposons, integrons and plasmids resulted in 'epidemics' of resistance genes spreading amongst different species and genera. The availability for the first time of molecular techniques for plasmid isolation and visualization, restriction endonuclease fingerprinting/ mapping of plasmids and Southern blotting with DNA probes enabled molecular epidemiology studies to be undertaken to identify antibiotic resistance gene flow.

This problem of nosocomial Gram-negative bacterial infections in hospitals was countered by the recognition that the bacteria were surviving as transient flora on the hands of medical and nursing staff. The development and application of handwashing using either aqueous or alcoholic disinfectant preparations (those containing chlorhexidine or triclosan being favoured) were instrumental in controlling the problem.

In addition, the early 1980s saw the introduction of extended spectrum cephalosporins, such as cefotaxime and ceftazidime, which had good activity against these multi-resistant nosocomial Gram-negative bacteria. It is perhaps far from coincidental that with rapidly increasing use of these antibiotics in hospitals (they were only available parenterally) the incidence of infection caused by methicillin-resistant *S. aureus* (MRSA) rose progressively in most countries with a developed or semi-developed hospital healthcare system.

MRSA

The rise of MRSA in the last decade and a half has been spectacular and demonstrates the threat from antibiotic-resistant bacteria. There has also been a similar but smaller increase in infections caused by methicillin-sensitive *S. aureus* (MSSA), primary blood stream nosocomial infections increasing in the USA twofold between 1980 and 1989. Also, in the USA in 1981, 5% of all isolates of *S. aureus* at a large teaching hospital were MRSA; by 1991 38% were methicillin-resistant.

Methicillin resistance is conferred on strains by the possession of a chromosomal copy of modified penicillin-binding protein, PBP2a. This protein has a low affinity for most β-lactam antibiotics (including isoxyl penicillins such as flucloxacillin and nafcillin) and therefore mediates cross-resistance to all such compounds. The *mecA* and associated genes are not frequently found to be transferred *in vivo*, although *mecA*

The battle against the rise of hospital-acquired infections caused by antibiotic-resistant micro-organisms is one of the major challenges faced by microbiologists today. Peter Hawkey takes a look at the problem and discusses how it may be tackled in the future.

LEFT:
Fig. 1. Typical intensive care unit patient. A portal of entry for nosocomial bacteria is the endotracheal tube providing the artificial ventilation (tracheal secretions are being removed by suction, another potential route for infection). Intra-vascular lines providing hydration, nutrition and a route for drug administration are the next most important portal of entry. The temperature (Bennett) probe is visible at the Y piece of the ventilator tubing.

is carried on a transposon. It seems likely that the gene has transferred into several clonal lines of *S. aureus*, although some hold the view that all of the clones seen today have descended from a common ancestor. Different countries and geographical areas have different clones (recognizable by the digestion of genomic DNA using the restriction endonuclease *Sma*I and display of the large fragments by pulse field gel electrophoresis).

At the moment the most successful clones seen in the UK are EMRSA ('Epidemic' MRSA) 15 and 16. In contrast, the clones seen in France are quite different, although some other clones have spread across continents (e.g. South America and Europe). The reasons for this are not altogether clear, but undoubtedly the ability of different strains to survive both at carriage sites and in the environment, as well as their ability to colonize new patients is important.

There is no evidence that MRSA strains are *per se* more pathogenic than MSSA. Most surveys show that >50% of MRSA are also resistant to aminoglycosides, fluoroquinolones, macrolides and lincosamides. This multiple resistance undoubtedly allows cross-selection by antimicrobial agents other than isoxyl penicillins. Delays in therapy also expand the number of patients acting as reservoirs. Therapy invariably involves vancomycin, heavy usage of which has probably led to the pre-eminence of vancomycin-resistant enterococci (VRE).

S. aureus is probably the most common cause of nosocomial infections and represents a huge challenge to the medical and scientific community. A recent study has shown that primary nosocomial blood stream infections result in an approximate threefold increase in direct cost (mean cost US$27,000) compared with those due to MSSA (US$9,600).

Problems with Gram-negative bacteria

As if these problems with Gram-positive pathogens were not enough, the heavy usage of extended spectrum cephalosporins has resulted in the selection of an interesting and growing problem caused by Gram-negative bacteria carrying the so-called extended spectrum β-lactamases (ESBLs). These arise by mutation and alteration of one or two amino acids in TEM and SHV plasmid-mediated β-lactamases. The extended spectrum cephalosporins had been specifically designed to be stable to degradation by the unmutated forms of these enzymes. The amino acid substitutions allow the extended spectrum cephalosporins to gain access to the active site of the enzyme as well as enhancing the rate of hydrolysis of the substrate. These enzymes are generally recognized by the fact that they are inhibited by 'conventional' plasmid-mediated β-lactamase inhibitors, such as clavulanic acid. The comparative ease with which mutation can lead to resistance and the evolution of ESBLs has been shown in a number of studies with examples of identical genotypes arising by convergent evolution from different wild type genes. There are currently some 80 or so types of TEM gene and nearly 30 SHV genes researched (see www.lahey.hitchcock.org/pages/lhc/studies/webt.htm).

In an effort to treat hospitalized patients with these infections caused by multi-resistant Gram-negative bacilli, many physicians have increased usage of carbapenem antibiotics. Inevitably, the bacterial population demonstrates a resilient response and resistance has developed via two unpredicted routes. By overexpressing certain types of β-lactamase normally encoded on the chromosome, but now mobilized onto plasmids (e.g. CMY), low levels of resistance to drugs such as imipenem are seen. Although these levels of β-lactamase are too low to allow clinically significant resistance, when combined with the loss of an outer-membrane protein (porin), clinically significant levels of resistance are seen, resulting in treatment failure. More sinister has been the appearance in widely dispersed locations around the globe in the last year or so of zinc-dependent β-lactamases (IMP2–4, VIM1 and 2) related (by nucleic acid sequence) to the highly transmissible enzyme IMP-1 first seen in Japan more than 10 years ago, but which has not spread outside of that country. These genes are often plasmid-associated and capable of moving from one replica onto another because of carriage as integrons.

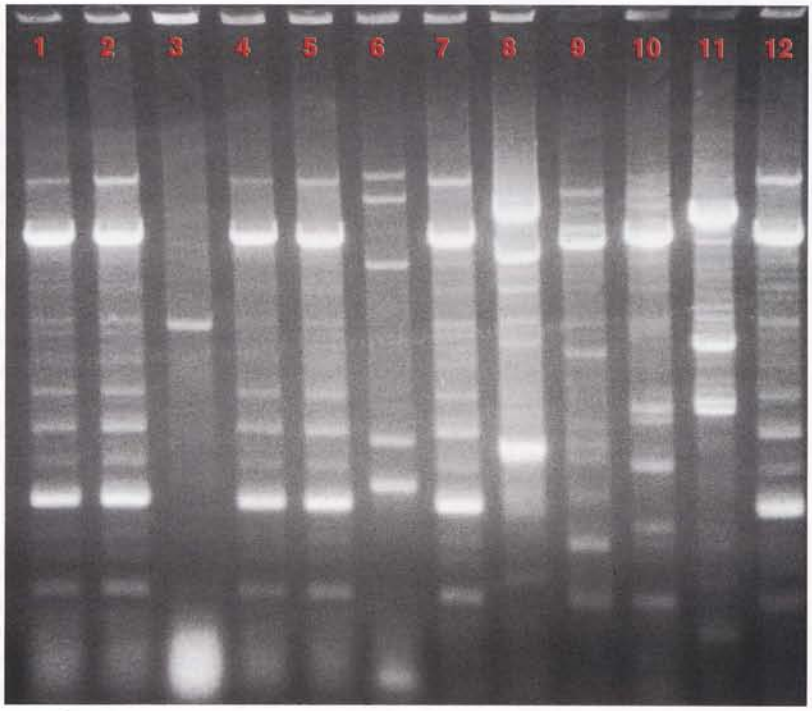
Intensive care units (ICUs)

Modern medical techniques have produced patients highly vulnerable to nosocomial infection who are managed in areas of the hospital where antibiotic usage is particularly high. Intensive care unit patients are particularly susceptible to infection with antibiotic-resistant bacteria by virtue of invasive procedures such as artificial ventilation and intravascular lines (Fig. 1). Some bacteria, such as *Pseudomonas* spp. and *Acinetobacter baumannii*, have become highly significant pathogens in this group. Treatment can be extremely difficult because they often carry a huge array of resistance mechanisms. Studies such as the EPIC study (a one day in 1992 point prevalue study of infections in ICUs in different European countries, including nearly 1500 units) showed that ventilator-associated pneumonia (VAP) accounted for nearly half of the ICU infections.

Combating the problem

The microbiologist can help reduce this burden of infection in several ways. The development of rapid molecular typing methods based on PCR has brought the prospect of 'real-time' investigation of environmental and patient sources of infection, and of routes of transmission. An example of such a successful investigation is shown in Fig. 2 and Table 1. Improvements in both the accuracy and speed of anti-

microbial susceptibility testing may in the future bring the prospect of being able to use antimicrobials more precisely. The clinical input from microbiologists is also crucial in maintaining appropriate levels of antimicrobial usage in all areas of the hospital. Microbiology laboratories, by processing routine specimens and performing antimicrobial sensitivity testing, form the front line of surveillance for antibiotic resistance and therefore are the 'intelligence' service in the battle against nosocomial infection.



LEFT:
Fig. 2. Repetitive element primer (REP)-PCR profiles of *Acinetobacter* spp. strains isolated from an outbreak of cross-infection in an intensive care unit. Lanes 1–6 are patient infections and 7–12 are environmental isolates. Table 1 shows the source of the isolates. An inadequate disinfection regime for the Bennett temperature probes was shown to be the cause. Improving the disinfection procedure eliminated the outbreak.

What does the future hold?

- Increasing mobility of the world population and the opportunity for the faster spread of resistance genes
- An ageing population with increased expectations of complex health care
- Better environments for antibiotic-resistant nosocomial bacteria to flourish in
- Increasing addiction to antibiotics by both patients and physicians – particularly in some developing industrial societies
- An apparent increase in the rate of emergence of novel antibiotic resistance mechanisms

Perhaps it does not look hopeful, but with the necessary political and professional will the battle against nosocomial infection cannot just be joined but even turned in the favour of mankind. If we lose it, the consequences for health care will be serious indeed.

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Table 1. Sources and properties of the *Acinetobacter* spp. causing an ICU outbreak, shown in Fig. 2

Lane	Specimen*	Date of isolation	Site	REP-PCR profile
1	*Acinetobacter baumannii*	1/5/93	Sputum	1
2	*Acinetobacter baumannii*	1/7/93	Tracheal secretion	1
3	*Acinetobacter baumannii*	1/8/93	Sputum	2
4	*Acinetobacter baumannii*	1/9/93	Sputum	1
5	*Acinetobacter baumannii*	12/31/92	Leg wound	1
6	*Acinetobacter haemolyticus*	12/20/92	Blood culture	3
7	*Acinetobacter baumannii*	1/12/93	Bennett temp probe	1
8	*Acinetobacter baumannii*	1/12/93	Sluice sink	4
9	*Acinetobacter baumannii*	12/6/92	Dust	5
10	*Acinetobacter baumannii*	12/8/92	Dust	6
11	*Acinetobacter lwoffii*	12/20/92	Blood culture	7
12	*Acinetobacter baumannii*	1/22/93	Bennett temp. probe	1

*Detected by randomly amplified polymorphic DNA (RAPD) analysis.

Fungal infections in the immunocompromised

Marc Mendelson

The number of severely immunocompromised patients is rising. This is leading to new problems with fungal infections, as Marc Mendelson describes.

Fungal infections (mycoses) often occur in healthy people. For example, over 70% of women in the general population have an episode of vaginal candidiasis in their lifetime. However, this article will focus on the clinical problem of fungal infections in patients whose immune system is compromised for whatever reason, because this often causes severe illness or death.

Immunosuppression is not only the result of diseases of the immune system, but is increasingly a consequence of treatment such as chemotherapy which impairs immune function. Limiting this so-called 'iatrogenic' or 'physician-induced' immunosuppression is a major challenge to modern-day physicians.

Host defence to fungal infections

The body's natural barriers, i.e. the skin and epithelial surfaces, form the first line of defence against many mycoses. Hence, any breach in these barriers, such as burns, intravenous catheters or the destruction of epithelial surfaces, as in gastrointestinal surgery, pose a major risk of fungal invasion. Fungal entry is followed by defence reactions such as phagocytosis and fungal killing, mainly by white blood cells, the neutrophils and mononuclear phagocytes. Therefore, the risk of infection is also increased by diseases and treatments that reduce the numbers of phagocytes, such as cancers, or those causing neutrophil dysfunction, such as diabetes mellitus. Optimal phagocytosis requires blood factors such as complement and chemotaxins that direct neutrophils to pathogens, which may be defective in an immunocompromised patient. More specific immunity to particular fungi relies on presentation of fungal antigens to T-lymphocytes by dedicated antigen-presenting cells which activate effector cell pathways in cell-mediated and humoral immunity, resulting in long-lasting immune defences.

Although a single factor may lead to immunocompromise, both suppression of immune function and the risk factors for the establishment of a fungal infection are often combined in seriously ill patients. For example, a patient with acute myeloblastic leukaemia, whose circulating immature blood cells (blasts) are dysfunctional, will undergo chemotherapy, which dramatically reduces the number of neutrophils (neutropenia). The treatment commonly involves a catheter made of foreign material being placed into the patient's vein to administer drugs and nutrition, providing a portal of entry for fungi. Furthermore, the use of antibiotics to combat infections that are a frequent consequence of neutropenia will alter the microbial flora of the gastrointestinal tract and allow fungal overgrowth. It is not difficult to see how such a patient is at particular risk of severe mycoses.

Clinical patterns of fungal infection in the immunocompromised host

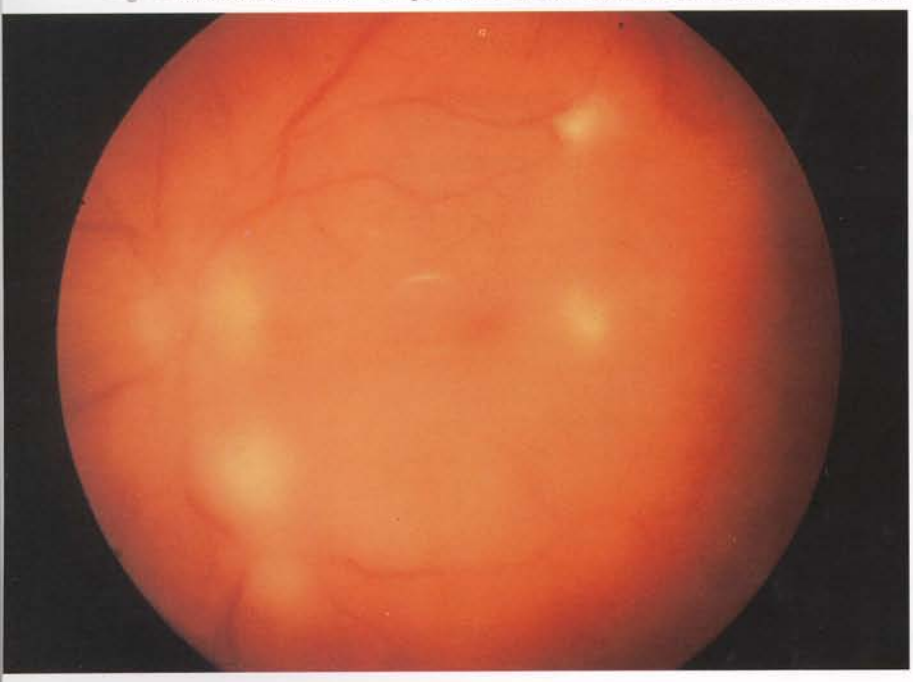
Serious fungal infections affecting the immunocompromised can be broadly split into those associated with a predominant quantitative or qualitative impairment of neutrophils, and those where impairment of T-lymphocytes and mononuclear phagocytes cause defective cell-mediated immunity.

Mycoses associated with quantitative or qualitative impairment of neutrophils

The three most common infections in this group are candidiasis, aspergillosis and zygomycosis. Immunocompromise allows the organisms to spread around the body, seeding multiple organs, which can result in clinical disease. The major risk factor for *Candida* and *Aspergillus* infections is the degree and duration of neutropenia, where neutrophil counts below 100 cells ml^{-1} for 7 days or more are particularly associated with both bacterial and fungal infection.

Disseminated candidiasis is most commonly caused by *Candida albicans*, a normal commensal of the alimentary tract. Gastrointestinal, cardiac and transplant surgery are all major risk factors, not only because of the surgery itself, but also because such operations commonly require periods of post-operative intensive care and the attendant use of in-dwelling catheters and antibiotics as described above. Disseminated abscesses occur in multiple organs, including the brain, eyes, kidney, heart, liver and spleen. Candidaemia (the presence of *Candida* cells in the blood) of immunocompromised patients is almost always associated with disseminated disease, carrying with it a high mortality of up to 40%. Sight-threatening

BELOW:
Fig. 1. *Candida* endophthalmitis.



endophthalmitis, as depicted in Fig. 1, is associated with candidaemia in over 25 % of cases.

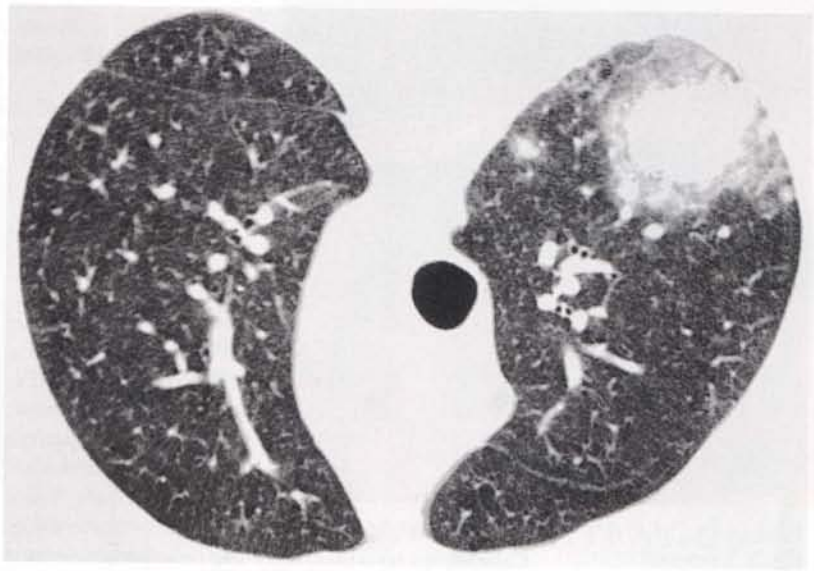
Unlike *Candida*, *Aspergillus* spp. are commonly found in the atmosphere, and so infection by *Aspergillus fumigatus* is predominantly via the respiratory route. Invasive aspergillosis from a focus of rapidly progressive *Aspergillus* pneumonia is most commonly found in the immunocompromised. The complications of this infection include damage to pulmonary vessels, leading to blood in the sputum (haemoptysis), and growth of the fungal hyphae through to the pleural surface which may cause collapse of the affected lung (pneumothorax). The chest X-ray may be normal until relatively late into the disease, but the greater sensitivity of computerized tomography (CT) may reveal characteristic features such as single or multiple nodules with a surrounding 'halo' (Fig. 2). As in candidiasis, dissemination of the fungus in the bloodstream may follow, causing skin and gastrointestinal ulceration, infected clots in the brain leading to a stroke, or microabscesses within multiple organs. Despite adequate treatment, invasive aspergillosis carries a high mortality.

Mucosal infection of the paranasal sinuses, more commonly by *Aspergillus flavus*, can spread rapidly to the surrounding tissues causing sinus pain, protrusion of the eyes (proptosis) and threaten sight. Zygomycosis, a collective term for *Mucorales* infections from the genera *Rhizopus* and *Absidia* may mimic this infection. Zygomycosis is most commonly associated with diabetic ketoacidosis, where *in vitro* studies have shown that raised blood glucose and acidaemia impair neutrophil function. A black blood-stained nasal discharge accompanied by a necrotic slough may occur as the infection spreads to the perinasal skin. Complications include growth into the brain, with a high case-fatality. Pulmonary, gastrointestinal and cutaneous disease sometimes occur and disseminated forms often develop suddenly. Prompt surgical and medical intervention may save lives but despite this there is still considerable morbidity.

Although less common, infection with soil-borne *Fusarium* species is an equally important mycosis in neutropenia, causing localized, focally invasive and disseminated infections. Surgical removal of the infected skin and soft tissue found in about 75 % of disseminated cases and restoration of neutrophil function are effective additions to antifungal medication.

Mycoses associated with defects in cell-mediated immunity

Impairment of the cell-mediated immune response to fungal infection can be congenital or acquired, primary or iatrogenic (such as from the use of corticosteroids or chemotherapy). In the modern era, the HIV pandemic has caused a major increase in fungal infections, which often occur in disseminated and atypical forms. Some of the less common mycoses are distributed worldwide, such as sporotrichosis, a chronic mycotic disease usually restricted to skin, subcutaneous tissues and the lymphatic system. However, many rare mycoses show geographic constraints. Examples include histoplasmosis from the river valleys of eastern USA; paracoccidioidomycosis, the commonest respiratory mycosis in Latin America; coccidioidomycosis from the dry valleys of south-western USA and Mexico; and penicilliosis from south-east Asia. A thorough travel history is therefore essential when evaluating suspected mycoses.

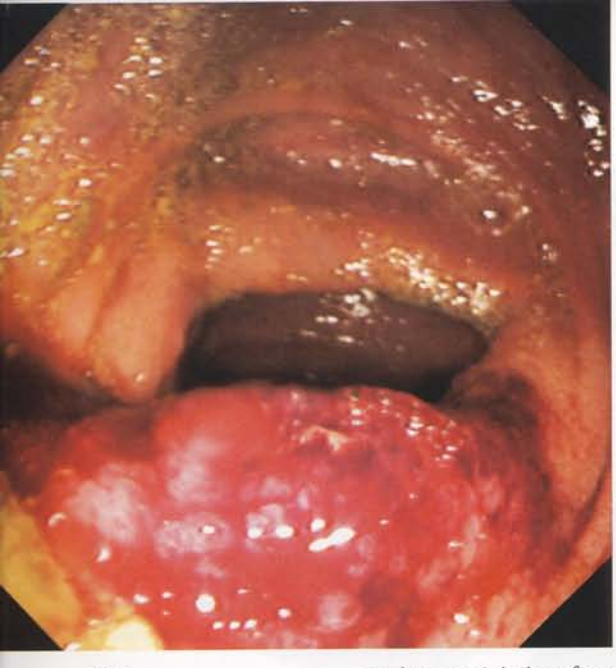


ABOVE:
Fig. 2. CT appearance of pulmonary aspergillosis showing nodule with characteristic surrounding halo.

These types of disseminated infections are rare in HIV cases compared with the incidence of seborrhoeic dermatitis, oesophageal candidiasis and cryptococcal infection. Seborrhoeic dermatitis caused by *Malassezia furfur* occurs in patients with HIV infection at four-times the rate of the normal population, and it is up to 10-fold more common in AIDS. Oesophageal candidiasis is a common AIDS-defining illness, although disseminated infection is rare, unlike the situation in neutropenic patients. Congenital T-lymphocyte dysfunction associated with disorders of the endocrine system predisposes infants to chronic mucocutaneous candidiasis, a condition also described at late onset in patients with AIDS, or in adults with cancer of the thymus or occult carcinoma.

Infection with *Cryptococcus neoformans* is the commonest of the deep mycoses in AIDS, generally presenting as meningitis in the severely immunosuppressed. A prolonged period of non-specific symptoms such as fever, malaise and headache, often in the absence of neck rigidity [which is a cardinal sign of inflammation of the lining of the brain and spinal cord (meninges)] raises the suspicion of cryptococcal disease. The cutaneous form may mimic the skin papules caused by Molluscum contagiosum virus. Similarly, penicilliosis, an increasingly recognized mycosis caused by *Penicillium marneffei* may also mimic Molluscum contagiosum virus. Penicilliosis is a systemic, primarily air-borne infection endemic in Thailand and south-east Asia. It is increasingly reported among AIDS patients, with approximately 3,000 patients diagnosed in northern Thailand in the past decade.

The diverse and atypical presentation of disseminated mycoses in the context of HIV underlies the importance of tissue examination in the diagnosis of fungal infections.



ABOVE:
Fig. 3. Disseminated histoplasmosis presenting as a pseudotumour of the large bowel.

This was recently exemplified in our unit by a West African patient with HIV-2 and advanced immunosuppression. The patient complained of abdominal pain in the right lower quadrant, weight loss, fever and iron deficiency anaemia. Colonoscopy revealed a cancer-like mass (pseudotumour) at the junction of the small and large bowel (Fig. 3). The cause was identified on biopsy as *Histoplasma capsulatum*, a rare cause of disease in the gastrointestinal tract of patients with HIV-2. Other diagnostic approaches, such as production of a specific antibody response to pathogens, is impaired in advanced immunosuppression, often rendering them an unreliable diagnostic tool.

Conclusion

The treatment of mycoses involves the use of antifungal drugs. However, dealing with the factors predisposing or contributing to infection should go hand-in-hand and is arguably as important to long-term outcome as the drugs themselves. This may include supporting neutropenia with colony-stimulating factors, changing in-dwelling catheters, improving control of blood glucose in diabetics, or reconstituting the immune system of HIV patients with highly active anti-retroviral drugs.

We are taught that for every action there is an equal and opposite reaction. As modern medicine advances with more transplantation, increasingly successful methods for treating cancer and improvements in the care of the critically ill, the 'reaction' of iatrogenic immuno-supression continues to take its toll in terms of morbidity and mortality from fungal diseases. In the developed world, immune reconstitution with highly active anti-retroviral therapy for HIV has radically altered the incidence of opportunistic pathogens, including mycoses, whilst the lack of such vital disease-modifying resources in the developing world will continue to take its toll on those in need.

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Further reading

Gupta, A.K., Baran, R. & Summerbell, R.C. (2000). *Fusarium* infections of the skin. *Curr Opin Infect Dis* 13, 121–128.

Ungpakorn, R. (2000). Cutaneous manifestations of *Penicillium marneffei* infection. *Curr Opin Infect Dis* 13, 129–134.

The use of molecular techniques to detect antimicrobial resistance in clinical bacterial isolates

Ad C. Fluit & Franz-Josef Schmitz

The broad range of current PCR and DNA chip applications in clinical microbiology includes the detection of pathogens and the analysis of genomic alterations, such as sequence and copy number alterations in bacterial genes and single nucleotide polymorphisms. This article focuses on the possible application of modern molecular methods for the detection of bacterial resistance genes and mechanisms.

As many of the genetic mechanisms of antimicrobial resistance have become better understood, new molecular methods are proving to be useful for the confirmation of antimicrobial resistance in laboratory isolates and for the direct detection of such resistance in clinical specimens. Conventional culture and susceptibility test procedures for most pathogenic bacteria generally take 48–72 hours. The performance of these tests may be erratic because factors such as inoculum size or variability in culture conditions can affect phenotypic expression of resistance.

The recent popularity of new molecular methods, such as nucleic amplification techniques or DNA chip technology, has been fostered by the increasing demand for new diagnostic tools which allow quick nucleic acid hybridization experiments and simultaneous analyses of large numbers of PCR products. The development of DNA chip-based assays in particular has been strongly driven by modern approaches aimed at the comprehensive analysis of multiple gene mutations and expressed sequences.

Detection of genetic determinants using modern molecular techniques may therefore be used to confirm antimicrobial resistance based on the organism's genotype, rather than relying on the variability of phenotypic expression of the resistance. Moreover, these tests can be done within hours, providing clinically relevant information days before conventional susceptibility test results become available. Molecular assays to detect antimicrobial resistance directly from clinical samples have been developed.

Testing is not only required for therapy but also to monitor the spread of resistant organisms or resistance genes throughout the hospital and the community. However, the presence of a resistance gene does not necessarily lead to treatment failure because the level of expression may be too low. For example β-lactamase production among *Enterobacteriaceae* is common, but the development of resistance is dependent on the mode and amount of expression. The application of nucleic-acid-based technology is particularly useful for slow-growing or non-culturable micro-organisms and the detection of point mutations or certain genotypes.

Causes of antimicrobial resistance

Antimicrobial resistance of bacterial isolates can be caused by a variety of mechanisms:

- the presence of an enzyme that inactivates the antimicrobial agent
- the presence of an alternative enzyme for the enzyme that is inhibited by the antimicrobial agent
- a mutation in the target of the antimicrobial agent, which reduces the binding of the antimicrobial agent
- modification of the target of the antimicrobial agent, which reduces binding of the antimicrobial agent
- reduced uptake of the antimicrobial agent
- active efflux of the antimicrobial agent
- overproduction of the target of the antimicrobial agent.

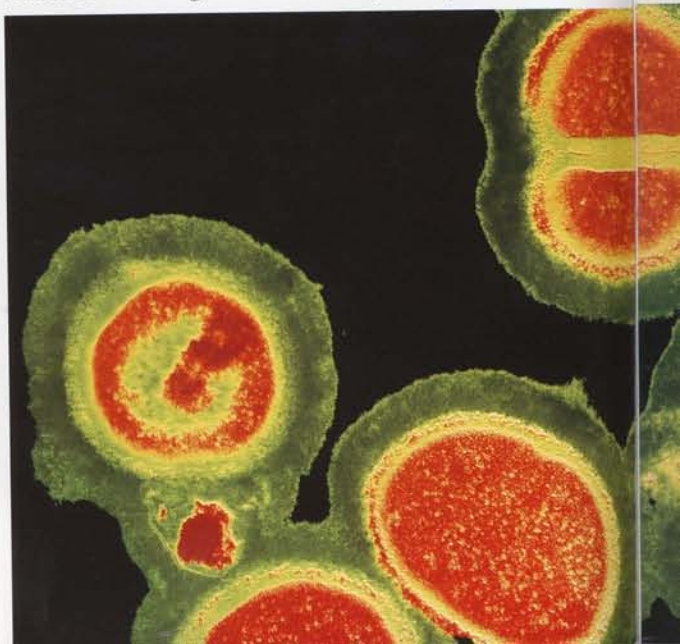
In addition, resistance may be caused by a previously unrecognized mechanism. As with any diagnostic test, the predictive value of molecular assays is dependent on the prevalence of the genes or mutations assayed. On the other hand, a gene, which is not expressed *in vitro*, may be expressed *in vivo*.

Specific applications of molecular techniques

The identification of methicillin resistance in *Staphylococcus aureus* and vancomycin resistance in *Enterococcus* spp. represent ideal applications of modern molecular methods.

Methicillin-resistant *S. aureus* (MRSA) is an important hospital-acquired pathogen capable of causing life-threatening infections and nosocomial outbreaks. The incidence of infections from this pathogen in European hospitals has increased dramatically in the past few years. The rapid and accurate identification of this pathogen is critical for patient management and for infection control programmes in hospitals. However, the reliable detection of MRSA using culture and susceptibility tests may be problematic because expression of resistance is usually heterogeneous and is influenced by culture conditions, especially in strains with low-level resistance. All strains of MRSA produce a unique penicillin-binding protein (PBP2) that is encoded by a chromosomal gene, *mecA*. The *mecA* gene is not present in susceptible strains. PCR has been used successfully to amplify and detect *mecA* gene sequences from clinical isolates within a few hours. These methods have also been used to detect MRSA directly from clinical specimens such as blood cultures and endotracheal aspirates.

Vancomycin-resistant enterococci have also emerged as important nosocomial pathogens in hospitals. Identification using culture and susceptibility tests is



even more problematic than that of MRSA, primarily because of difficulties in detecting low-levels of resistance and because accurate identification using conventional laboratory procedures may take as long as 4–6 days. Vancomycin resistance in enterococci is mediated by one of several genes: *vanA*, *vanB*, *vanB2*, *vanC1*, *vanC2*, *vanC3* or *vanD*. PCR assays have been developed to recognize the *vanA*, *vanB* and *vanC* genotypes and have demonstrated value in characterizing enterococci in the laboratory when conventional laboratory test results have been inconclusive. Another potential use of the assay is to assist in epidemiological studies when there is an outbreak.

PCR-based methods for the detection of antimicrobial resistance have also been applied to multidrug-resistant *Mycobacterium tuberculosis*. In the wake of the HIV epidemic and the breakdown of medical services in several Eastern European countries, the incidence of tuberculosis is rising rapidly, but treatment is threatened by the emergence of multidrug-resistant strains of *M. tuberculosis*. It can usually be treated with only a limited number of antimicrobial agents, the most important ones being rifampin, isoniazid, streptomycin and ethambutol. Because the organism is slow-growing, traditional diagnosis is time-consuming. Phenotypic determination of resistance may take up to 10 weeks after referral of a sample to the laboratory, but both commercial and in-house amplification assays can greatly improve detection time. It is not surprising therefore that within the past 10 years a multitude of different resistance assays based on molecular techniques have been specifically developed. However, many laboratories have trouble with the technical rigors imposed by these assays. Often isolates show multidrug resistance and with the number of potential genes and mutations involved, the number of assays needed to cover them all can be quite large. Therefore, a number of PCR assays have been developed which do not directly determine the presence or absence of resistance-causing genes and mutations, but identify either multidrug-resistant strains by other properties or monitor the effect of chemotherapy. One such completely different approach to determine resistance in *M. tuberculosis* was taken by developing a reverse transcriptase PCR-probe assay that was specific for *M. tuberculosis* precursor rRNA. Precursor rRNA carries terminal stems which are removed when mature rRNA subunits are formed. The number of these stems present in the bacterial cell is markedly affected by the inhibition of RNA synthesis.

Detection of resistance to antiviral agents by molecular methods has also been described for acyclovir-resistant herpesviruses and HIV resistance to reverse transcriptase inhibitors and to protease inhibitors. These assays have been used in a number of reference and research laboratories.

Limitations of the methods

Despite the obvious advantages of these newer procedures for the detection of resistance, there are potential limitations to DNA amplification technology and chip technology in the diagnostic microbiology laboratory. The accuracy and reproducibility of PCR assays depend on the technical expertise and experience of the operator. Specificity of the test may be affected by contamination of the specimen. In addition, very often the detection of resistance genes for diagnostic purposes is restricted to research and epidemiology. This is due to the overwhelming number of different resistance mechanisms and genes and their variants. Furthermore, most bacteria can be easily cultured. This, coupled with the cost of most molecular assays, puts such assays in an unfavourable position compared with phenotypic assays for detection of resistance.

Conclusions

Molecular analysis of bacterial resistance has yielded a wealth of information during the last decade. With the aid of molecular amplification techniques, great progress has been made in the knowledge of the distribution and spread of resistance markers among species. However, the original expectation that molecular techniques would routinely surpass phenotypic susceptibility testing has not (yet) been realized. Challenges that remain include the variety of point mutations or genes leading to resistance, and the labour-intensive nature of current amplification methods. DNA-chip technology, combined with automated amplification techniques, has the potential to meet these challenges. However, the development of DNA chips containing a broad range of resistance markers usable for many different species remains a formidable challenge and requires a broader knowledge of resistance markers than is currently available.

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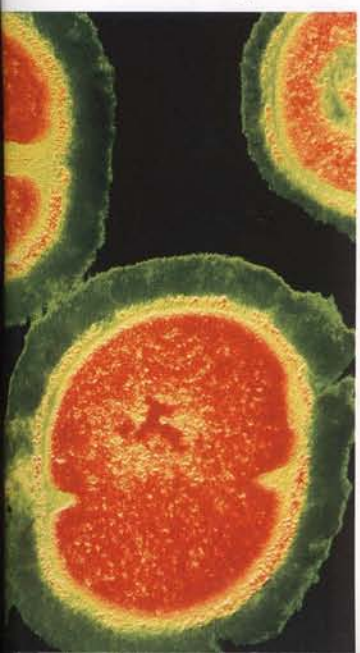


LEFT:
Coloured transmission electron micrograph (TEM) of a deadly cluster of MRSA bacteria.
COURTESY DR KARI LOUNATMAA/ SCIENCE PHOTO LIBRARY

How technology drives pathogen discovery

Paul Kellam & Robin A. Weiss

Innovations in technology have enabled scientists to advance their knowledge of micro-organisms. Now modern molecular techniques are being used to identify previously unknown pathogens.

Technological innovation in microbiology has been of supreme importance in the identification and study of pathogenic and non-pathogenic micro-organisms. The improvements that Anthony van Leeuwenhoek made to his single-lens microscope allowed him to observe bacteria for the first time in 1676. His report on oral microbiology to the Royal Society in 1684 enabled him to demonstrate that while saliva is essentially sterile, there is a vibrant and living biofilm of multitudinous microbes on the surface of teeth. Physical techniques dominated the early years of microbiology. Whilst the light microscope revealed bacteria, and electron microscopy later revealed the exquisite structure of viruses, the identification of individual virus particles by confocal immuno-fluorescence microscopy is very recent. The discovery of new micro-organisms is currently enjoying a renaissance. Novel flora in the oral cavity, too fastidious to grow in culture, can now be identified by molecular biology methods such as ribosomal RNA sequencing, rather than morphology.

The ability to culture

The concept of contagion dates from biblical times. Yet the 19th century witnessed debate between spontaneous generation and germ theory. Ferdinand Cohn and John Tyndall developed heat-inactivation techniques to argue against spontaneous generation, but were initially stymied by the problem of heat-resistant spores, which John Tyndall solved by allowing time for germination between sterilization procedures. Then the technical development of sterile defined media deliberately seeded with germs allowed Louis Pasteur and Robert Koch to resolve the debate firmly in favour of specific microbes that begat progeny in their own kind.

In time, culture techniques, genetics and molecular genetics came to dominate microbiological methodology. Robert Koch's discovery of anthrax bacilli and their propagation from spores in 1877, followed by his isolation and culture of tubercles, led him to enunciate his famous postulates of disease causation in 1884:

- that the microbe is detectable in each case of disease;
- that it can be isolated in pure form; and
- that it can cause disease anew when inoculated into susceptible animals.

However, even 100 years ago subtle alterations to Koch's postulates were necessary to account for viruses. Plant and animal viruses were first identified at this time on the physical basis of passing through filters with a pore size too small to allow the passage of bacteria. Of course, not all pathogens can be propagated in culture, but experimental infection of animals aided the recognition and ultimate identification of pathogens such as hepatitis B and C viruses. However, it was not until cloning and molecular biology technology became available that the true extent of culturable and unculturable microbes became apparent.

Microbiology was the driving force behind the new concepts of cloning and the development of molecular biology methods. Koch may be regarded as the grandfather of cloning technology. He first described the growth of discrete bacterial colonies on potato slices and rapidly adapted the technique to gelatin-coated slides in 1881. By 1887 Robert Petri had already designed his eponymous dish and recommended agar as an alternative to gelatin. Later cloning techniques can trace their conception to Koch's observations on the isolation of pure colonies that breed true. Cloning methods were also exclusively used in virology. D'Herelle described a quantitative plaque assay to enumerate infectious titre in his seminal 1917 report on bacteriophage. With the development of trypsinization and growth of human and animal cells in monolayer culture, Renato Dulbecco and Marguerite Vogt biologically cloned polio virus in 1952. Discrete colony assays of transformed cells were subsequently employed for studying oncogenic viruses such as Rous sarcoma virus by Temin and Rubin in 1958 and polyoma virus by Sachs and Winocour one year later.

The explosion of bacterial and bacteriophage genetics from the late 1940s, pioneered by nuclear physicists such as Max Delbruck and Leo Szilard, eventually led to cloning DNA and recombinant DNA technology. The inventions of specific DNA–DNA hybridization in 1958 through Watson–Crick reannealing of single-stranded DNA, molecular cloning in 1973 by Boyer and Cohen, and polymerase chain reaction (PCR) amplification in 1986, have provided highly sensitive, precise and rapid tools in molecular diagnosis and discovery that would surely have delighted Robert Koch. The development of serology by Paul Ehrlich and von Behring in the 1890s, and of monoclonal antibodies by Kohler and Milstein in 1975 gave us further specificity in distinguishing different microbes and for tracking the incidence and prevalence of infection.

In the latter half of the 20th century multiple approaches have been used successfully to identify hitherto unknown pathogens. This led to optimism about our ability to detect all micro-organisms. Indeed, 1983 was a vintage year for pathogen discovery, using both traditional and modern molecular methods. HIV was discovered by classical isolation in culture and observing a cytopathic effect, albeit corroborated by detecting reverse transcriptase activity; *Helicobacter pylori*, the cause of peptic ulcers, was identified by culture, microscopy and the age-old principle of investigator as experimental subject; and human papilloma virus (HPV) types 16 and 18 were initially identified in cervical carcinoma by weak DNA hybridization of tumour DNA with related HPV DNA from superficial warts. However, much of our

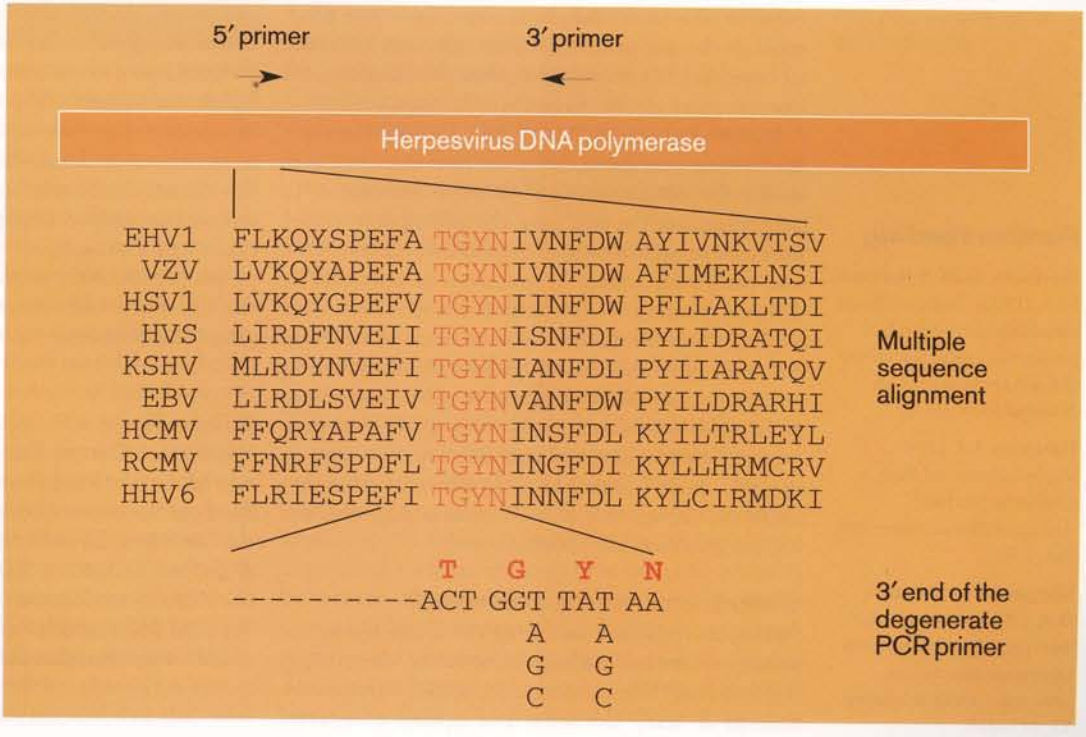
microbial world remains uncharacterized. Now seems to be a time of consolidating molecular-biology-based micro-organism detection whilst looking forward to the functional genomics era for our next dramatic advances.

Molecular biology and microbial identification

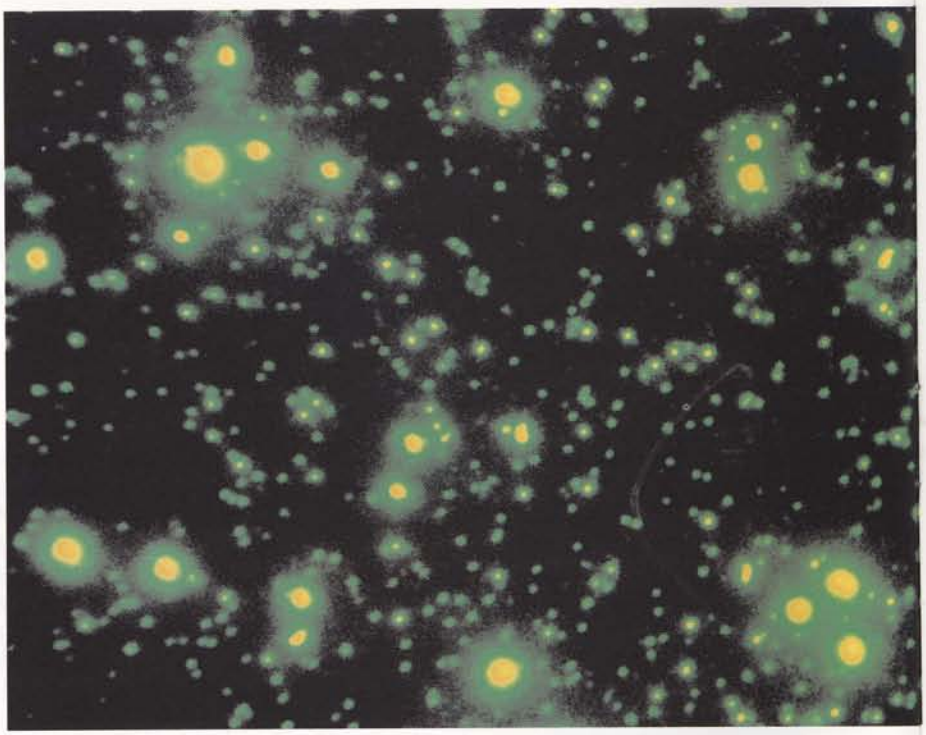
Certain features of genetic sequences make them particularly useful for identifying uncharacterized micro-organisms. First, the genetic code provides a limit to the number of different nucleotides available to define an amino acid. Second, functionally conserved regions of proteins in related microbial species often contain a stable amino acid sequence and third, PCR enables (through the rules of Watson and Crick base pairing) the amplification of a desired sequence to a level detectable above all other sequences present. These factors have been brought together in the methods of consensus (degenerate) primer PCR where it is possible to PCR-amplify, in theory, all known or new members of a family of micro-organisms (Fig. 1). This approach has led to the identification of new uncultivated bacteria responsible for bacillary angiomatosis in 1990, namely *Bartonella henselae*, and Whipple's disease in 1991/1992, namely *Tropheryma whippelii*. For bacterial identification, conserved regions of small subunit ribosomal RNA or DNA are used to design consensus primers. Consensus PCR has also been used to identify uncultivated viruses such as Sin Nombre virus in 1993, a hantavirus responsible for hantavirus pulmonary syndrome. To detect viruses, family- or subfamily-specific primers are often made to proteins conserved between all members of such viruses. However, for truly broad-range virus discovery a collection of different family-restricted degenerate primers needs to be compiled. Such a comprehensive system does not yet exist for virus detection.

In some part due to this lack of complete virus detection primer sets, other PCR-based methods have been used for pathogen detection. In particular a subtractive hybridization method known as Representation Difference Analysis (RDA) was used to identify the causative agent of Kaposi's sarcoma in 1996, namely human herpesvirus 8. RDA is based on using subtractive hybridization to isolate nucleic acid fragments present in one member of an otherwise related pair of samples. These isolated molecules are then selectively PCR-amplified. Multiple rounds of subtractive hybridization and selective amplification are performed until individual PCR products are produced which correspond to the genetic difference between the initial related samples. These PCR products are then sequenced to determine their identity.

Although sequence-based methods to detect unculturable micro-organisms have an advantage of speed and sensitivity, it is often far easier to generate a putative pathological microbial sequence from clinical samples than it is to determine their clinical relevance. This has led to a re-appraisal of Koch's postulates in defining the causal relationship between the presence of microbial sequences and a disease. While the principles behind Koch's postulates still hold, it is now less appropriate to make absolute statements regarding the forms of proof. For example, rather than rigidly adhering to '*After being fully isolated from the body and repeatedly grown in pure culture, the parasite can induce disease anew*', sequence-based methods can be interpreted as '*A putative pathogen's nucleic acid sequence should be present in most cases of an infectious disease*'. The use of such pure molecular biology methods is likely to yield further insights into the microbial aspects of life on earth. However, the latest technological revolution, functional genomics, should, if the trend is followed, be the next driving force behind microbiology and pathogen detection.



BELOW:
Fig. 1. Design of degenerate PCR primers to the herpesvirus DNA polymerase. Based on sequence alignments of herpesvirus polymerase genes, a conserved region was identified at the amino acid level. Back-translation of the conversed amino acid sequence produces a degenerate primer able to PCR-amplify from all possible codons for the amino acids TGYN. COURTESY P. KELLAM & R.A. WEISS



RIGHT:
Fig. 2. Fluorescence imaging of marine microbes, namely viruses (small numerous green dots) and prokaryotic cells (rarer, larger green dots).

Post-genomic pathogens

Cross-species analysis of complete micro-organism genomes, particularly bacteria, is beginning to identify core genes conserved amongst bacteria and pathogen/virulence genes associated with certain subspecies. For example, the difference between enteropathogenic and non-enteropathogenic *Escherichia coli* is a small set of virulence genes. Similar studies on viral genomes have been in existence for many years, but are only now being systematically analysed using modern bioinformatics methods. Compilation of such data, both bacterial and viral, allows the further design of broad-based detection methods (i.e. degenerate PCR) that should allow detection and discrimination between pathogenic and non-pathogenic microbes.

With the growing emphasis on genome detection and discrimination, the massively parallel methods of functional genomics, such as micro-arrays, also have the potential to revolutionize pathogen detection. Micro-arrays are essentially hundreds or thousands of individual DNA probes immobilized at defined locations on a solid support such as nylon membranes or glass slides. As such, pathogen detection arrays can easily be envisaged whereby a clinical sample could quickly be screened for all members of a virus family, for all pathogenic viruses, or perhaps more ambitiously, all pathogens. This last example of a 'broad-range pathogen detection array' could also be used to identify mixed infections and create an inventory of complex microbial communities, for example in the gut during health and disease.

Micro-arrays could also be directed towards monitoring host genes, using the host as an exquisite sensor and discriminator of different pathogens. To determine how the host 'sees' the pathogen it will be necessary to determine gene expression profiles of cells and peripheral tissues in response to infection by different microbes. Preliminary studies have shown it is not only possible to discriminate between different bacteria and viruses, but also to identify different host gene expression patterns induced by alternative strains of the same bacterial species. Microbe-specific host gene expression patterns could therefore not only serve to identify specific pathogens, but also provide details about the disease time course by identifying which of the host genes acts as a 'pathology clock'.

What remains to be discovered?

Having many different technologies available to discover pathogenic and non-pathogenic microbes, where do you begin to look? First, there are the large environments. Surveys of many terrestrial and aquatic ecosystems indicate that >99% of micro-organisms cannot at present be cultured and can only be identified using molecular methods. The sheer extent of microbial life was recently emphasized with the demonstration that 10^9 bacteria and 10^{10} viruses per litre occur in surface waters. Aside from the sheer variety of microbes present in these environments, they are dynamic, with viruses being responsible for up to 50% of the bacterial mortality rate (Fig. 2). Microbial populations of hosts are well documented with the concept of commensal bacteria well established. With the discovery of transfusion-transmitted virus (TTV) to add to the increasing list of persistent virus infections, the notion of commensal viruses is a recurring debate.

Finally, new human, animal and plant pathogens are almost certain to be discovered. Emerging infectious diseases (EIDs) are now a subject of much concern in the world. EIDs can be categorized as resurgent or recurrent existing diseases, newly identified agents associated with well-known diseases, or new human diseases caused by zoonotic agents. Already a wide range of acute and chronic diseases warrant investigation by culture-independent/molecular identification methods. In addition, doctors are often familiar with previously healthy individuals who present with acute, sometimes life-threatening diseases that have all the hallmarks of an infectious disease but no detectable pathogen. The Center for Disease Control (CDC) in Atlanta has initiated a project on 'Unexplained Deaths' to track such cases. The CDC suggest such deaths occur in 0·5–2 people per 100,000 per year in the USA. Translated to the UK this would account for 300–1200 deaths per year. Clearly discoveries in microbiology are far from over.

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Further reading

Fredricks, D.M. & Relman D.A. (1996). Sequence-based identification of microbial pathogens: a reconsideration of Koch's postulates. *Clin Microbiol Rev* 9, 18–33.

Fuhrman, J.A. (1999). Marine viruses and their biogeochemical and ecological effects. *Nature* 399, 541–548.

Manger, I.D. & Relman, D.A. (2000). How the host 'sees' pathogens: global gene expression responses to infection. *Curr Opin Immunol* 12, 215–218.

Microbiology before Pasteur

Milton Wainwright

LEFT:
Fig. 1. Louis Pasteur (1822–1895). Arguably the most influential, but certainly not the first, microbiologist.

Milton Wainwright takes a look at some of the microbiological discoveries made before Pasteur's seminal studies on fermentation.

When did microbiology begin? Most accounts of the history of microbiology start with Van Leeuwenhoek's observations of animalculae (which included bacteria) in the late 17th century, using rudimentary microscopes, and then jump nearly 200 years to the work of Louis Pasteur. The impression is thereby given that no work on micro-organisms, especially in relation to disease, was done prior to Pasteur's studies on fermentation, which began in 1857. Although Pasteur made a seminal contribution to our science, I hope to show here that a considerable amount of largely forgotten microbiology was done in the two centuries before his work began.

As early as 1720 the English physician, Benjamin Martin, was suggesting, in somewhat flowery language, that animalculae cause disease. Some 40 years later, Marcus Plenciz, a physician of Vienna, maintained that not only were infectious diseases caused by micro-organisms, but that '*nothing else but living organisms can cause disease*'. This was a direct challenge to the prevalent miasma theory which stated that disease was caused by 'bad air'. Plenciz also insisted that there were special germs for each infectious disease, and that they were conveyed through the air and multiplied in the body. Such views were largely speculative and were not based on experimental work. Surprisingly, even 18th century playwrights and novelists referred to the idea that animalculae were responsible for disease (see, for example, *A Devil on Two Sticks* by Samuel Foote, 1768). A limited amount of practical work was also done during this period, notably by the Danish microscopist Otto Frederick Muller (published posthumously in 1786) who observed and described 10 species of what he termed *Monas* and 31 species of *Vibrio*.

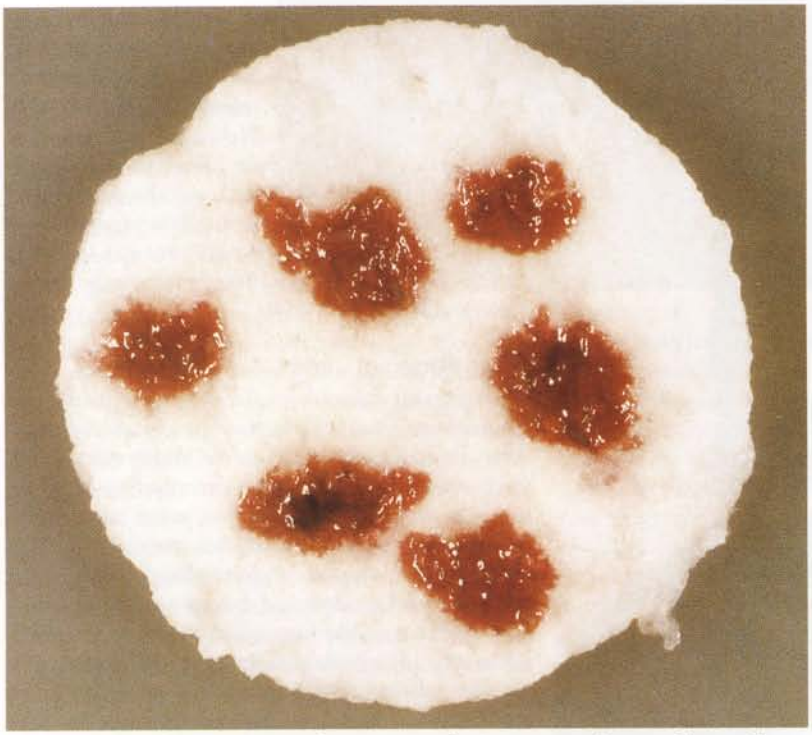
The 'Blood of Christ'

An important stimulus to the early development of microbiology came with attempts to discredit an infamous, alleged miracle. Since the Middle Ages people had noticed red, blood-like stains on moist bread. When these appeared on the bread and wafers used in the Catholic mass they were literally believed to be the blood of Christ. The Italian, Bartholomeo Bizio, looked at the red spots under a microscope and saw what he described as a fungus (terms like fungus and virus were often used in the early microbiological literature to describe what we now call bacteria), and on 20 August 1817, he moistened some bread and polenta (a porridge-like food made from crushed barley, chestnuts or maize) and left them in a warm, damp atmosphere. Twenty-four hours later, both the bread and polenta were covered in red growth. In 1823, he named the organism *Serratia marcescens*. Amazingly, Bizio showed that:

1. *Serratia* requires moisture and warmth for growth;
2. the growth propagates itself through contact of the red polenta with fresh polenta;
3. the red colouration can be passed to fresh bread by handling;
4. the reddening produces a mucilaginous substance and very small semi-spherical bodies, which according to experiments (by Spallanzani) are organic beings of botanical origin;
5. the spores of *Serratia* can germinate even after 3 years of drying;
6. the colouring matter is light-stable, insoluble in water, but soluble in alcohol, and dyes wool and silk without need of a mordant (Bizio was obviously thinking here of a biotechnological use for his *Serratia*).

The Prussian microscopist Christian Gottfried Ehrenberg (1795–1876) also showed an interest in the red spots found on 'bloody bread' and in 1848 he inoculated them on to potatoes, bread and Swiss cheese kept in metal vessels, the atmosphere of which was kept moist with damp paper. In so doing he probably became the first person to cultivate bacteria. Ehrenberg is also likely to have been the first to use the cover-all term bacteria (meaning little rods). In 1836 he had described 'infusoria' and named a number of genera of bacteria, including *Bacterium* and *Spirillum*. Even up to

RIGHT:
Fig. 2. The 'Blood of Christ' – *Serratia marcescens* growing on a moistened communion wafer.
COURTESY MILTON WAINWRIGHT



his death in 1876, however, Ehrenberg continued to '*view with disfavour the new-fangled idea that microbes can cause disease*'.

Further developments

By 1837, the French microscopist Alfred Donné had observed an organism, clearly a spirochaete, in syphilic lesions and made some tentative, if inconclusive attempts to demonstrate that it caused disease.

When we think of the history of microbiology we usually emphasize the bacteria. However, important early work was also done with fungi, notably yeasts. In 1838, for example, Cagniard-Latour discovered *Torula cerevisiae* and showed that it can ferment sugar to alcohol and carbon dioxide. In the following year, Schonlein and Remak observed the fungus which causes the skin disease favus [*Achorion* (*Trichophyton*) *schonleinii*] and showed it to be contagious, while in 1843 David Gruby, a Hungarian long resident in Paris, provided the first accurate account of the skin pathogen *Microsporon*.

By 1840 Jacob Henle had recognized that variolus pus '*is pus, plus the contagion for pus*' and that the contagion must be living. He then stated most of the postulates attributed in 1878 to Robert Koch, who had been one of Henle's pupils.

Béchamp – a neglected French microbiologist

In 1854, while studying the formation of invert sugar (equal amounts of fructose and glucose), Béchamp found moulds growing in some of his solutions and showed that invert sugar was only formed when these were present. No fructose was formed when solutions which prevented mould growth (such as zinc chloride and creosote) were added. Béchamp concluded that moulds act as 'ferments' and that they are necessary for the inversion of sugar to occur. The results were first published in 1855, and again in 1858.

Béchamp's contribution has largely been neglected because, in addition to being an ardent enemy of Pasteur, he was responsible for the heresy that disease is caused by the so-called microzyma (or microzyme) and that infections arise from within the body, not from without. Every living being, he claimed, arose from the microzyma and can be reduced to the microzyma. He claimed that microzymas are to be found in living cells as very small bodies which glisten when exposed to refracted light. Béchamp claimed that microzymas transformed into bacteria by enlarging into coccoid forms, i.e. when deprived of proper nutrition, microzymas transform into bacteria and cause disease. Such views obviously cannot be reconciled with mainstream microbiology.

An early sighting of the 'comma bacillus'?

In 1849, the English physicians Swayne, Brittan and Budd described what seems to be the comma bacillus of cholera which they claimed was present in large numbers in cholera stools and in the '*condensed air of rooms inhabited by cholera victims*'. The organism was found to be present in every water sample taken from cholera districts, but not from uninfected districts. The illustrations they provided clearly show a comma-shaped organism. Unfortunately a cholera sub-committee, while agreeing that a 'virus' may occasionally cause the disease, concluded that miasmas (or bad air) were the main cause. At around the same time, John Snow reported his epidemiological studies showing that cholera was spread in polluted drinking water. Snow also believed that cholera was caused by a *contagium vivum* and attributed to it '*the property of reproducing its own kind*' in the intestine of those suffering the infection.

Some five years after these observations, the Italian Filippo Pacini observed a comma-shaped organism in

cholera discharges and named it *Vibrio cholerae*. Its role in cholera was confirmed by Robert Koch in 1883.

Early fermentation studies

In 1842, a 19-year-old boy, under the care of the famous Scottish pathologist John Goodsir, complained of suffering from uncontrollable vomiting. On waking, the boy would involuntarily vomit from two-thirds to a whole wash-hand-basin-full of liquid smelling of '*fermenting wort*' which on standing became covered with a mass of froth which looked like '*the head of a pot of porter*'. Goodsir took some of the frothy liquid and examined it under the microscope. He described it as having '*the appearance of a wool-pack or of a soft bundle bound with cord crossing it four times at right angles and at equal distances*'. Goodsir suggested that the organism belonged to the *Bacillariae* and he gave it the name *Sarcina ventriculi*. He then attempted to cure the infections it caused by giving his patients carbolic acid and sodium hyposulphite.

In 1854 (three years before Pasteur published on fermentation), the English pathologist George Budd, while studying Goodsir's *Sarcina*, made some important observations on the nature of fermentations. He concluded that since torulae (i.e. yeasts) were also present in the vomit of patients suffering from *Sarcina* infections, not only was carbonic acid evolved, but also the '*common alcoholic fermentation*' was occurring, except that the alcohol so formed was rapidly transformed to acetic acid. Budd also observed that such acidification of alcohol '*would seem to be much more favourable when the matter is exposed to the air than when it is shut up in the body*' and that the condition caused by sarcinae often co-exists with chronic stomach ulcers, an observation which is echoed in our recent awareness of the role of *Helicobacter pylori* in this disease.

Urinary microbes

Another remarkable early paper on microbiology, which appeared in the *Lancet* of 1859, was written by Arthur Hill Hassall, a physician at the Royal Free Hospital in London. This paper was concerned with an organism Hassall called *Vibrio lineola* which he had isolated from urine as minute linear bodies. The vibriones in urine were of many different lengths, while others appeared filamentous like fungi. He also noticed that the vibriones were capable of movement and that this motion could be inhibited by the addition of iodine. Hassall's vibriones also formed a pellicle on the surface of stale urine which fell to the bottom of the tube on storage. The type and number of vibriones present in urine depended on the acidity and the presence of air. Hassall then described a second organism found in urine, which he called *Bodus urinarius*; these, he said, '*appear to fasten themselves to the surface of the plate of glass, their bodies swaying and oscillating like an inflated balloon kept down by its cords*' (i.e. flagella).

Babies, blindness and bacteria

The belief that miasma and physical factors caused disease was held as late as 1859 when Edwin Chesshire argued against the then dominant view that blindness in newly born children (*ophthalmia neonatorum*) was caused by exposure to light. Incredibly, most doctors of this period believed that daylight damaged the eye as the baby emerged from the womb. Chesshire demurred from this view, stating that '*my experience leads me to attribute the cause of this complaint only to the influence of vaginal discharges during parturition*'. Although Chesshire failed to implicate a specific organism, he suggested that the infection could be cured by applying silver nitrate, both prophylactically and after infection. Such treatment was used routinely in the USA to prevent *ophthalmia neonatorum* in the newborn until it was replaced in the 1940s by penicillin.

Conclusion

Clearly microbiologists (i.e. pathologists), working well before Pasteur, used microscopes to observe bacteria and fungi and concluded that such organisms could cause diseases in humans. Some even attempted to cure such infections using chemicals like silver nitrate and sodium hyposulphite. However, except for primitive attempts using moist bread and raw potatoes as substrates, they were largely unable to isolate and grow individual micro-organisms for closer study, a fact which obviously hindered the early development of our science. There is no doubt, however, that the history of microbiology extends further back in time and is a much richer tapestry than we have generally been led to believe.

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Further reading

Budd, G. (1854). On fermentation in the contents of the stomach with development of sarcinae. *Retrospect Med* 29, 141–145.

Chesshire, E.C. (1859). On the causes and treatment of ophthalmia in infancy. *Lancet* i, 122.

Fowke, F. (1885). On the first discovery of the comma bacillus. *Br Med J* i, 589–592.

Goodsir, J. (1842). History of a case in which a fluid periodically ejected from the stomach contained vegetable organisms of an undescribed form. *Edinb Med Surg J* 57, 430–443.

Harrison, F.C. (1924). The miraculous microorganism. *Trans R Soc Can* 18, 1–17.

Hassall, A.H. (1859). On the development of and significance of *Vibrio lineola*, *Bodus urinarius* and on certain fungoid and other organic productions generated by alkaline and albuminous urine. *Lancet* ii, 503–506.

Wainwright, M. & Lederberg, J. (1992). History of microbiology. In *Encyclopedia of Microbiology*, vol. 2, 419– 37. New York: Academic Press.

Protozoan parasites in the UK – cause for concern?

Tim McHugh

A range of protozoan parasites threatens the health of UK inhabitants. As Tim McHugh describes, the risks are increasing, due to a variety of factors, but measures are available to control the problem.

The protozoa are single-celled eukaryotes that inhabit a wide range of environments; they may be free-living or parasitic in lifestyle. Parasitic protozoa may be found in all parts of the body and include intracellular as well as extracellular species. They can cause a wide spectrum of disease ranging from species whose status as parasites is still equivocal, such as *Blastocystis hominis*, to those like *Plasmodium falciparum* which cause severe disease (malaria) and have a high mortality if untreated. Within species different strains or isolates may exhibit a range of pathogenicity, indeed considerable effort has been expended in the classification of pathogenic phenotypes and genotypes. The best example of this is *Entamoeba histolytica*; extensive and elegant studies were performed that separated this species into phenotypic groups, termed zymodemes. Some of the zymodemes contained non-pathogenic strains alone and subsequently sequence analysis has allowed these to be reclassifed as a separate species, *Entamoeba dispar*.

Exotic imports

When we think of parasites our minds turn to the jungles of South America and south-east Asia and the savannahs of sub-Saharan Africa. This is quite justified, as by far the biggest parasite burden is borne by the developing world. Malaria in all its forms is responsible for 1·5 million deaths per annum, of which 90% occur in Africa. The parasite responsible for Chagas disease, *Trypanosoma cruzi*, accounts for 140,000 disease episodes per year and this represents a substantial population of individuals with long-term debilitating disease. In Britain these parasites are seen in travellers returning from endemic regions and with the massive increase in foreign travel, both for pleasure and work, there is naturally an increase both in awareness and incidence of exotic imports.

The protozoa that we associate with travel are the vector-borne diseases: malaria, trypanosomiasis and leishmaniasis. There are 1,000–1,500 malaria cases per year in England and Wales; trypanosome and leishmania infections are in the tens rather than the thousands. These parasites all require an invertebrate vector in which they multiply, enabling transmission when the infected fly takes a blood meal from the unwary traveller. The range of suitable host insects is dependent on temperature and humidity; these provide a barrier to the widespread dissemination of these parasites in the UK. Although, with changing climate patterns, the day may yet come when the marsh parishes of Kent are once again a source of *Plasmodium vivax* malaria, there have been no indigenous cases of malaria in England since the 1950s. Malaria is the biggest threat and most infections associated with travellers from the UK could be avoided by use of appropriate prophylaxis and straightforward precautions whilst abroad (for advice contact the PHLS Malaria Reference Laboratory http://www.malaria-reference.co.uk).

These parasites represent the most dramatic face of parasitic protozoa, although returning travellers may well feel that the debilitating diarrhoea that so many bring back from their journey is of equal importance. This is often the result of bacterial infection, but protozoa are amongst the likely suspects. These include the flagellate *Giardia lamblia* and the amoeboid parasite *Entamoeba histolytica*.

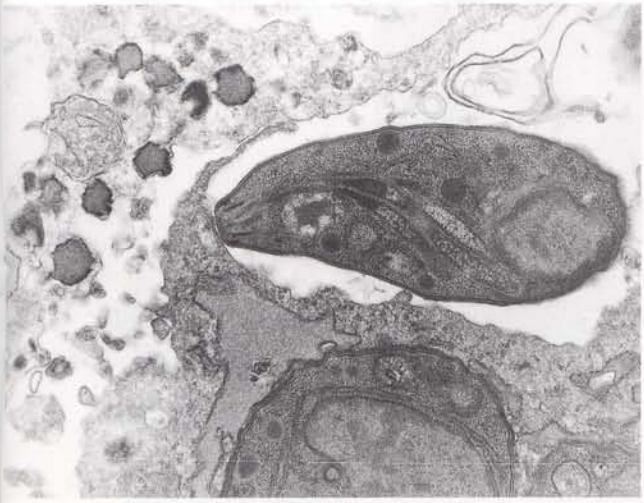
There were 536 laboratory reports of *Entamoeba* infection in 1998 in England and Wales. The majority of patients present with diarrhoea only, but in a significant number (10% of infections) disseminated disease occurs with formation of liver abscesses and meningoencephalitis.

Contaminated water

Some protozoan agents of diarrhoea are not only found in the tropics but are also indigenous to the UK. They are mainly associated with the contamination of water supplies, or foodstuffs that have been in contact with contaminated water, either as a result of irrigation or washing. The two principal organisms are *Giardia lamblia* and *Cryptosporidium parvum*. For each of these parasites there are 4,000–5,000 laboratory reports per year from England and Wales and each is associated with outbreaks.

Cryptosporidium has been the focus of attention recently as it gives us control problems. The infectious oocysts are resistant to chlorination and we do not have effective antiprotozoal agents to treat symptomatic infection. There are currently 5–10 outbreaks of cryptosporidiosis per year (compared with less than one per year for *Giardia*); these are largely associated with water supply treatment failures or contamination by sewage. However, outbreaks have been reported as a result of contamination of swimming pools and also from handling animals during farm visits. Recently, legislation has been introduced for continuous monitoring of water treatment sites. Companies are required to sample 1,000 litres of water over 24 hours for the presence of *Cryptosporidium* oocysts. If more than one oocyst is found per 10 litres of water then the company is liable to prosecution.

Giardia, though not so often associated with outbreaks, is still a significant cause of disease in the UK. Infections may be associated with foreign travel and lack of attention to such precautions as using bottled or boiled water and avoiding ice in food or drinks. Nevertheless, *Giardia* is indigenous to the UK and people become infected who have no history of travel. There is no clear example of a single reservoir species in the UK, but in the USA *Giardia* is regarded as a zoonosis. Beavers and other wild animals act as a reservoir and *Giardia* infection is particularly associated with those who undertake 'wilderness sports'.



At risk populations

The reality of parasitic infections for the generally fit and well patient in the UK is that the disease will usually be self-limiting or amenable to chemotherapy. However, a significant population of people may be regarded as at particular risk from these infections. We think automatically of the immunosuppressed, either as a result of HIV infection or immunosuppressive therapy. It is worth remembering that the immune responses in these two groups may be quite different and this is reflected in the parasites causing infections and the responses to them. However, significantly larger groups at risk of infection are those at the extremes of age. The young are at risk in the first years of life as their immune responses develop to maturity, but also because of their very tactile approach to exploring the world around them. The increasing population of the elderly is also vulnerable to infections that a younger person would shrug off. Indeed in recent outbreaks of *Cryptosporidium* it has been the elderly who have suffered the most; this infection is associated with passage of large volumes of watery diarrhoea for which the only option is to provide hydration support.

Several protozoa associated with intestinal disease have come to our attention as a result of immunosuppressed patients presenting with unusual diarrhoeas. These include the microsporidia, *Isospora belli* and *Dientameoba fragilis* as well as *Cryptosporidium*. It should be remembered that these organisms can also be seen in the immunocompetent.

Another parasite that has come to the fore in recent years is *Toxoplasma gondii*. This is because it impacts not only on the immunosuppressed but also because infection in pregnancy can have catastrophic effects. *Toxoplasma* is closely related to both *Cryptosporidium* and *Plasmodium*. It has a complex life cycle in which sexual reproduction only occurs in the cat family, while in all other hosts asexual reproduction occurs. Transmission is via two mechanisms. Cats pass infective oocysts in the stool which contaminate the environment, while the alternative route of transmission is consumption of meat containing the latent life cycle stage, the tissue cyst. Thus, those at risk are advised not to eat 'pink' meat or uncooked meat products. In Europe this applies particularly to lamb-based products, but in North America the focus is on pork. In the UK approximately 25–30% of the general population has been exposed to *Toxoplasma* and are positive in serological tests. The tissue cyst is immunologically inactive, is found in muscle and brain tissue and is responsible for sustaining a viable infection for the lifetime of the host. Those who are serologically positive are assumed to have a latent infection, held in check by the host immune response. This is the nub of the problem. Should the patient become immunosuppressed, then the 'time bomb' is released. Commonly a toxoplasmic encephalitis is observed but in transplant patients pneumonia and other manifestations may be seen.

Toxoplasma in pregnancy is a great cause of anxiety. If the mother acquires *Toxoplasma* infection for the first time during pregnancy then transmission to the foetus may result in mental and physical disability. Severe disease is most likely to result from infection early in pregnancy. Although most congenitally infected children will be asymptomatic at birth, in later life up to 80% will develop symptoms, particularly eye disease. Treatment for toxoplasmosis in pregnancy is problematical because of toxicity to the foetus; it is a better option for those pregnant or planning pregnancy to avoid undercooked meats and handling cat litter.

Often forgotten

A protozoan parasite that is often overlooked is *Trichomonas vaginalis*, which of course cannot be ignored in clinical practice. Trichomoniasis affects at least 170 million individuals globally, may increase the risk of transmission of HIV and predispose pregnant women to premature rupture of membranes and early labour. This flagellate parasite of mucosal membranes is very similar in biology to its close relative *Giardia*, but does not require the resistant cyst stage as it is transmitted by intimate sexual contact.

Public health

The title of this piece poses the question 'cause for concern?'. I have tried to outline the areas in which the parasitic protozoa pose a threat to the health of the population in the UK and I suggest that this challenge may best be met from a public health rather than an individual basis. Control of these infections is preferable to treatment. There are two components to effective control measures. First, public awareness; I hope the examples I have given show that if an individual chooses, they can avoid most of the risk of these infections. The second component is an appropriate infrastructure to minimize exposure; this may include measures to ensure the supply of clean water and surveillance for contaminated foodstuffs.

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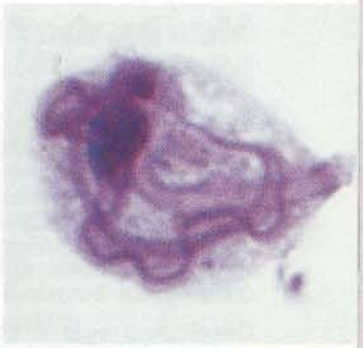

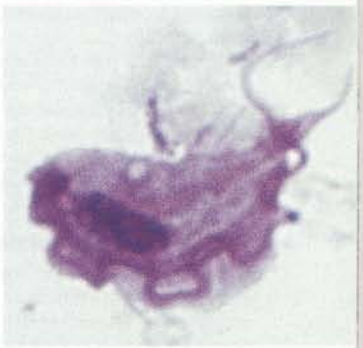

TOP LEFT:
Fig. 1. Transmission electron microscopy image of *Toxoplasma gondii* tachyzoite stage invading a host cell in a tissue culture preparation. The specialized structures of the apical complex can be seen; these are characteristic of this family of protozoans which includes *Plasmodium* and *Cryptosporidium*.
COURTESY DR T.D. MCHUGH

ABOVE:
Fig. 2. Haematoxylin and eosin (H&E)-stained smear showing the flagellate protozoan *Trichomonas*. The characteristic tear drop shape, flagellae and nucleus can be seen. The gut protozoan *Giardia* sp. has a very similar appearance.
COURTESY PROFESSOR S.H. GILLESPIE, ROYAL FREE & UNIVERSITY COLLEGE MEDICAL SCHOOL, LONDON

SocietyNews

November Council Meeting

Comings and goings

● The President welcomed **Professors Hilary Lappin-Scott** and **Tony Nash** and **Dr Keith Jones** as new Elected Members to their first Council meeting. This was also **Professor Chris Thomas**'s first meeting as the new Editor-in-Chief of *Microbiology* and **Professor Howard Jenkinson**'s as the new Scientific Meetings Officer. We wish them well in their new roles.

Developing regional activities

● Arising from a discussion about the value of regional branches of the Society, Council reaffirmed its belief that the interests of members are already well-served from the choice of main scientific meeting venues. However, Council was reminded by the Deputy Executive Secretary that funding is available from the Society to support one-day regional meetings on focused topics or to provide opportunities for postgraduate groups to meet. A note about this appears on p. 34.

Support for microbiology teaching in schools

● Council has provisionally allocated £90,000, primarily to enable teachers to attend in-service training courses in microbiology. The scheme has still to be finalized and full details will appear in a future issue of *Microbiology Today*.

New Food and Water Group

● Council has approved the establishment of a new Food and Water Group in recognition of the growing importance of this area both for members of the Society and for the wider public at large. Details of the new group will appear in a future issue of *Microbiology Today*.

Corporate and schools membership

● Council has agreed in principle to the establishment of two new categories of corporate membership, which it was intended should provide a linking between industrial sponsorship and the work of the Society in schools. Further details will appear in a future issue of *Microbiology Today*.

Research technicians

● It was also agreed in principle to create a fund for the support of 'research' and 'teaching' technical staff to attend scientific meetings of the Society, provided their Head of Department or another appropriate member of SGM could indicate that, through their level of commitment, they would benefit from attendance. Further discussions are taking place to make the arrangements for the scheme, which is likely to commence in 2002.

New Honorary Members

● Council was pleased to confer Honorary Membership on the following past Presidents of the Society, who had completed their full term in office, in recognition of their service to the Society: **Professor Derek Burke**, **Professor Howard Dalton**, **Professor Tony Trinci** and **Professor Roger Whittenbury**.

● *Alan Vivian, General Secretary*

Nominations for Members of Council

Three members, **Dr U. Desselberger**, **Professor G.P.C. Salmond** and **Dr K. Jones** retire from Council in September 2001. Dr Desselberger and Professor Salmond are not eligible for immediate re-election but Dr Jones, having filled a vacancy for one year which arose when **Professor Chris Thomas** was elected to the post of Editor-in-Chief of *Microbiology* in 2000, is eligible for immediate re-election. Nominations are invited from Ordinary Members to fill these three vacancies. All nominations must include the written consent of the nominee and the names of the proposer and seconder, both of whom must be Ordinary Members. Members submitting nominations should indicate the main area of microbiological interest of their nominee, who must have been a member of the Society for at least two years.

Nominations should be sent to the SGM General Secretary, Professor Alan Vivian, Department of Biological and Biomedical Sciences, University of the West of England, Coldharbour Lane, Bristol BS16 1QY to arrive **no later than 30 April 2001**.

New Years Honours

Professor Leszek Krzysztof Borysiewicz, Professor of Medicine, University of Wales, has been made Knight Bachelor for services to medical research and education.

Professor Brian Arthur Bridges, MRC Cell Mutation Unit, University of Sussex, has been awarded an OBE for his work on the cellular effects of radiation.

New on the SGM website ...

Microbiology in the News

For up-to-date fortnightly summaries of topical microbiology items as they appear in the UK broad sheets click on Microbiology in the News **http://www.sgm.ac.uk/PA/mic_news/micro.htm**. Microbiology in the News is written to appeal to those who are short on time, and also provides a valuable teaching resource for undergraduate lecturers.

Staff News

Welcome to **Yvonne Taylor**, new part-time PA to Janet Hurst, who will be helping to reduce the ever-mounting piles of paper in the External Relations office by converting them to an electronic format.

New Group Conveners

Petra Oyston

Microbial Infection

My microbiological interests lie in the molecular basis of bact erial pathogenicity. Since starting at CBD Porton Down in 1992, I have focused on the notorious pathogen *Yersinia pestis*, but work in my group is also under way on *Francisella tularensis* and *Burkholderia pseudomallei*. The final aim of most of our work is to develop effective vaccines and antibiotics against these bacteria. I have served on the Microbial Infection Committee for 4 years as an ordinary member and have been involved in the organization of group and main symposia. It has been very interesting and rewarding work and I must thank Peter Andrew for the sterling job he has done as Convener in this time.

Kirk Semple

Environmental Microbiology
from April 2001

My original training was in Biological Sciences at Napier in Edinburgh (1986–89). I quickly moved into environmental microbiology through my PhD research at the University of Newcastle (1989–93), investigating phenolic degradation under

the supervision of Ron Cain. From Newcastle, I moved to the Midlands to work at Horticulture Research International on a 2-year EU-funded bioremediation project (1993–95), looking at the potential for composts to clean up chlorophenol-contaminated soils, working with Terry Fermor.

In 1995, I moved to a lectureship in environmental microbiology and ecotoxicology in the Department of Environmental Science at Lancaster University. Over the past 5 years, I have moulded a small, but productive research group. My research interests involve understanding the fundamental processes concerning the fate of organic contaminants in the terrestrial biosphere, particularly interactions between soil-contaminant-biota (microbes, plants and invertebrates), considering bioavailability, biodegradation and ecotoxicity of the contaminants using novel techniques; leading into risk assessment and remediation of contaminated land.

Grants

Details of all Society grant schemes are available on the SGM website at **http://www.sgm.ac.uk** Application forms for most schemes can be downloaded. Click on the Grants & Funding button for details.

Any enquiries should be made to the Grants Office at SGM Headquarters, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (Tel: 0118 988 1821; Fax: 0118 988 5656; email: grants@sgm.ac.uk).

Watanabe Book Fund

A generous donation to the Society by Professor T. Watanabe of Japan has enabled the Society to set up a fund to make annual awards for the benefit of members in developing countries. This is distinct from our own International Development Fund.

Members of the Society who are permanently resident in a developing country may apply. The purpose of the fund is to enable members involved in higher education and/or research to acquire for their libraries books or possibly journals relating to microbiology. Applications should include:

1. A list of the publications required together with an estimate of their cost (the total cost for any one application should not exceed £300 sterling).
2. A letter from the Head Librarian of the organization certifying the need for the books and the address to which the books should be sent, a statement on where the books will be kept and an outline of the loan arrangements for members of the organization.
3. A description of the member's organization and its involvement in microbiology, the number of staff and students and details of the nature of any courses in microbiology provided by the organization, i.e. BSc Microbiology, technical training, etc.
4. A curriculum vitae of the principal applicant.

None of these items (1–4 inclusive) should exceed one side of A4 paper each.

Applications (two copies) should be sent to the Grants Office at SGM HQ. The closing date is **5 October 2001**.

International Development Fund Awards 2000

The following awards have been made from the Society's International Development Fund. The Fund exists to provide training courses, publications and other assistance to microbiologists in developing countries. The rules for the 2001 Fund will be published in the May issue of *Microbiology Today*.

Dr J. Campbell-Tofte, Royal Danish School of Pharmacy, Copenhagen, Denmark – up to £5,000 to carry out a PCR course in the Abeokuta, Nigeria.

Dr S. Cutting, School of Biological Sciences, Royal Holloway, University of London – up to £12,000 to develop molecular biology in Vietnam over two years.

Professor S. Gillespie and colleagues, Royal Free & University Hospital Medical School, London – up to £6,000 to help establish a reference and training centre for respiratory bacteriology in East Africa.

Dr A. Leck, Institute of Ophthalmology, University College London – up to £4,560 to provide microbiology training in the tropics aimed at preventing blindness from corneal ulcers.

President's Fund

The President's Fund offers financial support to younger members of the Society for the following:

1. Travelling to present a paper or a poster on a microbiological topic at a scientific meeting.
2. Attending a short course (up to two weeks).
3. Making a short research visit.

Larger awards are available for the short research visits and there are separate application forms for these.

1 & 2 – Smaller Awards

Maximum grants are £125 for attendance at meetings or institutions/attending an approved course in the country of residence, £200 for travel to another European country and £300 for travel outside Europe.

3 – Larger Awards

Up to £2,000 is available for making a short research visit of up to two months duration. The host institution may be overseas or in the applicant's country of residence.

All applicants must be resident and registered for a PhD or in a first postdoctoral position, in a country in the European Union. Only one application to the President's Fund may be made during the term of a postgraduate studentship or first postdoctoral position. The full rules of the scheme are published on the SGM website, from which application forms may be downloaded.

Postgraduate Student Meetings Grants

Postgraduate Student Members of the Society currently resident in the UK or another European Union country are eligible for a grant to cover the costs of accommodation and travel in attending ONE of the following SGM meetings:

- Heriot-Watt University, *Edinburgh, March 2001*;
- University of East Anglia, *Norwich, September 2001*;

and any other Society Group or Branch meeting in 2001. An application form giving full details of the scheme was sent to each European Student Member with their subscription invoice in October 2000, but a copy may be downloaded from the SGM website. Applications should be submitted well in advance of a meeting if members wish to ensure that their grant is received before making a booking.

Vacation Studentships 2001

Awards are available by competition to enable undergraduates (in their penultimate year) to work on microbiological research projects during the summer vacation. The studentships provide support at a rate of £135 per week for up to 8 weeks; limited funding for consumables is also available. Applications are invited from members on behalf of named students. The full rules were published in the November 2000 issue of *Microbiology Today* (p. 192). The closing date for applications is **28 February 2001**.

SGM Prizes

Kathleen Barton-Wright Lecture

The 2000 Kathleen Barton-Wright prize lecturer will be **Dr Moira E. Bruce**, Neuropathogenesis Unit, Institute of Animal Health, Edinburgh, for her distinguished contribution to our understanding of transmissible spongiform encephalopathies. The title of her lecture, which will take place at the Society meeting at Heriot-Watt University in March 2001, is *The secret life of the TSEs.*

Since 1970 I have been involved in research on transmissible spongiform encephalopathies (TSEs), working initially with Hugh Fraser and Alan Dickinson at ABRO and later at the Neuropathogenesis Unit in Edinburgh. My research has been based mainly on studies of the neuropathology and pathogenesis of TSEs in experimental rodent models, with an emphasis on the effects of agent strain variation. My colleagues and I have applied approaches developed for basic scientific studies to the very real TSE-related problems facing us today. For example, mouse transmissions demonstrated a link between variant CJD and BSE. I now head the Pathology and Pathogenesis Section at the Neuropathogenesis Unit, and lead a group investigating the involvement of the immune system in TSE pathogenesis. My lecture will include a description of studies on the transmission of TSEs within and between species, with particular reference to early events in lymphoid tissues and potential approaches to intervention.

Fred Griffith Review Lecture

The 2001 Fred Griffith Review Lecture has been awarded to **Professor Noreen E. Murray**, Institute of Cell and Molecular Biology, University of Edinburgh, in recognition of her long and distinguished service to microbiology. The title of her lecture, which will take place at the Society meeting at Heriot-Watt University in March 2001, is *Immigration control of DNA in bacteria; 'self versus non-self'.*

I studied Botany at King's College London in 1956, although my scientific interest was already in microbiology and genetics, despite my love of flowering plants.

I obtained my PhD in microbiology in 1959 under the supervision of Professor D.G. Catcheside in the University of Birmingham and while mapping mutations within a *Neurospora* gene obtained evidence for 'polarized gene conversion'. My interest in allelic recombination continued throughout my postdoctoral work with David Perkins in Stanford and Harold Whitehouse in Cambridge.

The concept of polarized gene conversion prompted my interest in sequence-specific endonucleases and on moving to Bill Hayes' MRC Unit in Edinburgh in 1968 it seemed time to initiate a genetic approach to map and manipulate restriction targets in phage I; my husband (Kenneth Murray) would determine the nucleotide sequence common to each target. Eventually, that is, when we encountered predictable (type II) restriction enzymes, we entered the field of genetic engineering via the construction and use of phage vectors. I did clone and overexpress the genes for some useful enzymes, e.g. DNA ligase and polynucleotide kinase, but maintained an interest in the technically useless, but biologically sophisticated type I, restriction systems.

Peter Wildy Prize

The first recipient of the newly established Peter Wildy Prize for Microbiology Education is to be **Dr Alan Cann**, University of Leicester, in recognition of his distinguished contribution to microbiology teaching. The title of his prize lecture, which will be delivered at the Society meeting at Heriot-Watt University in March 2001, is *Microbiology and the web: a nerd's eye view.*

Alan Cann was born in Plymouth in 1958. After a south Devon childhood, he travelled north to Manchester University to study geology. But a career hammering rocks was not for him, so he switched to microbiology. This required a hop over the Pennines to Sheffield. He then

undertook a PhD on poliovirus with Jeff Almond at Leicester. Three days into this, he experienced his first SGM meeting! He gained his BTA for work on human retroviruses at the University of California Los Angeles, but was lured back from the West Coast by the MRC AIDS Directed Programme and a post at the MRC Laboratory of Molecular Biology, Cambridge. There, he gained his first teaching experience on Part II of the Tripos and was appointed to a lectureship back in Leicester in 1990. Eight years ago he began using the web for teaching and has never looked back.

Promega Young Life Scientist of the Year 2001

1400, 10 April 2001

University of Bristol

Hosted by The Biochemical Society

The candidates for the 2001 competition have now been selected by the participating societies: Biochemical Society, British Society for Immunology, British Society for Histocompatibility and Immunogenetics and the Society for General Microbiology. Each of the eight contestants will give a short talk on their research.

Representing SGM will be:

- **Gina Manning**
  Veterinary Laboratory Agency, Surrey
  Evidence for a genetically stable clone of Campylobacter jejunii
- **Chris Smith**
  University of Cambridge
  HSV-1 latency in the central nervous system

The winner will receive a cheque for £2,000 and a unique glass trophy.

The competition is sponsored by Promega to encourage excellence in communication by young life scientists.

Elections 2001 to Group Committees

A number of members of Group Committees retire in September 2001 at the end of their terms of office. Nominations are now required to fill the vacancies arising. Where the number of nominations to a Group Committee exceeds the number of vacancies, there will be an election by postal ballot. The current members of each Group Committee and number of vacancies are listed opposite. In making nominations, members are particularly asked to bear in mind the desirability of a breadth of scientific interest on each committee. Nominations, including up to five words describing the general area of interest of the nominee, should be sent to reach the appropriate Group Convener **no later than 17 April 2001** (contact details on p. 43).

(C) Convener
(CR) Council Representative
*Retiring 2001

Cells & Cell Surfaces (4 Vacancies)

C.D. O'Connor (C) (Univ. Southampton)	Stress adaptation, proteomics
J.P. Armitage* (Univ. Oxford)	Bacterial motility and chemotaxis
J.I. Armstrong (Univ. Sussex)	Yeast membrane trafficking, signal transduction
S. Bruf* (Unilever, Vlaardingen)	Fungal cell walls, stress response
N.J. High (Univ. Manchester)	LPS genetics and phase variation
B. Kenny (Univ. Bristol)	*E. coli* pathogenesis, cellular microbiology
R. McNab (Eastman Dental Institute)	Bacterial surfaces, adhesion
P.B. Rainey (Univ. Oxford)	Plant–microbe interactions
A.W. Smith* (Univ. Bath)	Antimicrobials and host responses
C.J. Stirling* (Univ. Manchester)	Membrane translocation, heat shock proteins
M.J. Woodward (MAFF Central Vet. Lab.)	Food-borne zoonoses
U. Desselberger (CR) (Addenbrooke's Hospital, Cambridge)	

Clinical Microbiology (1 Vacancy)

S.H. Gillespie (C) (Royal Free Hospital, London)	Tuberculosis, pneumococcal infections, antibiotic resistance
D. Ala'Aldeen (Univ. Nottingham)	Bacterial infections: pathogenesis and immunity
K.B. Bamford (Imperial College, London)	Chronic infection, host response, *Helicobacter*
A.R.M. Coates (St George's Hospital, London)	Tuberculosis, chaperonins, bacterial dormancy, novel pathogens
B.I. Duerden (Univ. Wales, Cardiff)	Anaerobic bacteria, public health, antibiotics
C.G. Gemmell (Univ. Glasgow)	Methicillin-resistant *Staphylococcus*; host–bacteria interactions
T.L. Pitt (CPHL Colindale)	Nosocomial, respiratory and tropical infections, cystic fibrosis
Vacancy	
I.R. Poxton (CR) (Univ. Edinburgh)	

Clinical Virology (No Vacancies)

T.G. Wreghitt (Addenbrooke's Hospital, Cambridge)	Transplantation
S. Cameron (Regional Virus Laboratory, Glasgow)	Hepatitis, HIV, clinical virology
B. Cohen (CPHL Colindale)	Diagnostics, viral rashes, saliva testing
J. Connell (Virus Reference Laboratory, Dublin)	Diagnostic virology, hepatitis
C. McCaughey (Royal Victoria Hospital, Belfast)	Diagnostic virology, hantaviruses
P.J. Molyneaux (Aberdeen Royal Infirmary)	Diagnostic virology, hepatitis B
D. Westmoreland (University Hospital of Wales, Cardiff)	Molecular diagnosis, hepatitis, congenital infections
P.M.B. White (PHL, Norwich)	Public health, HLTV 1
U. Desselberger (CR) (Addenbrooke's Hospital, Cambridge)	

Education (3 Vacancies)

P. Wyn-Jones (C) (Univ. Sunderland)	Health-related water virology
A.J. Cann (Univ. Leicester)	Molecular virology, web-based learning
T.G. Cartledge* (Nottingham Trent Univ.)	Microbial physiology and molecular biology
I.W. Davidson (Unipath Ltd, Bedford)	Immunoassay, communication and public understanding
A.R. Eley* (Univ. Sheffield)	Medical microbiology, chlamydial pathogenesis
P.S. Handley* (Univ. Manchester)	Problem-based learning, environmental microbiology
R.O. Jenkins (De Montfort Univ.)	Biotransformation of antimony, arsenic, bioremediation
J. Verran (Manchester Metropolitan Univ.)	Communication, group work skills, student-centred learning
R.E. Sockett (CR) (Univ. Nottingham)	

Environmental Microbiology (2 Vacancies)

H.M. Lappin-Scott (C)* (Univ. Exeter)	Biofilms and starvation survival
A.S. Ball (Univ. Essex)	Soil microbiology, plant litter degradation, bioremediation
G. Black (Univ. Sunderland)	Bioremediation, plant-soil-microbe interaction, biomass utilization
F. de Leij (Univ. Surrey)	Bioremediation, biological control, rhizosphere, sustainability
K.T. Semple (Univ. Lancaster)	Biodegradation, environmental pollutants, ecotoxicology, bioremediation
I.P. Thompson (NERC, Oxford)	Microbial diversity, pollution degradation and impact
G.J.C. Underwood* (Univ. Essex)	Biofilms, exopolymers, sediments, algae, nitrification
D.D. Wynn-Williams (British Antarctic Survey)	Antarctic cyanobacterial ecology, astrobiology
L.E. Macaskie (CR) (Univ. Birmingham)	

Fermentation and Bioprocessing (6 Vacancies)

G. Hobbs (C) (Liverpool John Moores Univ.)	*Streptomyces* antibiotic production and morphology
N.J. Bainton (Univ. Surrey)	Bacterial signalling and communication
R.H. Cumming* (Univ. Teesside)	Bioprocessing
M.J. Dempsey* (Manchester Metropolitan Univ.)	Biochemical engineering
M.M.G. Duchars* (Zeneca, Billingham)	Large-scale fermentation, recombinant technology
R.M. Hall* (Glaxo-Wellcome, Stevenage)	Biotransformation, fermentation development, scale-up
D.J. Mead* (Delta Biotechnology, Nottingham)	Applied microbial physiology, process control
Vacancy	
G.P.C. Salmond (CR) (Univ. Cambridge)	

Irish Branch (4 Vacancies)

M.A. Collins (C)* (Queen's Univ., Belfast)	Food microbiology
A. Bell (Univ. Dublin)	Protozoal pathogens, *Plasmodium falciparum*
C.V. Carroll (Nat. Univ. Ireland Galway)	Physiological stress, gene expression, epidemiology
E.M. Doyle* (Univ. College, Dublin)	Applied enzymology, environmental biotechnology
S.M. Doyle (Nat. Univ. Ireland Maynooth)	Protein diagnostic/therapeutic agents
J. Morgan (Univ. College Cork)	Mucosal virology/immunology, SRSV, rotavirus, astrovirus
C. O'Reilly* (Waterford Institute of Technology)	Microbial metabolism of cyanide and nitriles
N.G. Ternan* (Univ. Ulster, Coleraine)	Environmental microbiology, biodegradation, organophosphonates, enzymology
A. Vivian (CR) (Univ. West of England)	

Microbial Infection (3 Vacancies)

P.C.F. Oyston (C) (CBD, Porton Down)	Bacterial pathogenicity, *Yersinia*, vaccines
P.W. Andrew* (Univ. Leicester)	Pathogenicity: *Listeria, Mycobacterium, Strep. pneumoniae*
M.R. Barer (Univ. Newcastle)	Bacterial physiology, infection, *M. tuberculosis, Salmonella*, STEC
D.A. Devine* (Univ. Leeds)	Antimicrobial peptides, anaerobes, stress, biofilms
P.R. Langford (Imperial College, London)	Human/veterinary pathogens, proteomics, DNA arrays, meningitis
S. Patrick (Queen's Univ. Belfast)	Anaerobic bacteriology, prosthetic joint infections
L.J.V. Piddock* (Univ. Birmingham)	Antibacteria action mechanisms, resistance
D.G.E. Smith (Royal 'Dick' School Vet. Medicine, Edinburgh)	Pathogenic mechanisms, bacterial pathogens of animals
I.R. Poxton (CR) (Univ. Edinburgh)	

Physiology, Biochemistry & Molecular Genetics (5 Vacancies)

D.A. Hodgson (C) (Univ. Warwick)	Molecular genetics and physiology
D.B. Archer* (IFR, Norwich)	Protein secretion in filamentous fungi
B. Ashraf (Univ. Bradford)	Bacterial heatshock proteins, molecular chaperones
N.C. Bruce* (Univ. Cambridge)	Biotransformation, microbial enzymology
S.J. Foster* (Univ. Sheffield)	Cell walls, starvation survival
J.C. Gottschal (Univ. Groningen)	Bioremediation, physiology of starvation and competition
N.P. Minton (CAMR Porton Down)	Molecular genetics, industrial bacteria
C.E.D. Rees (Univ. Nottingham)	Environmental control, bacterial gene expression
S. Spiro* (Univ. East Anglia)	Gene regulation, (de)nitrification
I. Stansfield (Univ. Aberdeen)	Translation, gene expression, yeast
G.M. Stephens* (UMIST, Manchester)	Microbial physiology, anaerobes, fermentation
C.R. Harwood (CR) (Univ. Newcastle)	

Systematics & Evolution (2 Vacancies)

G. Saddler (C) (CABI, Egham)	Systematics of plant-pathogenic bacteria
M.A. Aquino de Muro (CABI, Egham)	Entomopathogenic bacteria and fungi, molecular techniques
B. Austin* (Heriot-Watt, Edinburgh)	Taxonomy, ecology, fish pathogens, *Aeromonas, Vibrio*
R. Goodacre (Univ. Wales, Aberystwyth)	Organism fingerprinting, molecular systematics, chemometrics
M. Goodfellow* (Univ. Newcastle)	Actinomycetes, molecular and chemical systematics
F.G. Priest (Heriot-Watt, Edinburgh)	Molecular systematics of Gram positives
I.C. Sutcliffe (Univ. Sunderland)	Membrane-anchored molecules in Gram positives
A.C. Ward (Univ. Newcastle)	Data analysis in systematics and process control
H.M. Lappin-Scott (CR) (Univ. Exeter)	

Virus (4 Vacancies)

G.L. Smith (C) (Wright-Fleming Inst, Imperial College, London)	Poxviruses
I. Brierley* (Univ. Cambridge)	Coronaviruses, retroviruses, translation, RNA structure
I.N. Clarke (Univ. Southampton)	Caliciviruses, rotaviruses, microviridae, chlamidiaphage
S. Efstathiou (Univ. Cambridge)	Herpesviruses, pathogenesis, latency, viral vectors
D.J. Evans* (Univ. Glasgow)	Picornaviruses, paramyxoviruses replication, receptors, pathogenesis
J.K. Fazakerley* (Royal 'Dick' School Vet. Medicine, Edinburgh)	Pathogenesis, neurovirology, alphaviruses, picornaviruses, apoptosis
M. Harris (Univ. Leeds)	Retroviruses, hepatitis C
E. Hoey* (Queen's Univ. Belfast)	Enteroviruses, molecular biology, picornavirus taxonomy
K.N. Leppard (Univ. Warwick)	Adenoviruses, gene expression, RNA nuclear export, cell cycle
J.C. Neil (Univ. Glasgow Veterinary School)	Retroviruses, cancer, immunodeficiency viruses/vaccines
M.A. Skinner (Inst. Animal Health, Compton)	Poxvirus, replication, morphogenesis, immunomodulation, vaccines
R.M. Elliott (CR) (Inst. of Virology, Glasgow)	

Going Public

Public Understanding of Science Award Report

ABOVE:
Heddon-on-the-Wall butterfly haven and some of the participants (top) and participants in the '*Build a Tree*' game (bottom).

RIGHT:
A young participant proudly displays his find (centre) and two ladies colouring in fungal habitats in the W.I. hall (bottom).

ALL PHOTOS COURTESY M. MILNER

The Fungal Village – Heddon-on-the-Wall

Heddon-on-the-Wall in Northumberland is the centre of an on-going conservation project that has actively involved the local community and the British Trust for Conservation Volunteers (BTCV). Derelict land has been converted into a wildlife garden (the Heddon Butterfly) surrounded by a wildflower meadow. Nearby is the village common that overlooks the river Tyne.

As a regular weekend volunteer for BTCV I have often talked to other volunteers and visitors about my '*regular job*'. As this involves environmental microbiology, I have explained that micro-organisms can play a highly beneficial, and indeed essential role in the environment, occur in immense numbers and diversity, and not all microbiologists are interested in '*cloning Molly the multiply-drug-resistant rabbit that lives in supermarket cheese*'.

Macrofungi are a highly visible and accessible group of micro-organisms and the principles behind their examination are broadly the same (and incur the same difficulties) as other micro-organisms. Also, in contrast to other European cultures, the UK is particularly fungiphobic, and there are mainly negative perceptions of their roles (e.g. the name toadstools).

With fungi as the focus, we decided to run a weekend of events in October to promote the environmental importance of micro-organisms to the villagers of Heddon-on-the-Wall. Suggesting the name '*The Fungal Village*' provoked an interesting response! Nevertheless, the participants and location proved ideal, a mixture of ages and backgrounds who explored the vast diversity of micro-organisms in their area. The weekend of informative fungal fun involved talks, walks, educational activities for the young (and young-at-heart) and a good time for all. All that remained was the weather…

…Which was brilliant for the entire time!! Several weeks of warm(ish), wet weather was followed by a bright sunny autumnal weekend that brought out plenty of fungi and, more importantly, visitors to the fungal village.

Friday night kicked off with talks about the significance and role of micro-organisms in the environment. This was followed by an introduction to fungi and how to collect and observe them responsibly from an expert field mycologist, Mariano Quintana of Madrid.

Saturday dawned bright and crisp and we all awoke refreshed, particularly those who were interviewed by BBC Radio North at 0730 prompt! A large group gathered at a local plantation to have guided fungal walks led by Mariano Quintana and Gordon Rutter (from Edinburgh). The group was deliberately divided in two and visited either a mainly coniferous or deciduous area. After wandering around about 500 m from the car park in 2 hours we lunched on mushroom soup and returned to the 'laboratory'.

The lab for the weekend was the W.I. hall fitted with two microscopes (kindly loaned by the University of Newcastle upon Tyne). Our groups examined their fungal collections and followed a number through the (sometimes tortuous) identification process. This included introducing them to systematics, keys and looking at the microscopic features of the fungi (using spore prints and the microscopes). However, before that we all took part in '*Toadstool or Tree*', a game being trialled by our visiting British Mycological Society education officer, Sue Assinder. This required lots of running about in circles and even more brain power – this was a problem for the event organizer! Other young persons' activities in the afternoon included how the mushroom got its spots and painting a fungal habitat.

Phewww!!! After all this hard work we needed to relax. *No chance*! The BTCV volunteers prepared a barbecue and broth supper for all participants. About 40 people came out to enjoy the excellent food, drink and conversation.

Sunday once again dawned bright and crisp, and we awoke refreshed, particularly those who had been drinking the real ale the previous evening.

'*What's on Your Patch?* was a guided walk to discover the diversity of fungi on the village common. As on the

Saturday, the people were split into two groups and taken around the common in, looking at either mainly mixed woodland or a small meadow area. Once again, everyone (even the mycologists) was impressed by the fungal diversity, with more than 50 species found in about 2 hours. After lunch a choice of events was available: further identification using microscopes; a mycological treasure hunt, where clues were traced by following the mycelia (if one didn't get entrapped in it); and painting banners to illustrate the fungal life cycle. The group game was '*Build a Tree*' where members were used to construct a tree trunk, tap root, xylem, bark, roots and associated mycorrhizal fungi that all made various noises when happy. There's nothing quite like group silliness to prove a point.

On Sunday evening we all parted, after a highly enjoyable weekend. Everyone was amazed by the diversity of fungi, even in 'their backyard', and had acquired an understanding of the processes and problems of fungal identification. Above all, the weekend brought people of all ages and backgrounds together to learn about microbiology in the environment. After such overwhelming enthusiasm we have started to ensure that the Fungal Village is not an isolated event and it will be repeated next year.

P.S. So that was it?

No way! 72 hours after the Fungal Village, five able volunteers travelled (at their own expense!) to the Sierra Guadarrama mountains north of Madrid, Spain, to continue their mycological training in a different environment.

● *Dr Mike Milner is carrying out research into the molecular microbial ecology of in situ bioremediation in NRG Fossil Fuels, University of Newcastle-upon-Tyne. Tel. 0191 285 1999; Fax 0191 222 6669; email m.g.milner@ncl.ac.uk*

LEFT:
Young mycologists with their model Amanitas (top) and the microscopy lab (bottom).

CENTRE RIGHT:
Inside identification at the W.I. hall.

BOTTOM LEFT:
A fungal foray with Gordon Rutter (top) and a typical scene inside the W.I. hall (bottom).

ALL PHOTOS COURTESY M. MILNER

SGM Public Understanding of Science Awards

If you are planning any projects to promote the public understanding of microbiology then SGM may be able to help you. Grants of up to £1,000 are available to fund appropriate activities. Applications are considered on a first come, first served basis. The current funding year runs from January to December 2001.

See SGM website for details and an application form.

ScienceWorld – From medicine to media

Tune in to ***ScienceWorld*** this Sunday from 6.00–7.00 pm for a look at this week's discoveries, breakthroughs and inventions from the realms of science and technology, some top tunes and a chance to win a meal for two at Garfunkels Resaurant.

With Chris Smith, Shibley Rahman and Catherine Hawkins

Don't You Dare Miss it!

We usually get to the station at about 5.30 pm every Sunday, in theory giving us half an hour to organize the material and select music for the show, before we go live on air at 6.00 pm. In practice, somebody is usually late, the photocopier is usually out of paper and nobody knows the weather forecast.

If you'd asked me at the beginning of 1999 what I saw myself doing in the forthcoming new millennium, probably the last thing I'd have said would have been presenting a science show on local radio every Sunday evening. Like most of these things the show began as a series of lucky coincidences. A couple of us who had been involved with presentations during National Science Week were invited along to a local radio station to talk about science for an hour or so. It had been intended to be a one-off appearance, but the show went so well that we left with an invitation to appear weekly, as guests on a weekday evening show. We worked our way through every single interesting biomedical topic that we could think of. We tackled brain disorders, gene therapy, the microbial world, and even sexually transmitted infections and contraception. The show on contraception was extremely popular, but almost got us into trouble. By that time, as an experiment, we were also being broadcast live on cable television, as well as radio, and we had filled the studio with every conceivable kind of contraceptive (kindly supplied by Addenbrooke's Hospital genito-urinary medicine clinic). Interestingly, viewer and listener surveys revealed that for that show our most substantial TV audience was in Harlow, Essex (a phenomenon that remains unexplained, but is open to interpretation!), and more shockingly, that a staggering 55,000 people were tuning in to the show each week.

At about this time it occurred to me that, since the show had been very popular and there was an obvious niche for a product like it in Cambridge, it might be possible to obtain some sponsorship so we could set ourselves up with our own dedicated science show, giving us the freedom to improve and develop the concept without the constraints of having to fit in as guests on someone else's show.

As luck would have it, the Biotechnology and Biological Science Research Council (BBSRC) launched a new grant scheme to fund ventures into public understanding of science and were inviting applicants to apply for awards of up to £10,000 to help put their ideas into action. I put the idea to the radio station and after endless meetings and phone calls we eventually had a deal. They promised us an hour-long Sunday evening slot, at a very reasonable rate, subject to us raising the necessary sponsorship. We then wrote the world's fastest grant application, submitted it to the research council, and went home for Christmas.

In January 2000 we received news that we had been awarded a grant of £7,000. The radio station were pretty shocked – I don't think they really believed we would get the money, but on Sunday 27th February the *ScienceWorld* show was launched.

We begin each show with a news round up of the weeks' discoveries, publications, innovations and inventions. We play popular chart music between items, run a competition and phone-in throughout the show and feature a special live guest interview, including recently James Watson, Sir Alec Jeffreys and Richard Dawkins. The material, which we write ourselves, is gleaned from journals, newspapers, periodicals (including *Microbiology Today*!) and the internet.

The success of the show stems from the fact that we keep the science simple and humorous, and intersperse the talking with popular chart music, generating an accessible broadcast that appeals to a broad spectrum of listeners. Also, as far as we know, *ScienceWorld* is the only dedicated science show to be broadcast on a commercial radio station in the UK.

In a short space of time we have had to make the transition from medical and PhD students to DJs which has involved learning how to run all the gadgetry required to 'drive' the show and make it sound good. It's not easy to talk intelligently whilst you are watching the clock, cueing the next song, adjusting the mic levels and monitoring the backing music, but if the listener figures are anything to go by, we're definitely getting there. The skills we have learned have also proved surprisingly useful in the lab, providing the perfect training in giving talks and presentations, working under pressure and in good time-keeping ! Doing the show live is an enormous buzz, mainly because you know that when you push up the microphone slider, thousands of people will hear you make a mistake if you say the wrong thing (a bit like speaking at a conference really) – it's a pretty strong incentive to get it right.

● ***Chris Smith, Medical and PhD student, Division of Virology, Department of Pathology, University of Cambridge.***

'ScienceWorld' is written, produced and presented by Chris Smith, Shibley Rahman and Catherine Hawkins, sponsored by the BBSRC, and broadcast live on 107.9 (FM) The Eagle, (Cambridge) every Sunday evening from 6.00–7.00 pm.

TOP RIGHT:
The *ScienceWorld* team prepare for a show. *From left to right:* Catherine Hawkins, Guest, Shibley Rahman and Chris Smith.

BELOW:
Chris Smith in the 'The Eagle' studio in Cambridge.

PHOTOS COURTESY CHRIS SMITH

New International Masters Programme in Biotechnology

The Technical University of Denmark (DTU) is offering a two-year Master of Science Degree in Biotechnology starting in September 2001. Biotechnology is a major focus area at DTU for both teaching and research. Our research interests cover the major areas of the multidisciplinary field of biotechnology, from bioinformatics to microbial interactions in foods.

Within our education, there is an emphasis on the function of whole cells, that is, a systems approach is applied. This comes through a close integration of many different disciplines such as protein chemistry, molecular biology, ecology, taxonomy, anaerobic microbiology, enzyme technology and fermentation physiology.

Our aim is to educate skilled graduates to a high level, with the following key subject areas in the Masters Programme:

- Bioprocess Engineering
- Immunology
- Bioseparation
- Environmental Biotechnology
- Bioinformatics
- Microbial Physiology
- Metabolic Engineering

We are keen to attract the best students from around the world to the Masters Programmes at DTU, and therefore we have secured a number of scholarships for students who are accepted on the course. In addition, the course does not carry tuition fees. However, potential students are urged to apply early, as places may be limited (deadlines and further information are available on our website). We have close collaboration with a number of Danish industries, offering the possibility of placements or employment during or after the study programme.

DTU is located in Lyngby, around 10 km north of the Danish capital, Copenhagen, and so is ideally placed for accepting international students. The surrounding area has many places of cultural and historical significance (Hamlet's Elsinore castle is close by), and the region benefits from close links to Scandinavia via the recently opened 17 km bridge to Sweden. If you require further temptation, Copenhagen enjoys a drier climate than much of Britain, a real treat if you hail from the west of Scotland!

Further information can be found at **www.ibt.dtu.dk/masters_programme** or by contacting Mhairi McIntyre, Centre for Process Biotechnology, Building 223, Technical University of Denmark, 2800 Lyngby, Denmark (email mhm@ibt.dtu.dk).

Soapbox!

Whether you're an undergrad or postgrad, the SGM wants to hear from you. Anything goes (as long as it's microbiology).

- Any interesting news items e.g. events that you've taken part in.
- Tell us what you think about your degree/research, your university.
- Your experiences e.g. giving presentations or finding a job.

Win **£25** plus **one year's student membership to the SGM** for the best letter published in each issue of our magazine. Send your entries to: **soapbox@sgm.ac.uk**

SGM reserves the right to edit entries prior to publication. Here's the first contribution.

Dear Soapbox

As a microbiology honours student who has chosen a lab-based research project, I have gained (and am gaining) an uncensored, no-frills, 'Access All Areas' style insight into the world of working microbiologists in their natural habitat ... the lab. This experience is enabling me to decide whether or not this is a world I want to willingly enter. Like many students I went into this degree with my eyes only half open to exactly what it entailed.

Living with arts students for the past year has made me almost resent the subject for its long hours compared to other degree courses, the running between buildings for lectures (which almost always over-run leaving you even less time to run to the next building) and of course that overwhelming state of confusion you are left with after many a practical has ended and it's time to write it up.

But that was then and this is now, the now that gives us more responsibility, more importance and inevitably a lot more weight on our shoulders. We no longer have the ability to blend into the general mass of life science students, because we have specialized and suddenly have to face the scary truth that our lecturers are on first name terms with us (without referring to a list). So as we don our 'I'm a third year' lab coats (tight around the neck and wrists to avoid lethal spillages) and have signed all the relevant safety contracts we are obliged to take on our practical work with a new found sense of professionalism.

Can't help like feeling like a bit of an imposter though, working in a lab full of hard working, dedicated PhD students who are all genuinely full of enthusiasm for their work. Yes, it's time to get serious about my studies for the first time in ... well for the first time! But the underlying issue here is whether I really want to be a professional microbiologist. It is now that I have to ask myself questions such as: could I ever get as excited and enthralled as my peers when a PCR actually works, or receive a new TGGE machine with all the nervous anticipation you would expect with a new born baby!? Do I pride myself on my aseptic technique? Could I live with the smell of dodgy latex lingering on my hands for so long after I have taken my gloves off, as well as all the other sickening smells that come with the territory?

But probably the most important thing for me is whether I could spend days, months and years following protocol after protocol without really thinking. A lack of creativity in my daily schedule may cause me to lose track of why I am studying in this field and the vast scope for development this hugely influential subject has to offer.

Well, as I said, I'm getting a glimpse of what it could be like, and hopefully by the end of the year I'll know whether or not it is something it should be like, for me anyway.

■ ***Julie Srivastava***
University of Liverpool

If anyone out there would like to respond to the views raised in this letter please email soapbox@sgm.ac.uk

The content of letters in this section does not reflect the opinion of the SGM.

A job in ... Science Policy

In a new series of articles, Gradline editor Tracey Duncombe explores the range of careers available to microbiology graduates. Here she interviews Rebecca Bowden who works for the Royal Society.

I met up with Rebecca in the auspicious setting of No. 6 Carlton House Terrace. Even science purists can't help but be taken aback by the grand architecture and admire the many paintings that adorn the walls, which combine to give you a feel for the historic nature and well respected traditions of the Royal Society. My visit coincided with the Royal Society's MPs briefing on stem-cell research and there was a very up-beat, bustling atmosphere to the place.

Profile

Name Rebecca Bowden

Age 31

Present Occupation
Senior Manager Science Policy, The Royal Society

Previous Employment
Senior Scientific Officer, Department of the Environment (now DETR)
Manager of administration section of the biotechnology unit

Research Associate, Dept Agriculture and Environmental Science, University of Newcastle
Development and risk assessment of genetically engineered avian probiotics

Education
PhD, Dept Genetics and Microbiology, University of Liverpool
Ecological impact of transfer of antibiotic resistance genes within natural populations of bacteria in the soil environment

BSc (Hons), University of Liverpool
Microbial biotechnology

Q *What prompted you to leave research?*

'I wanted a broader overview, I didn't want to continue looking at just single genes or bacteria in the laboratory, but I wasn't sure what kind of jobs were out there. I saw an advert for a post as higher scientific officer at the Department of the Environment (DoE) to review applications to release and market genetically modified organisms (GMOs), and applications for contained use. This related a lot to what I'd already done in Newcastle and during my PhD, and it was also a good opportunity to see if I liked office work.'

Q *You stuck with it. What was it that you enjoyed about the post?*

'I was the only person for the DoE who was reviewing applications for contained use in the UK and increasingly I was looking at applications to market. This involved a lot of paperwork and working to very strict deadlines. There is a legal framework for these applications, which can be as little as 30 days, and this can't slip so I had to be very good at time management. It was a bit like juggling experiments back in the lab.

Whilst at the DoE I became involved in negotiations under the UN convention for biological diversity. This involved preparing the biosafety protocol, an international agreement, on how to handle GMOs. I was seconded and promoted to the scientific adviser for the UK delegation. At the time the UK was President of the EU and therefore we took the lead and had a joint chair with members of the European Commission. My role was to speak for the EU in the scientific working group, which was terrifying but really enjoyable. I liked watching the people involved in negotiations, it was good fun. It also got me more interested in policy work.'

Q *What prompted your move to the Royal Society?*

'It seemed to be a way forward which would give me a much broader experience in science policy. I became part of a small unit in general science policy. This included working on all aspects of public policy, including the Kyoto agreement and renewable energy. I thought this would allow me to get away from GMOs, but then I discovered that the RS hadn't commented on GMO policy. I gathered a group together, which included RS fellows, members of the NFU, the Institute of Grocery and others, to review the state of the science on GM plants (1998) and concerns for the future. I became known as *biotech woman* because biotechnology policy exploded out of control.'

Now I'm Senior Manager of the section covering anything in innovation, how to develop the science to make money; energy policy; and the science base itself, including the RAE. I'm responsible for six managers and four support staff. I've one manager now just for biotechnology, which I'm happy for them to take over.'

Q *How does policy tie in with the Society's other work?*

'The RS has a big budget for its fellowship schemes and public meetings, but the budget for the policy unit is much smaller. We don't lobby directly or run advertisements. Rather, we gather expert groups together and produce an authoritative, independent view. Our primary aim is to inform policy makers and this has to be done with independent money, even though we do receive offers from various organizations. We may hold public meetings on the back of our statements and so this has affected how we interact with the public. We're still viewed as an *old boys' club* in some quarters but now we're getting out there and helping facilitate discussion, as well as trying to inform policy.'

Q *Your career to date seems so well planned. Was that intentional?*

'Not at all. I think you need to step back and look at what skills you have. I could've hated my job at DoE. It just happened that I enjoyed it and was good at it.'

So you want to work in Science Policy?

Here's what you need.

Science Policy Officer, The Royal Society

Degree in science, engineering or technology (dependent on the post applied for).
An MSc is a bonus. Administration experience is necessary.

Manager, The Royal Society

3–4 years postgraduate experience. A PhD is not necessary.

Higher Scientific Officer, DETR (formerly DoE)

Postdoctoral experience. The candidate must show management experience; this could be supervising students in the laboratory. Good writing skills are required.

For further information about the Royal Society or DETR, see their websites at:

http://www.royalsoc.ac.uk/

http://www.detr.gov.uk/

● If you have any stories or news for publication in Gradline, please send them to Tracey Duncombe at pa@sgm.ac.uk

Meeting preview
New challenges to health: the threat of virus infection

Geoff Smith

A preview of the topics to be discussed in the Main Symposium at the SGM Meeting at Heriot-Watt University, 26–27 March 2001.

The virus group has organized the main symposium at the Spring 2001 SGM meeting at Heriot-Watt University, Edinburgh. The purpose of the meeting is to review the continuing threat of viruses (and prions) to human and animal health. Although several virus diseases have been controlled by vaccination (such as polio, measles, mumps, rubella and yellow fever) and one (smallpox) has been eradicated, viruses remain a potent threat to human and animal health due to their ability to evolve and adapt rapidly. For viruses such as influenza and HIV, the ability to undergo rapid antigenic variation enables them to evade existing immunity and cause disease. Viruses may adapt to new situations, such as changes in the density of human, animal or insect hosts, or the presence of immunosuppressed populations, and cause disease where hitherto they were unable to do so. Rapid virus evolution also enables virus strains to arise that are resistant to existing drugs. The meeting will consider the mathematical modelling and surveillance of virus infections.

There will follow talks that review the molecular, cell biological mechanisms by which viruses and prions induce disease. These include influenza and HIV, the devastating haemorrhagic diseases caused by Ebola and Marburg viruses, prion diseases such as BSE and new variant CJD, psychiatric illness and how drug-resistant virus strains pose a major problem for anti-viral chemotherapy

The organizers are most grateful to all the speakers for their contribution to the symposium and for their chapters for the book that will be available at the meeting. The meeting will be of interest to all those interested in virus and prion disease and is an important reminder to all that viruses are and will remain a continual threat to human and animal health.

● *Professor Geoffrey L. Smith, Convener of the SGM Virus Group, helped to organize this symposium and can be contacted at the Wright Fleming Institute, Imperial College School of Medicine, St Mary's Campus, Norfolk Place, London W2 1PG.*
Tel. 0207 594 3971; Fax 0207 594 3973; email glsmith@ic.ac.uk

Other symposium organizers:
● *P.M. Goodwin, The Wellcome Trust*
● *W.L. Irving, University of Nottingham*
● *J.W. McCauley, Institute of Animal Health, Compton*
● *D.J. Rowlands, University of Leeds*

Further details of this meeting together with a booking form are given in the enclosed Programme Booklet. The symposium will be published as a book. A review and order form will be available in the May issue of 'Microbiology Today'.

Meetings

Meetings on the web

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

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. 43 for contact details of Group Conveners. Administration of meetings is carried out by Mrs Josiane Dunn of the Meetings Office at SGM Headquarters, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (Tel. 0118 988 1805; Fax 0118 988 5656; email meetings@sgm.ac.uk).

Abstracts Book

147th Ordinary Meeting
University of Exeter
12–15 September 2000

Community Structure and Co-operation in Biofilms

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 sent to the appropriate Convener, preferably by e-mail. 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, Professor 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

SPRING 2001 – 148th Ordinary Meeting

Heriot-Watt University, Edinburgh
26–30 March 2001

● Main Symposium
New Challenges to Health: the Threat of Virus Infection

● PROGRAMME BOOKLET

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

● OFFERED POSTER PRESENTATIONS

Delegates whose offered posters have been accepted should note that an area of 1 m × 1 m only is available on the poster boards for their display.

● MICROSCENE NOTICEBOARD

At the meeting, a board will be set up with notices of jobs, postdoctoral positions, studentships, courses, conferences. etc. Contributions are welcome and may be either brought to the meeting or sent beforehand to Janet Hurst at Marlborough House.

● SOCIAL EVENTS

The Heriot-Watt campus is sited a distance away from the delights of central Edinburgh and so a programme of evening social events has been arranged to keep the delegates happy when they are not attending scientific sessions. These include:

Monday 26 March
Trade & Welcome Reception

Tuesday 27 March
Society Dinner, followed by a ceilidh

Wednesday 28 March
Whisky tasting
70's Night (disco & bar)

Please support these events.

Launch of New Clinical Microbiology Group

Please support the new Group which will be launched at this meeting. It has been formed to bring together clinical microbiologists and basic medical scientists. The Group aims to stimulate the collaborations that underlie good quality medical research. The activities will be relevant to medical, dental and veterinary microbiologists and all science trained microbiologists with an interest in clinical infection.

The Group will cover:
- fundamental and applied aspects of medical, dental and veterinary infections
- the diagnosis of microbial infections
- immune response to micro-organisms
- treatment and prevention of microbial infections
- resistance to anti-microbial agents
- epidemiology of infection
- taxonomy of clinically relevant micro-organisms

The Group's first symposium on 27 March deals with *Antibiotic resistance*, followed by an offered papers session on 28 March and a workshop on *Microbiology research funding*.

● Special Symposium
Genomics: beyond the sequence

Systematics & Evolution Group and the International Committee on Systematic Bacteriology with joint funding from the National Science Foundation

26–27 March

AUTUMN 2001 – 149th Ordinary Meeting

University of East Anglia
10–13 September

● Main Symposium
Mycobacteria – New Developments

Organizers: M. Goodfellow, P.M. Goodwin, H.M. Lappin-Scott, G. Saddler and E.M.H. Wellington

10–11 September

10 September am – Systematics
N. STOKER (LSHTM) *Mycobacteria in the 21st century*
M. GOODFELLOW (Newcastle) *Systematics of mycobacteria*
S.T. COLE (Institut Pasteur) *Comparative mycobacterial genomics*
P.J. BRENNAN (Colorado, USA) *Mycobacterial cell wall*

10 September pm – Epidemiology
P. FINE (LSHTM) *TB epidemiology and environmental influences*
R.S. CLIFTON-HADLEY (VLA, Addlestone) *Bovine tuberculosis: current epidemiological issues*
D. VAN SOOLINGEN (Bilthoven, The Netherlands) *Contribution of DNA fingerprinting to examine the transmission of tuberculosis*
L.G. WAYNE (Long Beach, USA) *Dormancy in mycobacteria*

11 September am – Pathogenesis
B. GICQUEL (Institut Pasteur) *Mycobacterial genetics*
P.D. BUTCHER (St. George's, London) *M. tuberculosis gene expression during infection: proteomics and microarrays*
M.J. COLSTON (NIMR) *Interactions between host cells and mycobacteria*
J.M. SHARP (Moredun, Edinburgh) *Pathogenesis and immuno-pathogenesis of M. paratuberculosis (title to be confirmed)*

11 September pm – Control
I.M. ORME (Colorado, USA) *Early events in the lung and consequences for vaccine strategies*
D.B. YOUNG (Imperial College London) *Lipoproteins, glycoproteins and new vaccines*
K. DUNCAN (GlaxoWellcome UK) *New approaches to drug design*
S.H. GILLESPIE (Royal Free, London) *Anti-tuberculosis chemotherapy: past success and future challenges*

● Other symposia

● Microbial lifestyles

Cells & Cell Surfaces Group

13 September
Organizers: J. Armitage (armitage@bioch.ox.ac.uk) & P. Rainey (paul.rainey@plant-sciences.ox.ac.uk)

● Lower respiratory tract infections

Clinical Microbiology Group

13 September
Organizer: S. Gillespie (stepheng@rfc.ucl.ac.uk)

● Research supervision – how to get it right

Education Group

12 September, followed by a Supervisor Training workshop on 13 September
Organizer: A. Eley (a.r.eley@sheffield.ac.uk)

● Microbial interactions in aquatic environments

Environmental Microbiology Group with British Phycological Society

11 & 12 September
Organizer: G. Underwood (gjcu@essex.ac.uk)

● Bioprocess monitoring & control

Fermentation & Bioprocessing Group

10 & 11 September
Organizer: D. Mead (dave.mead@aventis.com)

● Mobile genetic elements in bacterial virulence

Microbial Infection Group

12 September
Organizers: M. Barer & P. Langford (p.langford@ic.ac.uk)

● Metabolic flux

Physiology, Biochemistry,& Molecular Genetics Group

12 September
Organizers: N. Bruce & G. Stephens (gmstephens@umist. ac.uk)

● Classification and identification of clinically significant actinomycetes

Systematics & Evolution Group

12 September
Organizer: G. Saddler (g.saddler@cabi.org)

● Offered Posters

These are welcome for all group sessions. Please submit titles and abstracts to the appropriate symposium organizer or Group Convener by the deadline of **11 May 2001**. See notice on p. 34 for general conditions for submitting posters.

SPRING 2002 – 150th Ordinary Meeting

University of Warwick
8–12 April

● Main Symposium Signals, switches, regulons & cascades: control of bacterial gene expression

Irish Branch

Functional Genomics of Microbial Pathogens

Trinity College Dublin
22–23 March 2001

Internationally known speakers in the area of functional genomics will address the questions of how the vast amounts of information being generated on the genome sequences of microbial pathogens will be used to advance our knowledge of the biology of these organisms and to devise new methods of control.

D. McDEVITT (SmithKline Beecham, USA) *Genomics: new strategies for small molecule drug discovery: opportunities and hurdles*
M. PALLEN (Queen's University of Belfast) *Data mining bacterial genome sequences*
P. DORR (Pfizer, UK) *3D structure analysis coupled with high-throughput screening*
R. RAPPUOLI (Chiron SpA Italy) *Reverse vaccinology*
P. RATHOD (Catholic University of America) *Global transcriptional changes in the human malaria parasite Plasmodium falciparum*
G. WEINSTOCK (Texas) *Genomic studies of spirochaetes*
B. WREN (London School of Hygiene & Tropical Medicine) *The full Campy: post-genome analysis of a food-borne pathogen*

Full details of this event and a registration form are on the SGM website.

Organizer: Angus Bell (abell@tcd.ie)

Microbial Genome Environment Interactions

Queen's University of Belfast
Autumn 2001

Organizers: Martin Collins (m.collins@qub.ac.uk) and Mike Larkin (m.larkin@qub.ac.uk)

For details of Irish Branch activities contact the Convener, Martin Collins (m.collins@qub.ac.uk)

Other Events

● Joint ASM/SGM Meeting

2–6 October 2001
Caribe Hilton, San Juan, Puerto Rico

Biodegradation, Biotransformation and Biocatalysis (B3)

Organizers: David Gibson (University of Iowa), Hilary Lappin-Scott (University of Exeter), Gary Sayler (University of Tennessee), James Tiedje (Michigan State University) & Gary Toranzos (University of Puerto Rico)

Following on from the successful first joint meeting of the American Society for Microbiology and the SGM at the University of Aberdeen in 1995, the two societies are pleased to announce the second joint meeting. Tropical San Juan, Puerto Rico, with its diverse landscape and numerous natural wonders, will be the site of the conference.

The conference will include a 3-day meeting with plenary sessions on each topic, invited speakers and an opportunity for short offered papers and posters.

● PROPOSED TOPICS:

Biodegradation and environmental fate of organic pollutants
Anaerobic biodegradation and biocatalysis
Genetics of biodegradation and biotransformation
Microbial communities/biofilms
Metabolic engineering
Fungal transformations and secondanry metabolism
Biocatalysis and industrial enzymes
Oxygenases in biocatalysis and biodegradation
Stereoselective biosynthesis
Directed evolution for novel reaction
Mining genomes/bioinformatics

Further details of speakers will be finalized shortly and will be available on the SGM website. For further information, contact Hilary Lappin-Scott (University of Exeter; email h.m.lappin-scott@exeter.ac.uk).

● REGISTRATION

SGM members are entitled to register for the meeting at the same concessionary rates as ASM members and Student Members may apply for ASM travel grants. See **www.asmusa.org** for registration details.

● BURSARIES

Grants will be available from the SGM for young members (postgraduate and first postdocs) wishing to attend this meeting.
Full details of the scheme will be published on the SGM website:
www.sgm.ac.uk

● Viral Zoonoses

9–11 January 2002
Royal College of Physicians, London

SGM Clinical Virology Group, European Society for Clinical Virology and the European Society for Veterinary Virology

Organizers: T. Wreghitt (Fax 01223 242775) & J. Best (jenny.best@ kcl.ac.uk)

11 September pm – Control
I.M. ORME (Colorado, USA) *Early events in the lung and consequences for vaccine strategies*
D.B. YOUNG (Imperial College London) *Lipoproteins, glycoproteins and new vaccines*
K. DUNCAN (GlaxoWellcome UK) *New approaches to drug design*
S.H. GILLESPIE (Royal Free, London) *Anti-tuberculosis chemotherapy: past success and future challenges*

● Other symposia

● Microbial lifestyles

Cells & Cell Surfaces Group

13 September
Organizers: J. Armitage (armitage@bioch.ox.ac.uk) & P. Rainey (paul.rainey@plant-sciences.ox.ac.uk)

● Lower respiratory tract infections

Clinical Microbiology Group

13 September
Organizer: S. Gillespie (stepheng@rfc.ucl.ac.uk)

● Research supervision – how to get it right

Education Group

12 September, followed by a Supervisor Training workshop on 13 September
Organizer: A. Eley (a.r.eley@sheffield.ac.uk)

● Microbial interactions in aquatic environments

Environmental Microbiology Group with British Phycological Society

11 & 12 September
Organizer: G. Underwood (gjcu@essex.ac.uk)

● Bioprocess monitoring & control

Fermentation & Bioprocessing Group

10 & 11 September
Organizer: D. Mead (dave.mead@aventis.com)

● Mobile genetic elements in bacterial virulence

Microbial Infection Group

12 September
Organizers: M. Barer & P. Langford (p.langford@ic.ac.uk)

● Metabolic flux

Physiology, Biochemistry,& Molecular Genetics Group

12 September
Organizers: N. Bruce & G. Stephens (gmstephens@umist. ac.uk)

● Classification and identification of clinically significant actinomycetes

Systematics & Evolution Group

12 September
Organizer: G. Saddler (g.saddler@cabi.org)

● Offered Posters

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Hot off the Press

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.

Chlamydial controversy

Chlamydia are a group of bacteria with the unpleasant lifestyle of obligate intracellular parasites. Their activities result in disease in many vertebrate species, ranging from being the leading cause of blindness in humans to causing spontaneous abortion in farm livestock. Their parasitic nature has made it impossible to apply many important bacteriological techniques to them. The sort of plus/minus biological markers normally used to classify bacteria do not work. A small set of biochemical, physiological, morphological, serological and DNA–DNA hybridization methods is used for their identification. With the advent of DNA-based methods there is increasing evidence for chlamydia in animals as diverse as amoebae, bivalves, alligators and chameleons, as well as their long-established hosts of humans and farm animals. As knowledge of their identification, diversity and activities has developed, the number of species, and how to define them, has also changed.

In 1999, Everett *et al.* published in IJSB a paper that reclassified the order *Chlamydiales*, with the proposal of two new families, a new genus and five new species. A group of scientists, led by J. Schachter from the Chlamydia Research Laboratory of the University of California, in a Letter to the Editor, question whether this upheaval in chlamydial taxonomy is necessary at this time: as they say, the single genus *Chlamydia* worked, and it has taken years to reach its current status of immediate recognition among the medical profession and public. In reply to this Letter and in a supporting paper, the authors of the 1999 paper have justified and strengthened the basis for the new chlamydial taxonomy.

Bush & Everett (2001) have combined analyses of genes, including one that seems to respond rapidly to evolutionary pressure and others that are important in virulence, with information on the sequences of the ribosomal genes favoured by molecular taxonomists. Their analyses indicated that all these genes were evolving in concert, albeit at very different rates.

Individual species are characterized by a mixture of their typical host animals, molecular details of ribosomal genes, and major rearrangements in the genes on their chromosome. Since the bacteria are obligate parasites, one question about the diversity of chlamydial species is whether it matches and dates from the evolution of their host species. The difficulty here is that there is currently no agreement on the date when some of the host species originated. There is also increasing evidence that some chlamydia live in amoebae and so may be widespread in soil and water. It was found that closely related chlamydial species were no more likely to share a host, or other virulence traits, than distantly related species. Indeed, there is some indication that advantageous genes may have spread laterally among isolates.

However, with any revision to bacterial classification, especially to a group that affects public health, there is always a question of whether this is the right time to change. Whether this change is accepted is in the hands of the microbiologists.

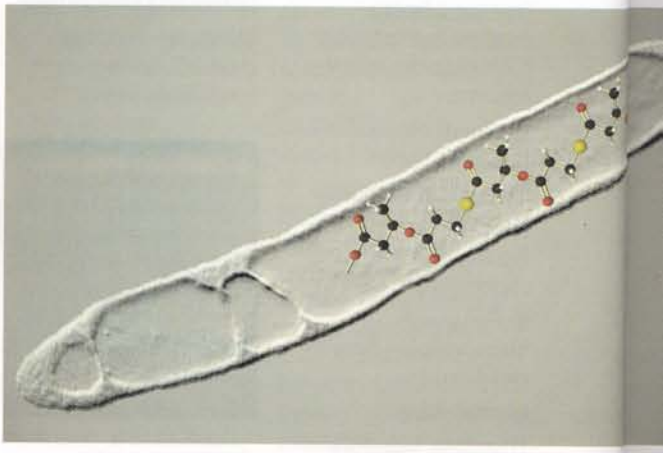
The paper by Bush and Everett is the first in ***USEM Online*** to use the supplementary data system – six sequence alignments can be viewed, printed or downloaded.

This new added-value feature of all SGM's online journals allows authors to append not only supporting data and data that would be unsuitable for the printed journal, but also electronic files such as video. Details are available from the Editorial Offices.

Bush, R.M. & Everett, K.D.E. (2001). Molecular evolution of the *Chlamydiaceae*. *Int JSyst Evol Microbiol* **51**, 203–220.

Schachter, J. and 31 other authors (2001). Letter to the Editor: Radical changes to chlamydial taxonomy are not necessary just yet. *Int JSyst Evol Microbiol* **51**, 249.

Everett, K.D.E. & Andersen, A.A. (2001). Letter to the Editor: Radical changes to chlamydial taxonomy are not necessary just yet – reply. *Int JSyst Evol Microbiol* **51**, 251–253.



THIS PAGE:
Electron micrograph showing a thin section of a cell of *Ralstonia eutropha* fully packaged with cytoplasmic inclusions of polyhydroxyalkanoic acids with the structure of the new polythioester, consisting of 3-mercaptopropionic acid and 3-hydroxybutyric acid, superimposed.
COURTESY T. LÜTKE-EVERSLOH AND A. STEINBÜCHEL, UNIVERSITÄT MÜNSTER, GERMANY

OPPOSITE PAGE:
Top: Kiba, an 11-year-old Asian elephant who died from systematic haemorrhagic disease, now known to be the work of a newly discovered virus, endotheliotropic elephant herpesvirus (EIHV-1). Below: Kiba's offspring, Plai Kiri, who fortunately shows no sign of the virus.
COURTESY B. EHLERS, ROBERT KOCH-INSTITUT, BERLIN, GERMANY

Microbial alternative to plastics

Cells are rather good at making polymers. Although biologists concentrate on ones like nucleic acids and polysaccharides, a less well known type is attracting considerable industrial attention. These are the polyhydroxyalkanoates (PHAs). Many bacteria make them as stores of carbon and energy, in a similar way to the fat deposits in some animal cells. The feature of PHAs that attracts biotechnologists is that their plastic-like characteristics make them ideal for uses in packaging, medicine and the food industry. Not only do they come from a renewable resource, and are of course biodegradable, but also bacteria can be induced to synthesize over 130 different forms. Some of these have valuable physical characteristics that would be too expensive to make by conventional chemistry.

The reason for this variety is that the enzyme that makes PHAs is not very fussy about its substrate. Biotechnologists have learnt how to exploit this lack of specificity by adding likely precursors to the growth medium for the bacteria to

churn out an ever-growing range of polymers. A new PHA has resulted from a collaboration between polymer chemists and microbiologists at the University of Münster in Germany, and has a very novel chemical feature. It is the first to contain sulfur atoms inserted into the backbone of the polymer. The researchers fed small amounts of 3,3′-thiodipropionic acid (TDP) to the bacterium *Ralstonia eutropha*, alongside a second carbon source such as fructose. The fructose supplied most of the carbon and energy requirements of the cells, while the TDP ended up in the storage polymer. The researchers found that if they strictly limited the nitrogen in the growth medium, the yield of polymer increased from 9 to 19% of the dry weight of the cells.

Another intriguing aspect is that although this polymer is new to science, it may be a natural product. Some marine algae synthesize sulfur-containing compounds in response to changes in salinity and, since TDP is one of the normal breakdown products, some aquatic bacteria may make the polymer. The researchers now want to investigate whether the physical properties of this new polythioester are as unusual as its chemistry.

Lütke-Eversloh, T., Bergander, K., Luftmann, H. & Steinbüchel, A. (2001). Identification of a new class of biopolymer: bacterial synthesis of a sulfur-containing polymer with thioester linkages. *Microbiology* 147, 11–19.

Natural transformation

About 40 bacterial species have so far been shown to take up DNA from their surroundings and incorporate it into their chromosomes. This process, called transformation, occurs naturally during growth, without the intervention of microbiologists. The mechanism evolved a long time ago and the genetic diversity created by this recombination helps the bacteria adapt to environmental changes, or overcome a host's defence mechanisms. Specific proteins are required to recognize suitable DNA, take it into the cell and then fit it into the chromosome. Of course, if things went too far, different species of bacteria would blend into one, and this has certainly not happened. Scientists at the Universities of Bremen and Oldenburg have been looking at the limitations on natural transformation.

Strains of the species *Pseudomonas stutzeri* have very variable traits, including the ability to live on various toxic compounds. They fall into seven groups, called genomovars, each with the same genes, but arranged differently. The ability to live in varied environments seems linked to acquisition of foreign genes and rearrangements in the chromosome. Michael Lorenz and Johannes Sikorski have been examining exactly how efficiently the seven genomovars manage this. They grew strains, mixed with their own purified DNA, on conventional laboratory media and measured how efficiently they took it up. Half of the strains were transformed, but the efficiency varied over a thousand-fold. Adding extra, totally unrelated DNA to the mixtures decreased the uptake of their own DNA to some extent. When the researchers tested the most easily transformed strains to see how well they could incorporate DNA from other genomovars, transformation was usually best with DNA from strains of the same group.

The results indicate that despite the advantage a strain might gain, there are barriers to the free exchange of genes in *P. stutzeri*, thus maintaining diversity within the species. Understanding the exact nature of these barriers is the next step.

Lorenz, M.G. & Sikorski, J. (2000). The potential for intraspecific horizontal gene exchange by natural genetic transformation: sexual isolation among genomovars of *Pseudomonas stutzeri*. *Microbiology* 146, 3081–3090.

A 'jumbo' virus problem

The Asian elephant is endangered in the wild by habitat destruction. There are now fewer than 50,000 of these animals left. Even when they are brought into the protection of zoos, other dangers can assail them. Researchers in Berlin have been studying the reason for the sudden death of an 11-year-old Asian elephant called Kiba. He died within 24 hours from a systematic haemorrhagic disease, which has caused the death of other elephants in American and European zoos.

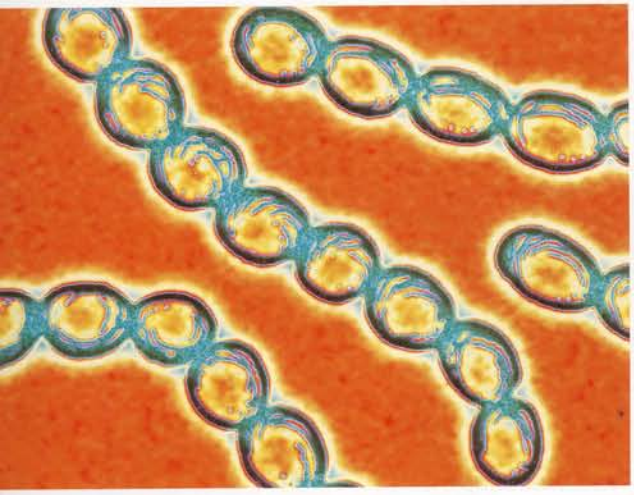
The disease is now known to be the work of a newly discovered virus, endotheliotropic elephant herpesvirus (EIHV-1). It was detected using the polymerase chain reaction (PCR) to amplify part of a viral gene from Kiba's blood and tissues. The German researchers have now used electron microscopy to examine thin slices of the elephant's organs. The spherical virus particles in the nuclei of some liver cells looked just like herpesvirus, supporting its identity. To find out how similar this particular virus is to other herpesviruses, they investigated its other genes using PCR. This revealed that although the virus was related to a particular group called the betaherpesviruses, the relationship was quite distant. It must be the first member of a new genus, or even a new family, of herpesviruses.

One worrying question was whether the virus had also infected the other elephants in Kiba's herd. The researchers designed a test that would detect an EIHV-1 gene with great specificity and sensitivity. To their relief, when they tested blood samples from the herd, including Kiba's offspring Plai Kiri, there was no sign of the virus. The test now offers a way to monitor captive elephants for signs of this lethal disease.

Ehlers, B., Burkhardt, S., Goltz, M., Bergmann, V., Ochs, A., Weiler, H. & Hentschke, J. (2001). Genetic and ultrastructural characterization of a European isolate of the fatal endotheliotropic elephant herpesvirus. *J Gen Virol* 82, 475–482.

Collagen look-alike involved in streptococcal infection?

Although the complete sequence of the genome of *Streptococcus pyogenes* was finished in 1999, scientists are still deciphering what it actually means. *S. pyogenes* is an important pathogen of humans. As well as causing superficial skin and throat conditions, it can cause serious invasive infections and can trigger auto-immune attacks, resulting in illnesses such as rheumatic fever. Despite decades of research into the pathogenicity of this organism, the genome sequence has revealed many new, possibly important, proteins.



Coloured transmission electron micrograph of chains of *Streptococcus pyogenes*. COURTESY ALFRED PASIEKA/ SCIENCE PHOTO LIBRARY

The bacterium's surface is decorated with a varied collection of proteins, many of which are known, or presumed, to be involved in its pathogenicity. They may help it attach to human cells or evade the immune system. Adrian Whatmore of the Infectious Disease Research Group at the University of Warwick, has picked out a gene, named *sclB*, that encodes a protein with similarity to the mammalian protein collagen. The extensive similarity of the SclB protein to collagen is unprecedented among bacteria. The structure, as deduced from the DNA sequence, indicates that SclB also contains a sequence to direct it to the surface of the bacterial cell. This is probably removed once the protein passes through the cell membrane, leaving a portion to anchor it while the rest protrudes from the surface. An indication of its importance is that this protein seems to be present in most isolates of *S. pyogenes*.

It can be an advantage for a pathogen to continuously change the face it presents to its host. The DNA coding for SclB contains repetitions of the same DNA sequence, and molecular biologists now know that these often regulate the expression of a gene in some way. Mistakes, and thus changes in the number of repeats, are often made during DNA replication, and are an easy way to generate subtle variants of the cell.

Although the function of SclB is unknown, the author speculates that its similarity to collagen, a ubiquitous protein of human skin, tissues and joints, could help trigger an auto-immune response, potentially resulting in damage to joints or the heart valves.

Whatmore, A.M. (2001). *Streptococcus pyogenes sclB* encodes a putative hypervariable surface protein with a collagen-like structure. *Microbiology* 147, 419–429.

Turning up the heat for BSE

One of the most intriguing features of the BSE epidemic is the stability of the infective prion protein. It is still infectious after exposure to temperatures and chemicals that make most other proteins curl up and disintegrate. One of the reasons seems to be that it forms aggregates in both the brain of infected animals and in tissue extracts. Its chemical structure makes the protein hydrophobic, which means that it dissolves in fats, rather than water, or sticks to itself if nothing else is available. The disturbing aspect of this is that the EU still processes 1·4 million metric tons of bovine fat into soap, detergents, cosmetics and animal feed each year. Although the process usually involves heating the fat in water under pressure for at least 20 minutes at 200 °C, a forthcoming paper in *Journal of General Virology* is the first comprehensive investigation of whether this does indeed remove all detectable prions.

A group of German researchers at Heinrich-Heine University in Düsseldorf investigated how well authentic prion protein survived being heated at temperatures up to 160 °C for 20 minutes. The scientific basis for this method is that the heat initiates chemical reactions between water and protein that will break the protein into its harmless chemical constituents. The researchers used a very sensitive immunological method which could detect even one hundred millionth of a gram of prion protein. After heating the prion in water, or bovine fat, or mixtures of the two, they could estimate how much of it still survived. They could calculate a degradation factor, to indicate how effectively the protein was destroyed in each of their experiments. Lipid definitely protected the protein, reducing the factor by over 100 at the lowest temperature of 100 °C. Its influence, fortunately, disappeared above 160 °C, so that the protein vanished. The researchers wonder if the fat covers the hydrophobic surface of the protein, protecting it from degradation for a time.

The best current estimates of the infectiousness of BSE indicate that it is directly proportional to the amount of prion protein. Public health regulations in Germany assume that autoclaving at 133 °C for 20 minutes will be sufficient to degrade all prions, and there are similar recommendations in the UK and USA. This study gives a way to check that this is really correct, especially with fatty materials, as well as providing the basis for assessing the biological safety of the industrial processes that render beef fat.

Appel, T.R., Wolff, M., Rheinbaben, F., Heinzel, M. & Riesner, D. (2001). Heat stability of prion rods and recombinant prion protein in water, lipid and lipid–water mixtures. *J Gen Virol* 82, 465–473.

Introducing the Society for Industrial Microbiology

Kristien Mortelmans

The Society for Industrial Microbiology (SIM) is a professional association dedicated to the advancement of microbiological sciences, specifically as applied to industrial material, processes, products and their associated problems. Our membership is international, diverse and includes many of the top scientists from industry, government and university laboratories who are employed in different areas of microbial biology.

SIM was founded in 1949 for industrial microbiologists involved in basic and applied research for product development. Its founders established a society that would continually serve and respond to the needs and concerns of companies that produce products from micro-organisms or their metabolites.

SIM serves as liaison between the various specialized fields of theoretical and applied microbiology. It promotes the exchange of scientific information through workshops, meetings and publications, in such areas as fermentation processes, bioremediation, biodeterioration, recombinant DNA technology, secondary metabolism, genomics, biotransformation, quality assurance/quality control, cosmetic microbiology, environmental microbiology and food microbiology, among others.

The Society is governed by an elected Board of Directors who serve as volunteers. In addition, there are numerous committees that are chaired by SIM members, appointed by the President-elect for 3 years.

The Society currently offers four types of membership: Regular individual membership, Student membership, Emeritus membership and Corporate membership. With a membership of under 2,000, SIM maintains an atmosphere of friendliness and cordiality that is evident at the annual meetings and special conferences.

Meetings

The SIM Annual Meeting is recognized by attendees and trade journals as offering the best and most current topics in microbial biology while providing commercial, high quality exhibits featuring the latest products and services available to microbial biologists. SIM also hosts special conferences on topics of international concern and interest.

Publications

SIM News features special articles written by key experts in their respective fields, events of importance and interest such as meeting announcements, new books, new products, and reports on our national science and technology policy.

The *Journal of Industrial Microbiology and Biotechnology* (JIM&B) is an international journal that publishes original, peer-reviewed research specializing in areas of theoretical and applied microbiology, short communications, critical reviews and letters to the Editor. The articles cover all aspects relating to the study of micro-organisms and the industrial application of microbiology such as: biotechnology, fermentation and biotransformation processes, environmental microbiology, biodegradation, biodeterioration, quality control and government regulations, strain development, novel microbial products, tissue culturing improvements, food microbiology, microbial disposal of pollutants, and antibiotics.

Placement service

This service is free to members and there are no forms to complete. Those members searching for a new position simply send a copy of their CV to SIM. The placement service will match their qualifications with employer requests. Employers with positions available can send a letter detailing the position's specifications to the Placement chair or to SIM for inclusion in the job bank and for posting on the SIM website.

Website

SIM's homepage, located at **www.simhq.org**, provides members with access to up-to-date information on SIM meetings, services and career opportunities. Other pages include publications, careers, membership services, meetings, corporate members and kids' zone, among others.

Local sections

The Society has a number of local sections established across the United States which provide services to their members and are governed by their own elected officers. They hold annual meetings and smaller seminars throughout the year.

For more information about SIM contact:
Society for Industrial Microbiology (SIM), 3829 Old Lee Highway, Suite 92A, Fairfax, VA 22030-2421 USA.
Tel. +1 703 691 3357; Fax +1 703 691 7991; email info@simhq.org; website http://www.simhq.org

● *Dr Kristien Mortelmans (right) is President of SIM and edits SIM News. email kristien@unix.sri.com*

SGM President Sir David Hopwood was keynote speaker at the 2000 annual meeting of the Society for Industrial Microbiology (SIM) in San Diego, California, in July. There he met Dr Kristien Mortelmans, President of SIM, where they agreed to establish an alliance between the two societies. As a first step in accomplishing this goal there will be an occasional exchange of material between the societies' respective news magazines, *Microbiology Today* and *SIM News*. Here Dr Mortelmans introduces SIM to SGM members.

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.

Biohazard

By K. Alibek with S. Handelman
Published by Arrow/ Random House UK (2000)
£6.99, pp. 307
ISBN: 0-09-941464-3

This intriguing and thought-provoking book provides an autobiographical, detailed insight into the Soviet Union's biowarfare program (1972–1992) from their top scientist. It contains some of the Soviet Union's most guarded secrets of the cold war. The author describes the history of biological weapons, how they were produced and tested, the catalogue of agents involved, how they concealed their 'offensive' work from US inspectors, the effects of the demise of the Soviet Union on their biowarfare programme and his defection to the US in 1992. The author communicates the subject well, providing sufficient scientific background and explanation where necessary. I can thoroughly recommend this book both to scientists and to the general public, although some may find the content alarming.

■ ***Kerstin Williams***
London School of Hygiene and Tropical Medicine

Practical *Streptomyces* Genetics

By T. Kieser, M.J. Bibb, M.J. Buttner, K.F. Chater & D.A. Hopwood
Published by the John Innes Foundation (2000)
£60.00 + p&p, pp. 613
ISBN: 0-7084-0623-8

Practical Streptomyces Genetics is a technical manual for laboratory-based studies with these fascinating bacteria and close relatives. This book supersedes and excels its previous manifestation, incorporating a far greater diversity of genetic techniques. For example, the chapters on transposon insertion, microscopy, gene disruption and analysis of *Streptomyces* DNA are all new. There is also more background and extensive updating of the established approaches. The verdict, after its 3 month road-test in my lab, is that this book is essential to old hands and novices alike. A minor criticism is that the prolific cross-referencing and detailed index can sometimes make it hard to find specific information (but this does lead to wider reading!). More seriously, the book is only available in paperback so, unless well protected, it will almost certainly go the way of our copy of Sambrook *et al.* from frequent consultations, i.e. a stack of loose, printed sheets and missing pages.

■ ***Maggie Smith***
Queen's Medical Centre, University of Nottingham

Parvoviruses: From Molecular Biology to Pathology and Therapeutic Uses. Contributions to Microbiology, Vol. 4

Edited by S. Faisst & J. Rommelaere
Published by S. Karger AG, Basel (2000)
CHF178.00/ DM213.00/ US$155.00, pp. 208
ISBN: 3-8055-6946-7

The *Parvoviridae* are a large family of viruses infecting a wide spectrum of animal species from insects to man. This volume reviews their epidemiology and pathology, molecular biology and potential use as gene transfer vectors. The molecular biology and replication is meticulously described for different genera. Applications of their use as tools are covered, for example the DNA of adeno-associated viruses (AAV) can be integrated into cellular genomes and be reactivated upon superinfection with helper adenovirus. This finding and progress in the identification of AAV receptors has allowed targeting of particular cells and expression of inserted genes for gene therapy. In summary, this book is very useful in spanning the areas of the molecular biology of parvoviruses and their potential uses for gene therapy. The volume will enrich departmental and larger institutional libraries, as well as being of interest for molecular biologists, virologists and physicians involved in gene therapy.

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

Diseases of Poultry: World Trade and Public Health Implications. Scientific and Technical Review, Vol. 19(2)

C.W. Beard & M.S. McNulty
Published by World Organisation for Animal Health (2000)
Ecu 40.00, pp. 664
ISBN: 92-9044-516-5

The book contains 17 chapters and most deal with one disease pathogen or a closely related group. Two chapters are concerned with disease entities, i.e. neoplastic diseases and poult enteritis syndrome. The final chapter is different in that it deals with diseases of a bird species, namely the ostrich. Each chapter is well written by one or more experts on the disease, starting with an initial summary. The pathogen or disease are all recorded using variations on a relatively similar format. The disease in the bird is first described and its cost to the poultry industry. Next follows a description of the agent, including its antigenic structure, culture characteristics, antibiotic resistance pattern for bacteria, typing and pathogenesis. Then the epidemiology of the disease followed by a description of the diagnosis, including cultural methods, serology, etc. The public health considerations are reported together with treatment and control. In some cases this section is placed early in the chapter where this is the really important problem, as with *Campylobacter* infection. There is a comprehensive reference list which goes up to at least 1999. The book is a very useful update on many of the most economically important diseases in poultry or those which cause food-borne disease in man. The selection of disease appears to be on this basis, so many problems which confront the veterinary surgeon or laboratory microbiologist are not mentioned. However, the volume will be of value to those who are interested in knowing more about all aspects of some of the most important poultry problems worldwide.

■ ***Anthony Andrews***
Welwyn

Microbiological Aspects of Biofilms and Drinking Water. The Microbiology of Extreme and Unusual Environments Series

By S.L. Percival, J.T. Walker & P.R. Hunter
Published by CRC Press (2000)
£75.00/ US$119.95, pp. 229
ISBN: 0-8493-0590-X

Over the past few years there has been a growing awareness of the role that biofilms play in our lives. In drinking water systems biofilm formation is normal and can hold and/or protect many dangerous, indicator and nuisance organisms such as *Legionella*, coliforms, *Escherichia coli*, mycobacteria, *Pseudomonas aeruginosa*, protozoans, *Salmonella*, *Shigella* and *Campylobacter*.
Biofilm formation can seriously inhibit the effects of the chemicals used to control bacterial levels in drinking water. Also, our increasing tendency to attach complicated water treatment or dispensing systems made of modern biofilm encouraging materials (i.e. vending machines and filters) to our mains water is giving greater opportunity for biofilms to develop. Problems are only now beginning to emerge. All of this means that we may have to rethink some of our perceptions of water treatment and look closely into water contact materials and disinfection methods.
This book by three leading UK workers in this field is by far the best I have seen on the subject and is strongly recommended to anybody working in the fields of potable water and is essential reading, as well as being a highly desirable text book.

■ ***Mike Hurst, Watermark***

Data Analysis in Molecular Biology and Evolution

By X. Xia
Published by Kluwer Academic Publishers (2000)
NLG315.00/US$135.00/£93.25, pp. 277
ISBN: 0-7923-7767-2

This book is an accompaniment to the software program of the same name and while the program is available on the internet without charge, there is a rather steep price of £93.25 on the book. However, taken together, the book and software combined represent excellent value for money and this reviewer is definitely recommending this book for any researchers interested in molecular biology and evolution. The text is detailed, but easily read, with lots of helpful insights and discussions of problems with data analysis (bias in datasets, problems with maximum likelihood, etc.). The scope of the book is vast, covering database interrogation, multiple sequence alignment, codon usage bias, amino acid substitutions, theoretical aspects of maximum likelihood and distance matrix methods and much more. It is an excellent example of how a book in this area should be written.

■ ***James McInerney***
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Salmonella in Domestic Animals

Edited by C. Wray & A. Wray
Published by CABI Publishing (2000)
£95.00/US$175.00, pp. 480
ISBN: 0-85199-261-7

A great deal has happened in the area of animal mycoplasmosis in the 40 years since the publication of Professor Buxton's *Salmonellosis in Animals*; indeed most of it, including ministerial resignations, has occurred in the last 15 years. It is timely then for the publication of this volume covering recent developments in virulence, infection, epidemiology and control, laboratory diagnosis and, perhaps, most importantly antibiotic resistance. It is of course impossible to discuss animal salmonellosis without considering the human dimension and this is covered well. The leading workers in the field in Europe, North America and Australia have contributed to the comprehensiveness of this volume. At over £100, the book will not become a student text but should be bought by institutions and those working in the animal and human fields.

■ ***Robin Nicholas***
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Basic Techniques in Molecular Biology

By S. Surzycki
Published by Springer-Verlag (2000)
DM129.00/£44.50/US$79.95/öS942.00/SFr117.50, pp. 434
ISBN: 3-540-66678-8

This is a manual for research scientists. The general introduction sections provide background information on each technique, although all but the most conscientious researcher might skip these and go directly to the method they require. Basic protocols are complemented with sufficient information to allow an appreciation of the purpose of each solution or manipulation involved. The user could modify the protocol for their own application and also troubleshoot if the methodology does not work well. The manual also comments on the relative costs of different procedures, although the idea of molecular-biology-on-a-budget is a bit of an oxymoron. The methods described are fundamental and would form the 'basic instruction kit' of an aspiring molecular biologist. If I was only recommending one methods manual for a laboratory in molecular biology, I would still probably choose Sambrook. Although more expensive, it provides very similar information and is much more extensive in its coverage.

■ ***Anne Glover***
University of Aberdeen

Infectious Causes of Cancer: Targets for Intervention. Infectious Disease Series

Edited by J.J. Goedert
Published by Humana Press (2000)
US$125, pp. 515
ISBN: 0-89603-772-X

This is a substantial collection of papers reviewing the causal role of micro-organisms in the development of cancer. Experts in the field cover viruses involved via different mechanisms like carrying their own transforming genes (HTLV-1, HBV, HPVs), acting via insertional mutagenesis (retroviruses, HBV) or chromosomal translocation (EBV). It becomes clear that the oncogenic process is multifactorial: tumours like lymphoma and hepatocellular carcinoma may also occur without EBV or HBV/HCV infection. Viruses have developed ingenious ways to evade the host's immune recognition in the infected cell (HHV-8, EBV), and, in turn, tumours develop at higher frequency in the immunodeficient host. The influence of chronic infection and inflammation on oncogenesis is also widely discussed.
The volume is a treasure for reading. Most authors have made an effort to present up-to-date references (1998/99). The book is highly recommended to all microbiologists and clinicians with an interest in aspects of the molecular pathogenesis and rational therapy of cancer.

■ ***Ulrich Desselberger***
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Infectious Diseases and Arthropods

By J. Goddard
Published by Humana Press (1999)
US$75.00, pp. 240
ISBN: 0-89603-825-4

Many newly emerging or re-emerging infectious diseases are transmitted by arthropod vectors. This book is unusual in bringing all arthropod-borne diseases into a single volume, as they are more often classified by the aetiological agent (viruses, rickettsia, bacteria, protozoa, nematodes) rather than by the vector. Successive chapters are dedicated to diseases carried by mosquitoes, ticks, fleas, sand flies and other miscellaneous vectors, as well as to problems directly related to arthropods – myiasis, infestations, bites and stings. The book is biased heavily towards entomological aspects, providing significant information on vector biology and control. Details of the diseases themselves – clinical, pathological, immunological – are very superficial and should be read only by way of introduction to the field. It is therefore of greatest interest to professional vector biologists, epidemiologists and public health workers, but would provide a useful adjunct to in-depth clinical texts consulted by infectious disease physicians and scientists.

■ ***Andrew Taylor-Robinson***
University of Leeds

Clinical Parasitology. A Handbook for Medical Practitioners and Microbiologists

H. Sheorey, J. Walker & B.-A. Biggs
Published by Melbourne University Press (1999)
£22.95, pp. 163
ISBN: 0-522-84834-6

As much of the scientific literature on parasites tends to appear in weighty textbooks, this pocket-sized guide to clinical parasitology will be highly welcomed. *Clinical Parasitology* is aimed very much at Australian readers; however, the majority of the information contained within its pages is universally applicable. Organized alphabetically from *Acanthamoeba* to *Wuchereria* this text contains well researched and up-to-date information on most parasites which cause human infections. Including short but informative clinical notes and lists of the currently available therapies. This book would be a useful reference for those in the clinical setting. Modern diagnostic techniques are discussed but there is not enough detail for it to be used as a laboratory manual and the inadequate photographs could not be employed as an aid to parasite identification. *Clinical Parasitology* is therefore unsuitable for use as a laboratory manual. This book is not library material, but as an introductory text for those new to the exciting world of parasites it is well worth £22.95.

■ ***Dany Beste***
CPHL London

Mycorrhizal Biology

Edited by K.G. Mukerji, B.P. Chamola & J. Singh
Published by Kluwer Academic/Plenum (2000)
£100.00/US$145.00/NLG336.00, pp. 340
ISBN: 0-306-46294-X

In the developed world, the mutualistic symbioses between fungi and plants have been relatively neglected until recently, as their roles in phosphorus nutrition and plant protection have been supplanted by agricultural chemicals. In India the importance of mycorrhizal symbioses for soil conservation and agricultural production has been recognized for longer. This book is largely written by Indian scientists, and it would be hard to find another country that could muster so many mycorrhizal researchers. It begins with general reviews of mycorrhizal biology, covering material that is widely available elsewhere and sometimes less than accurate (mycorrhiza does not come from Greek words *mike* and *rrhiza*). Later chapters are mostly literature reviews of more specialized aspects, though occasionally they include some otherwise unpublished experimental data. This book is a useful and detailed reference for the specialist and a reminder of the extensive contributions of Indian scientists to this field.

■ ***Peter Young***
University of York

Physical Biochemistry: Principles and Applications

By D. Sheehan
Published by John Wiley & Sons Ltd (2000)
£32.50, pp. 349
ISBN: 0-471-98663-1

This excellent textbook sets out to explain the basic principles behind many of the physical methods used in a modern biochemical laboratory. Included are the major spectroscopic techniques, structure determination by X-ray and NMR, chromatography and electrophoresis. Each chapter starts with a description of the background physics, then covers the instrumentation involved and ends with some typical examples of the uses of the techniques. The physics is not always easy, but is presented in such a way that non-mathematical readers should be able to gain some understanding. Particularly timely is the discussion of mass spectrometry and its applications in proteomics. The book will obviously be of most interest to those active in the laboratory and wishing to understand more of the basic principles behind the methods that they are using. It will also be of use to undergraduates taking specialist courses in physical methods in biochemistry.

Anthony G. Lee
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Infectious Disease in the Aging: A Clinical Handbook Infectious Disease Series

Edited by T.T. Yoshikawa & D.C. Norman
Published by Humana Press (2000)
US$99.50, pp. 352
ISBN: 0-89603-744-4

The book has multiple but entirely North American authorship and is of markedly variable quality. Reviewers tend to gauge a book by searching initially for a favoured topic. I was dismayed to find only four lines dedicated to *Clostridium difficile* infection, which include one inaccuracy and one inappropriate reference. How this can be for such a text is perverse and sits uncomfortably alongside eight pages on sexually transmitted diseases. A stated aim was to include up-to-date references, but this is variably achieved (the chapter on urinary tract infections has two 1997 references and none more recent). The chapter on vaccination contains a level of detail often lacking elsewhere and is well referenced. By comparison, the chapter on meningitis does not mention conjugate group C meningococcal vaccine and contains errors on recommended therapy for penicillin-resistant pneumococcal infection. Thus, this book is often not superior to current authoritative general texts and cannot be recommended to those with particular interest in infection in the elderly.

■ ***Mark H. Wilcox***
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Streptococcal Infections: Clinical Aspects, Microbiology, and Molecular Pathogenesis

Edited by D.L. Stevens & E.L. Kaplan
Published by Oxford University Press (2000)
£69.50, pp. 449
ISBN: 0-19-509921-4

This book really does live up to its comprehensive title and ranges from historical accounts of the fluctuations in prevalence and severity of human diseases such as rheumatic fever over the last 100 years to recent developments in the molecular dissection of pathogenic mechanisms. The Editors have assembled a distinguished list of contributors and the individual chapters are substantial and uniformly thoughtful in setting out the background and historical perspective of their topic to cover both the manifestations of disease as well as recent developments in laboratory studies. Any laboratory working on streptococci will find this volume useful, not just for their own pet organisms but as background information on related species. With genomic data now becoming available for the streptococci, this book serves as a timely reminder of the huge array and diversity of human diseases caused by this group of organisms.

■ ***Roy Russell***
University of Newcastle

The Biology of Nitric Oxide Part 7. Proceedings of the 6th International Meeting on the Biology of Nitric Oxide, Stockholm, Sweden, September 1999

Edited by S. Moncada, L.E. Gustafsson, N.P. Wiklund & E.A. Higgs
Published by Portland Press Ltd (2000)
£110.00, pp. 234
ISBN: 1-85578-142-5

This is a book of snapshots of NO research. The Stockholm conference that generated it was further proof of the giddy pace of NO research and the immense variety of roles that this tiny mediator molecule displays. NO is important in microbiology but most of this volume is devoted to NO enzymology, pathology and apoptosis. As for Part 6, the book contains only one-page abstracts based on the meeting's oral communications and posters, each crammed with information. Microbiologists will find only a handful of overtly microbiological pages, but those wishing to understand NO and related reactive species would do well to study their interactions with oxidative stress, the multitude of biological processes affected by NO, NO chemistry and NO synthases (especially since some bacteria have such enzymes). The subject index is reasonable but the price will select against all but the most specialist readers and libraries.

■ ***Robert Poole***
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Quantum Evolution

By J. McFadden
Published by HarperCollins (2000)
£16.99, pp. 338
ISBN: 0-00-255948-X

This is a book which intends to make science accessible. In all such endeavours, authors walk a line between generalities which make underlying processes clear and detail which convinces the reader that the generality is reasonably true. This book doesn't manage that balance for me, but that is a personal view. There is nothing wrong as such, just missing details which, for me, weaken the argument. Given the scope of the coverage, the origin of life, the role of quantum mechanics in evolution, right through to neurophysiology and consciousness, though, missing details are a necessity. I confess, I did not find the anecdotal style endearing either, but for all that I hope the book will be read and discussed. It will, I think, make a stimulating subject for student debate.

For the curious, 'quantum evolution' refers to quantum tunnelling which moves a proton making mis-match base-pairing energetically feasible.

■ ***Dave Roberts***
The Natural History Museum, London

Sexually Transmitted Diseases: Vaccines, Prevention and Control

Edited by L.R. Stanberry & D.I. Bernstein
Published by Academic Press (2000)
£74.95, pp. 468
ISBN: 0-12-663330-4

This is a comprehensive and well rounded textbook. It contains fascinating information on the history of sexually transmitted infections and their close link with the socio-economic health of the people. This is particularly highlighted in the Russian experience of sexually transmitted diseases where the need to change society rather than introduce antibiotics is demonstrated concisely. There is a good balance between physiology and pathogenesis of infection and treatment and prevention aspects. It is well referenced, although I find these irritating when included in the flow of the text, particularly when reading the opening chapters with their more general statements. Read from cover to cover, this book will give the reader an extensive and broad understanding of the subject. It is more likely to be read a chapter at a time and would be a useful source of information for trainees starting out in this particular specialty.

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Macrophages. A Practical Approach
Edited by D.M. Paulnock
Published by Oxford University Press (2000)
H/B £65.00; P/B £29.95, pp. 211
ISBN: H/B 0-19-963689-3; P/B 0-19-963688-5

Microbiology: An Introduction, 7th Edition
By G.J. Tortora, B.R. Funke & C.L. Case
Published by Benjamin Cummings (2001)
Distributed by Pearson Education
£33.99, pp. 887
ISBN: 0-8053-7554-6

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Diary

march 2001

2001, YEAST ODYSSEY IN MOLECULAR GENETICS. THEORETICAL AND PRACTICAL COURSE [INTERNATIONAL CELL RESEARCH ORGANIZATION (ICRO)]

Buenos Aires, Argentina
8–23 March 2001

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PESTIVIRUS CONTAMINATIONS OF BOVINE SERA AND OTHER BOVINE VIRUSES CONTAMINATIONS

Paris, France, 29–30 March 2001

CONTACT: The Public Relations Unit, European Directorate for the Quality of Medicines (EDQM): Caroline Larsen Le Tarnec (Tel. +33 3 88 41 28 15); Francine Baumgarthen (Tel. +33 3 88 41 28 24); Emily Walker (Tel. +33 3 90 21 48 39) (Fax +33 3 88 41 27 71; email publicrelations@pheur.org; http://www.pheur.org)

april 2001

MOLECULAR BIOLOGY UPDATE
A FOUR-DAY LABORATORY COURSE

Hatfield, Herts, 9–12 April 2001

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://www.herts.ac.uk/natsci/STC)

673rd BIOCHEMICAL SOCIETY MEETING: MOLECULAR COMMUNICATIONS

University of Bristol
10–12 April 2001

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

INTERNATIONAL TRAINING COURSE ON THE USE OF EXPRESSION SYSTEMS FOR STUDYING STRUCTURE, FUNCTION AND REGULATION OF MEMBRANE PROTEINS (ICRO)

Shanghai, China
11–24 April 2001

CONTACT: Dr Jian Fei, Shanghai Institute of Cell Biology, 320 Yue-Yang Lu, 200031 Shanghai, China (Fax +86 21 62713169; email fei@guomai.sh.cn), or Prof Dr Wolfgang Schwarz, Max-Planck Institute of Biophysics, Kennedyalle 70, 60596 Frankfurt/Main, Germany (Fax +49 69 6303 340; email wolfgang.schwarz@mpibp-frankfurt.mpg.de)

may 2001

THE APPLIED CLINICAL TRIALS EUROPEAN SUMMIT

Paris, France, 14–16 May 2001

CONTACT: Jo Edge (01244 393150; email jedge@advanstar.com)

INTERNATIONAL COURSE ON LABORATORY ANIMAL SCIENCE

Utrecht, The Netherlands
14–25 May 2001

CONTACT: Prof Dr L.F.M. van Zutphen or Mr Stephan van Meulebrouck, Dept of Laboratory Animal Science, Faculty of Veterinary Medicine, PO Box 80.166, 3508 TD Utrecht, The Netherlands (Tel. +31 30 2532033; Fax +31 30 2537997; email pdk@las.vet.uu.nl)

june 2001

4th INTERNATIONAL CONFERENCE ON ANTHRAX

Annapolis, Maryland, USA
10–13 June 2001

CONTACT: Anthrax Conference, c/o ASM, 1752 N Street NW, Washington, DC 20036, USA (Tel. +1 202/942 9257; Fax +1 202/942 9340; http://www.asmusa.org/mtgsrc/anthrax01.htm)

6th EUROPEAN CONFERENCE ON EXPERIMENTAL AIDS RESEARCH 2001 (ECEAR'2001)

Heriot-Watt University, Edinburgh, 23–26 June 2001

CONTACT: Conference Secretariat, c/o Index Communications Meeting Services (Scotland) Ltd, 32 Queen's Crescent, Newington, Edinburgh EH9 2BA (Tel. 0131 667 9887; email scotland.icms@dial.pipex.com)

EARTH SYSTEM PROCESSES

Edinburgh, Scotland
24–28 June 2001

CONTACT: Ian Dalziel and Ian Fairchild (scientific content); Helen Wilson and Michael Stevens (administration); (http://www.geosociety.org/meetings/edinburgh)

july 2001

AN INTRODUCTION TO BIOINFORMATICS
A TWO-DAY COMPUTER/LECTURE COURSE

Hatfield, Herts
3–4 July or 10–11 July 2001

CONTACT: Dr Henry Brzeski, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284554; Fax 01707 286137; email h.brzeski@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

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

Hatfield, Herts, 5 July 2001

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://www.herts.ac.uk/natsci/STC)

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

Hatfield, Herts
6 July 2001 or 13 July 2001

CONTACT: Dr Ralph Rapley (see above)

MOLECULAR MEDICAL MICROBIOLOGY
A TWO-DAY LECTURE/LABORATORY COURSE

Hatfield, Herts, 18–19 July 2001

CONTACT: Dr Madhu Goyal, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284624; Fax 01707 286137; email m.goyal@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

AMERICAN SOCIETY FOR VIROLOGY 20th ANNUAL SCIENTIFIC MEETING

Madison, Wisconsin, USA
21–25 July 2001

CONTACT: Sidney E. Grossberg, Secretary-Treasurer, American Society for Virology, Dept of Microbiology and Molecular Genetics, Medical College Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226-0509 USA (Tel. +1 414 456 8104; Fax +1 414 456 6566; email segrossb@mcw.edu; http://www.mcw.edu/asv)

3rd INTERNATIONAL GEMINIVIRUS SYMPOSIUM: A MEETING ON PLANT SINGLE-STRANDED DNA VIRUSES AND THEIR INSECT VECTORS

John Innes Centre, Norwich
24–28 July 2001

CONTACT: carol.aab@hri.ac.uk or gemini-2001.enquiries@bbsrc.ac.uk (http://iltab.danforthcenter.org/symposium.html)

august 2001

BIO CHINA 2001

Beijing, China
22–25 August 2001

CONTACT: Dr Liang Hui, Guantong Building, No. 44 Hua Yuan Beilu, Haidian District, Beijing, China 100083 (Tel. +86 10 82081644/62046728; Fax +86 10 82079384; email bio2001@china.com or bjwrc@public.fhnet.cn.net; http://chinabio.org or http://china-expo.com)

september 2001

11th INTERNATIONAL WORKSHOP ON *CAMPYLOBACTER, HELICOBACTER* AND RELATED ORGANISMS (CHRO2001)

Freiburg, Germany
2–5 September 2001

CONTACT: Prof Dr Manfred Kist, National Reference Centre for *Helicobacter pylori*, Institute of Medical Micribiology and Hygiene, Hermann-Herder-Str. 11, D-79104 Freiburg, Germany (Tel. +49 791 203 6590; Fax +49 791 203 6562; email kistman@ukl.uni- freiburg.de; http://www.chro2001.de)

PROTEIN TECHNIQUES
A TWO-DAY LABORATORY COURSE

Hatfield, Herts, 3–4 September or 10–11 September 2001

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://www.herts.ac.uk/natsci/STC)

NUCLEIC ACID TECHNIQUES
A THREE-DAY LABORATORY COURSE

Hatfield, Herts
5–7 or 12–14 September 2001

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://www.herts.ac.uk/natsci/STC)

SEVENTH EUROPEAN WORKSHOP ON VIRUS EVOLUTION AND MOLECULAR EPIDEMIOLOGY

Leuven, Belgium
5–12 September 2001

CONTACT: Dr Anne-Mieke Vandamme, Rega Institute and University Hospitals, AIDS Reference Laboratory, Minderbroedersstraat 10-12, B-3000 Leuven, Belgium (Tel. +32 16 332180; Fax +32 16 332131; email annemie.vandamme@uz.kuleuven.ac.be)

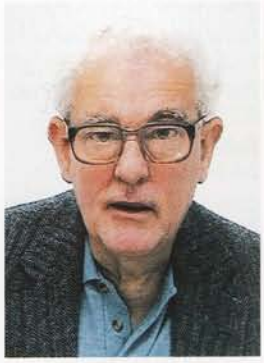
PSEUDOMONAS 2001

Brussels, Belgium
17–21 September 2001

CONTACT: Pierre Cornelis, Laboratory of Microbial Interactions, Flanders Inter-university Institute for Biotechnology, Vrije Universiteit Brussel, Paardenstraat 65, B-1640 Sint-Genesius-Rode, Belgium (Tel. +32 2 3590221; Fax +32 2 3590390; email pcornel@vub.ac.be; http://homepages.vub.ac.be/~pcornel/pseudomonas2001.htm)

Comment

Was the BSE inquiry worth it?



The Rt. Hon. Tam Dalyell

I do not pretend to have read all 16 volumes of Lord Phillips' Report. I am not ashamed. Like most others – all but a few, a very few, I suspect – I have read chunks of it and this brings me to the point.

Whoever asked Lord Phillips to produce 16 (yes, 16!) often indigestible volumes at a cost – wait for it – of £27 million? Heavens above, £27 million could have been spent in other ways – not least in trying to help farmers facing bankruptcy.

Herein lies the trouble. Distinguished judges of the High Court – and Lord Phillips is extremely distinguished – give way to the temptation to wallow in their subject, producing a learned treatise. What the country and the farming community really needed was a few clear guidelines as to future action, not a ponderous $2^1/_2$ year inquiry, which seems to have been overtaken by events in Europe and the realization that Britain is not so unique, after all, in relation to BSE.

Phillips goes on and on about '*the growing public suspicion and dissatisfaction that important information was not being shared and discussed openly*' and that this led to '*a public feeling of betrayal*' when a possible link to human health was announced in the House of Commons, when Stephen Dorrell and Douglas Hogg made their statements. Well, well! Hindsight is a wonderful thing. Some would argue that it is hugely to my discredit, but the brutal truth is that my concern was about gratuitous damage to the British farming community, which had, heaven knows, and has, enough problems to worry about. Governments should not create panic, at least, until such time as all the facts are in their possession. I had sympathy for John Gummer, though less for his use of his daughter being photographed guzzling a meat burger!

What has Phillips achieved, that would not have been achieved had he not reported? Zilch, I suspect.

When I first heard that Lord Phillips had been made chairman of a committee to inquire into BSE/CJD, I thought 'he'll be quick, sensible and decisive, expeditious in asking the right questions of the right people! He'll know a lot of the background, and is exactly the right guy to cross-examine my friend, Bob (now Professor) Will, of the Neuropathogenesis Unit of the Western General Hospital in Edinburgh, and other researchers in the field.' Will had been an enormous success in putting his concerns to 129 West Lothian farmers and butchers, at a meeting I organized at Oatridge Agricultural College in 1996.
Imagine my consternation when I discovered that it was a Baron Phillips of Worth Matravers. 'But, David's title is surely of Ellesmere!' Wrong one. It had never occurred to me that it was not David Phillips, ex-chairman of the Advisory Board for the Research Councils, sometime Professor of Molecular Biophysics in Oxford, and a member of the Lords Select Committee on Science and Technology as Lord Phillips of Ellesmere.

Had it indeed been he, we would have got, if not notes on the back of a proverbial envelope, at least a succinct constructive plan for action, in one-tenth of the time, at one-hundredth of the cost.

As the fond son-in-law of a judge who sat in the High Court and the Court of Appeal for a third of a century, I say for pity's sake, keep the lawyers out of inquiries, which, if we must have them, should be expeditiously conducted by scientists.

● ***The Rt. Hon. Tam Dalyell is Member of Parliament for Linlithgow***

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