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Contents

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Above: Petri dish culture of colonies of *Escherichia coli*. *Dr Jeremy Burgess / Science Photo Library*

Vol. 31, Part 3, August 2004

Most people associate the gut bacterium *Escherichia coli* with disease or even death, but in the laboratory it provides an ideal organism for advancing research into cell and molecular biology. Model or menace? In this issue we explore some of the many facets of *E. coli*.

Gavin Thomas has devoted his research career to *E. coli* and has even created a specialist website. On pp. 114–115 he gives an overview of his favourite microbe.

Thanks to genomics, scientists now understand why some strains of *E. coli* are harmless whilst others are pathogenic. Jeremy Glasner and Nicole Perna describe (pp. 124–125) how, as more and more strains are sequenced, the variability is surprising even researchers.

E. coli O157:H7 is infamous, thanks to a fatal outbreak in Scotland in 1996. David Gally and his colleagues have been finding out where the bacteria live inside their cattle host (pp. 126–128). The somewhat unexpected results may well offer a means of controlling the organism. However, this strain of *E. coli* is not the only cause of diarrhoeal disease, as Henry Smith *et al.* describe on pp. 117–118.

Not all *E. coli* are bad news. K-12 is probably one of the most studied bacteria in science. On p. 116 Nobel Prizewinner Joshua Lederberg recounts the history of this fascinating strain and its contribution to genetics research. Other strains of *E. coli* hold promise as probiotics and may well prove a beneficial component of our diet, according to Bob Rastall and Glenn Gibson on p. 119. *E. coli* has been long in use as an indicator of faecal pollution of food and water. Keith Jones and Richard Smith (pp. 120–122) show how testing for these bacteria can be used not only to show pollution, but also to track its source.

Getting away from *E. coli*, but staying with research, Tony Minson examines the implications of new codes of practice for microbiologists in Comment on p. 156.

And finally, on a less serious note, Milton Wainwright speculates on how the conversation might have gone in 1934 had Alexander Fleming been involved in a research assessment exercise (pp. 130–131).

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

Articles

Regular Features

Other Items

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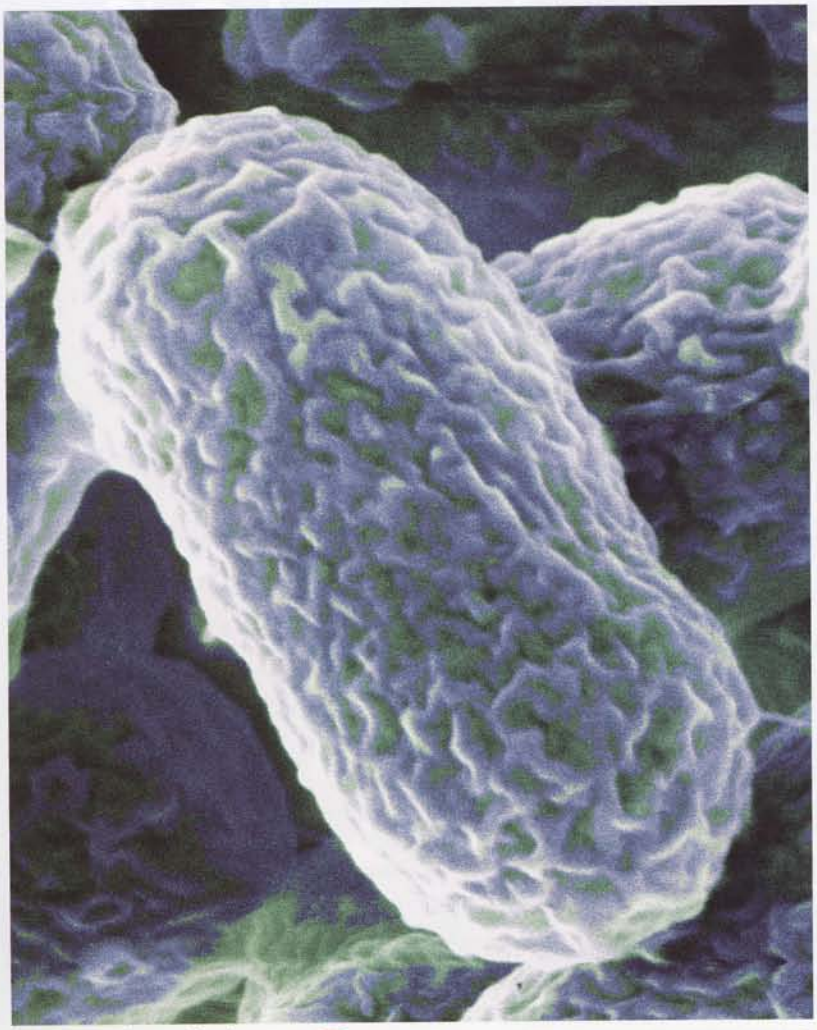
Escherichia coli: model and menace

Gavin Thomas

'All cell biologists have at least two cells of interest, the one they are studying and *E. coli*' (*Fred Neidhardt*)



Microbiology Today Editor and *E. coli* expert Gavin Thomas explores the various facets of *E. coli*, the subject of this issue.

Mention *E. coli* to the man in the street, and he's most likely to make some references to a dodgy burger and the resulting diarrhoea. The menace is familiar, but the model is not. By contrast, the ubiquitous use of *E. coli* as a model organism and workhorse of molecular and cell biology means that most biologists are more likely to know the model and not much about the menace.

E. coli K-12: the researcher's friend

The *E. coli* that most of us come across in the lab are usually derived from strain K-12 or strain B, with the former being predominant. The history of this particular strain is described in the article by Joshua Lederberg, one of the many researchers who have made great leaps in our understanding of biology using *E. coli*. The development of bacterial genetics made *E. coli* an even more tractable organism to study and by the early 1990s almost half of its 4·6 megabase (Mb) genome had been sequenced by groups around the globe interested in particular aspects of its biology. The rationale for it being the first bacterium to get its own genome sequencing project was obvious and it was one of the first organisms where interesting questions could be addressed by comparing a number of sequences from 'menace' strains to those of the 'model'. Glasner and Perna describe how these studies have highlighted the relatively large differences between genomes of the same species and how they have evolved.

E. coli's natural habitat is the mammalian gut, and each of us have billions of them growing happily inside us at this very moment. As commensal organisms in our gut flora they are a relatively minor component, although their contribution is important, and Rastall and Gibson describe interesting old and new data to suggest that they could be used as probiotics to treat certain conditions. As *E. coli* grows in our intestines it is being continually shed in huge numbers in the faeces and hence directly out into the environment (in most mammals). The presence of *E. coli* in faeces and the readiness with which it can be selectively cultured has resulted in it also being used as a marker of environmental faecal pollution. Jones and Smith explain this application of *E. coli* and the interesting work they are now doing to trace the sources of contamination by genetically typing the isolated strains.

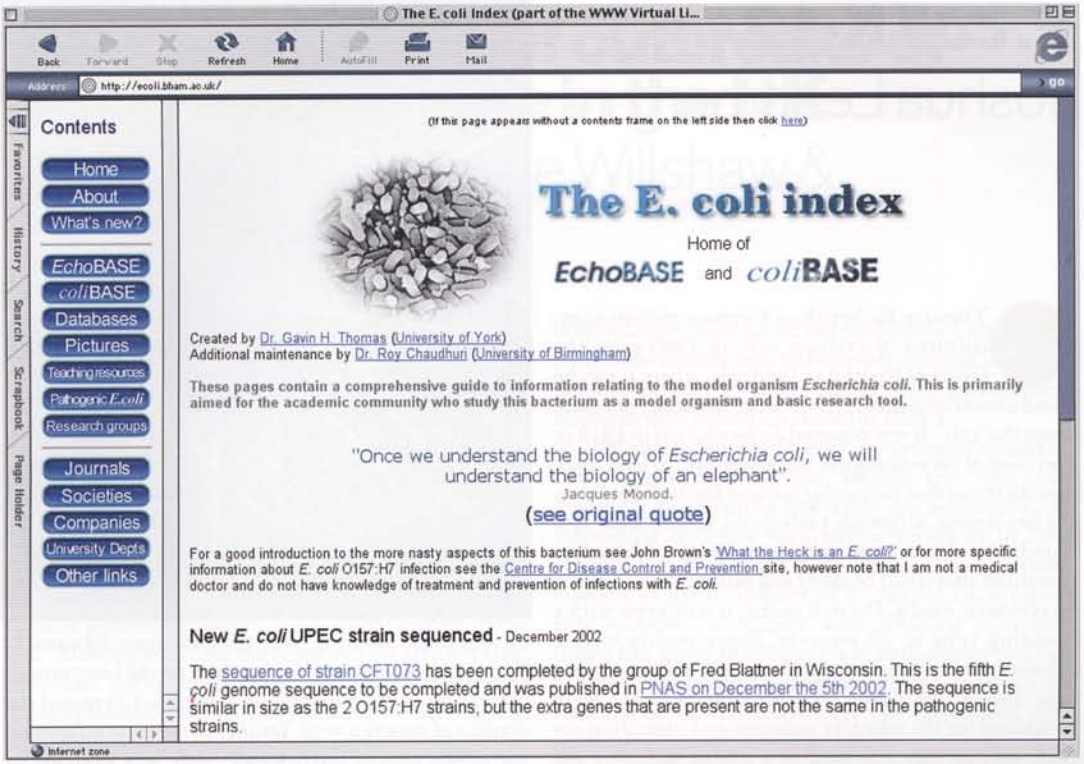
Biotechnology has also benefited greatly from scientific advances in *E. coli* K-12, particularly in the recombinant DNA era that started in the 1970s. The synthesis of human therapeutics in *E. coli*, such as insulin and human growth hormones, has had a major impact on medicine.

Pathogenic *E. coli*: an emerging menace

The widely perceived fear of *E. coli* as a dangerous microbe is a relatively recent development. It first really came to the attention of the UK general public after the major outbreak of O157:H7 in Lanarkshire in 1996 when 20 people died. O157:H7 is far from being the only pathogenic *E. coli* strain and Henry Smith and colleagues describe the different pathotypes present in the environment. For O157:H7, it is now clear that the major reservoir for this bug is in cattle, where the bacterium does not cause disease. David Gally and colleagues describe their exciting work in tracking down exactly where O157:H7 lives in the cow and how this localization is mediated. Their work suggests a physical method to reduce the risk of contamination while cows are at the abattoir, which with other measures implemented as part of SGM president Hugh Pennington's government report, should help reduce the incidence of disease caused by this bacterium in the UK.

A model organism for the 21st century

Now that microbiology is in the post-genomic era, scientists are developing more holistic approaches to studying microbes, alongside the traditional reductionalist methods. The ultimate objective of this new direction is to be able to completely understand a 'cell' to



FAR LEFT:
Coloured scanning electron micrograph of *E. coli* O157:H7 bacteria.
COURTESY DR GARY GAUGLER / SCIENCE PHOTO LIBRARY

LEFT:
The home page of 'The *E. coli* Index' (http://ecoli.bham.ac.uk/).

the extent that its behaviour can be modelled and hence predicted *in silico*. In selecting a candidate 'cell' on which to base these new experiments, *E. coli* seems like a strong choice. This belief is held by a large grouping of scientists who have formed the International *E. coli* Alliance (IECA), a worldwide consortium that is pooling expertise and resources relating to *E. coli* and is already providing post-genomic tools that will match those available for *Saccharomyces cerevisiae* and *Bacillus subtilis*. Most recently a major project from Keio University in Japan has resulted in the creation of a library of mutant strains containing single knockouts in over 4,000 *E. coli* genes.

To be able to construct an *in silico* model of a microbial cell, much still needs to be done to complete the 'parts list' of the cell to be modelled. Even for an organism as well studied as *E. coli*, this is not a trivial exercise. Of the 4,400 or so *E. coli* genes, over 1,500 have no clear physiological function. High-throughput post-genomic technologies are providing clues to the functions of many of these genes, but in the end a clear functional description of a gene product requires biochemical, genetic and physiological data, limiting the rate at which these discoveries can be made. An alternative strategy is to create a reduced *E. coli*. That is, to remove all the genes that we do not think have an important function for the cell. This will make modelling easier as the number of working parts is reduced. Fred Blattner and colleagues in the USA have removed over 0·5 Mb of the original 4·6 Mb genome with no reduction in growth rates on a range of commonly used growth media. It is likely that these two methods will be combined in practice. Comparative genomics highlights regions of the genome that have been acquired relatively recently, which can be removed without having a major effect on phenotype in respect to growth in standard lab conditions. Then genes that are still uncharacterized in *E. coli* and are widely distributed across different microbes can be studied in detail on the assumption that their ancient and ubiquitous presence implies an important conserved cellular function. A number of these proteins have now been crystallized and their 3D structures solved, which is aiding the design of experiments to determine function.

Metabolic reconstructions of *E. coli* have been created by several groups and the most complete reconstruction, from Bernhard Palsson and his colleagues in San Diego, also overlays transcriptional regulatory information, adding a further layer of detail. These models already seem to be able to make simple *in silico* predictions that agree well with *in vivo* measurements, but they are still a long way from what one would consider a complete cellular simulation.

With this renewed interest in *E. coli* and the current 'coming together' of the previously disparate *E. coli* research community, there is every reason to believe that *E. coli* will retain its central place in biological research into this new millennium.

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Further reading

For a summary of the Pennington Report, see **www.abdn.ac.uk/mmb/people/pennington-group-report.shtml**

Price, N.D., Papin, J.A., Schilling, C.H. & Palsson B.O. (2003). Genome-scale microbial *in silico* models: the constraints-based approach. *Trends Biotechnol* 21, 162–169.

Resources

The *E. coli* index serves as a gateway to resources for both the model and the menace and can be found at **http://ecoli.bham.ac.uk/**.

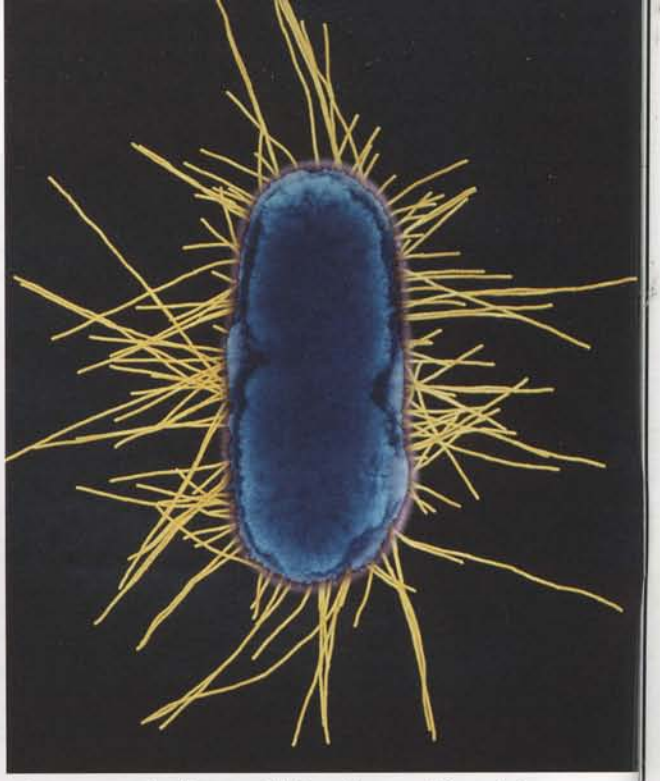
The text of the *Escherichia coli and Salmonella: Cellular and Molecular Biology* book, otherwise known as the '*E. coli* bible' can be found online at **www.ecosal.org/ecosal/index.jsp**

Details of the UK grouping within IECA, called Integrated Biology of *E. coli* (IBEC), can be found at **http://ecoli.bham.ac.uk/ibec/**

Information about access to the new mutant library and other tools from the Japanese initiative can be found at **http://ecoli.aist-nara.ac.jp**

E. coli K-12

Joshua Lederberg



K-12 is possibly one of the most studied bacteria in science. Joshua Lederberg, whose pioneering work on bacterial genetics led to his winning the Nobel Prize in 1958, describes the fascinating history of this strain of *E. coli*.

TOP RIGHT:
Coloured transmission electron micrograph of a section through an *E. coli* K-12 bacterium.
COURTESY KWANGSHIN KIM / SCIENCE PHOTO LIBRARY

Theodor Escherich, a German pediatrician, cultured 'Bacterium coli' in 1885 from the faeces of healthy individuals, where it can be found almost universally in the large intestine, or colon, hence the 'coli'. It was renamed *Escherichia coli* in 1919 in a revision of bacteriological nomenclature, to lend more specificity to this particular form of Bacterium. From the beginning, although pathogenic strains were also found, *E. coli* was used as a representative, harmless bacterium that could be safely and easily cultivated even on synthetic media. On rich media, it will grow with a doubling time of 20 minutes; hence readily visible colonies can be seen overnight when it is plated on agar. Specialized media, like MacConkey's agar, were developed for the selective isolation and identification of *E. coli*, as this was used as a global indicator for the pollution of water supplies. Hence, during the first half of the 20th century, *E. coli* was well known to bacteriologists. However, it was rarely, if ever, mentioned in general biology texts, as bacteria were generally regarded as pre-cellular in complexity and devoid of the nuclei and other genetic apparatus of 'real' organisms.

The conceptual revolution that has catapulted bacteria into the spearhead of molecular genetic study dates to 1944. Avery, Macleod and McCarty reported that pneumococcal bacteria could be transformed in serological type with preparations of DNA, the first robust evidence that DNA had anything to do with genes. Unfortunately, there was little to connect that transformation with genes as known in higher organisms, and the opportunity to cross-breed bacteria and look for recombination and segregation in the style of Mendel was absent. Those challenges motivated my own work, which by 1946 filled that vacuum, with experiments on comprehensive genetic exchange and linkage mapping using *E. coli*.

E. coli was chosen for these studies because of its favourable husbandry just mentioned. Soon the Matthew Effect came into play: the very accumulation of knowledge, mostly concentrated on a single strain, 'K-12', made it more likely that it would be a prototype for still further studies. This strain was found to harbour a lysogenic bacteriophage, lambda, which has seeded a scientific industry of its own; it is also the seat of a number of plasmids – intracellular DNA particles transmitted by conjugation. The latter in turn provided the basis for gene-splicing, genetic engineering and modern biotechnology.

There are many myths about the provenance of 'K-12' – it has nothing to do with 'Kindergarten-12th Grade' primary education, which is the usual association with the acronym in the USA. Actually, strain K-12 was isolated at Stanford University in 1922 from human faeces, and was kept under that label for many years as a stock strain in the bacteriology department there. In the 1940s, Charles E. Clifton used it for studies of bacterial nitrogen metabolism, and his colleague Edward L. Tatum then borrowed it for his work on the biosynthesis of tryptophan from indole and serine. K-12 entered the domain of genetics with Tatum's pioneering studies on the production of nutritionally deficient mutants in 1944. That work led to my collaboration with Tatum, and the discovery of sexual recombination in 1946. Since then, K-12 has been used by thousands of other investigators for innumerable genetic studies, and its genome sequenced. In retrospect, we know how lucky was the choice of strain K-12. With the methods used in 1946, only one *E. coli* strain in twenty, chosen at random, would have been successfully crossed, owing to the idiosyncrasies of the F-plasmid which govern its sexual behaviour. Likewise, if it had carried prophages different from lambda, like P1, the integration of bacterial viruses into the chromosome might have been obscured.

During many years of cultivation in the laboratory, the strain has lost its 'O' surface antigens, which is just as well as it provides further assurance of its harmlessness to people. On the other hand, this has left K-12 out of the arena of study of pathogenesis, which comes to the fore with special strains of *E. coli* like O157, which betray close relationships to other pathogens like *Shigella*.

Some of the most important of the scientific applications of K-12 genetics have been in the field of gene regulation, and the elaboration of the concept of the 'operon', with work centred at the Pasteur Institute in Paris. The Nobel Prizes earned by Francois Jacob and Jacques Monod are but two of the dozen that by my account are affiliated with *E. coli*. The overall scientific literature alluding to *E. coli* now encompasses over 100,000 publications; Google reports almost 3 million hits with '*coli*' on the World Wide Web.

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Based on material published in *Instruments of Science. An Historical Encyclopedia* (1997). Used with the permission of Taylor & Francis, New York, USA.

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E. coli as a cause of outbreaks of diarrhoeal disease in the UK

Henry Smith, Geraldine Willshaw & Tom Cheasty

Many cases of gastrointestinal infection in the UK are due to various strains of *E. coli*. Henry Smith and his colleagues at the Health Protection Agency review the recent pattern of outbreaks and consider what action should be taken to protect us in the future.

Since Escherich first described in 1885 the bacterium now known as *Escherichia coli* it has become one of the best studied organisms in microbiology. *E. coli* is present as a commensal in the intestinal tract of man and animals. However, certain strains of *E. coli* can cause severe disease in these hosts. This has led to detailed investigations of this 'Jekyll and Hyde' species and particularly in the last 25 years with the emergence of *E. coli* O157. This brief overview aims to consider the contribution of *E. coli* as a cause of general outbreaks of diarrhoeal disease in the UK. Although outside the scope of this article extra-intestinal pathogenic *E. coli* are also a significant cause of human diseases such as infantile meningitis, septicaemia and urinary tract infections.

Diarrhoeagenic *E. coli*

Comparison of the virulence properties of diarrhoeagenic *E. coli* strains has resulted in the recognition of several categories associated with disease. Those to be considered here are the enteropathogenic (EPEC), enterotoxigenic (ETEC), enteroinvasive (EIEC), enteroaggregative (EAggEC) and verocytotoxin-producing (VTEC).

Outbreaks caused by EPEC, ETEC, EIEC and EAggEC

Pioneering work by Bray established the importance of EPEC as a cause of outbreaks of infantile gastroenteritis in the UK in the 1940s. These continued until the early 1970s, but since then outbreaks caused by 'classical' EPEC strains have become very rare. The serotyping scheme, devised by Kauffmann, played an important part in these early EPEC studies. Outbreaks were caused by certain serotypes including O114:H2, O119:H6, O127:H6, O128:H2 and O142:H6. These EPEC strains form attaching and effacing (A/E) lesions that result in destruction of the microvilli on the intestinal epithelium and intimate attachment of bacteria to pedestals at the apical cell membrane. The possession of a gene termed *eae* that encodes the outer-membrane protein intimin is essential for the formation of A/E lesions. 'Classical' or 'typical' EPEC also possess the EPEC adherence factor (EAF) plasmid, but this is not required for A/E lesion production as so-called 'atypical' EPEC strains lacking the EAF plasmid can produce lesions. Outbreaks caused by atypical EPEC strains that were *eae*-positive but lacked the EAF plasmid have been identified in the UK in recent years (Table 1). These have involved food-borne transmission and generally affected adults. In one such outbreak, at a wedding reception, isolates of the 'outbreak' strain were obtained from food as well as infected individuals.

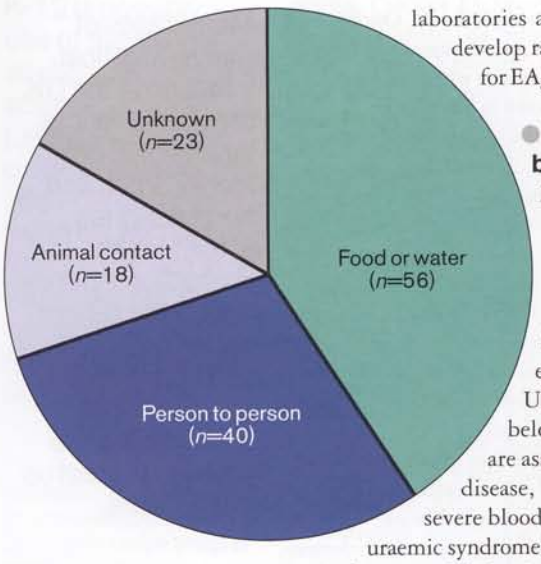
ETEC remain a major cause of diarrhoea in developing countries and also of travellers' diarrhoea. The pathogenesis of ETEC requires colonization of the small intestine and production of one or both of the two types of enterotoxin, heat-stable and heat-labile. Outbreaks of ETEC infection are very infrequently reported in the UK but an example, involving adults where two different serotypes were isolated, is shown in Table 1.

EIEC rarely cause outbreaks in developed countries. EIEC strains are very like *Shigella* spp. and cause dysentery by invading intestinal epithelial cells. An interesting outbreak occurred in Yorkshire in 2003 (Table 1) and appeared to involve food-borne transmission of EIEC. Isolates of *E. coli* O124, a typical enteroinvasive serogroup, were obtained from cases linked to a group of restaurants as well as from two food handlers. All isolates possessed a genetic marker associated with the enteroinvasive phenotype and were resistant to four antimicrobial agents.

EAggEC were defined in the late 1980s based on the pattern of adhesion to tissue culture cells. This group of *E. coli* shows a characteristic 'stacked brick' adhesion pattern and histopathological lesions have been demonstrated in animal models. EAggEC usually cause a watery diarrhoea with vomiting and the disease can be persistent, particularly in children in developing countries. Outbreaks of EAggEC infection have been reported in the UK and contaminated foods appear to be the transmission route (Table 1). In a study of four outbreaks of gastroenteritis in the UK, EAggEC was the predominant pathogen isolated. However, additional pathogens, including *Shigella sonnei*, *Campylobacter* and other diarrhoeagenic *E. coli*, were also isolated in a small proportion of cases in these four outbreaks. This suggests that there had been considerable contamination of the food vehicles implicated in these outbreaks. So far EAggEC have not been detected in animals and it appears that, like classical EPEC, ETEC and EIEC, the reservoir for EAggEC strains is the human gut. Food handlers who carry these types of diarrhoeagenic *E. coli* may present a significant risk of spreading infection. In a national study of infectious intestinal disease in England EAggEC were detected in 5·1 % of cases presenting to GP practices, a higher percentage than was found for *Salmonella* spp. in the same study. This group of *E. coli* represents an emerging problem as a cause of diarrhoeal disease. However, tests for these *E. coli* are not available in diagnostic

Table 1. Examples of food-borne outbreaks caused by diarrhoeagenic *E. coli* in the UK

E. coli group	Setting	Serotype
EPEC	Wedding party, 1997	O?H10
EPEC	Conference, 2001	O88:H5
ETEC	Catered function, 1995	O6:H16; O?:H-
EIEC	Restaurants, 2003	O124:H-
EAggEC	Conference, 1994	O86:H34
EAggEC	Hotel, 1994	O98:H-



ABOVE:
Fig. 1. Main transmission routes in 137 general outbreaks of infection with VTEC O157 in England and Wales between 1995 and 2003.

laboratories and work is in progress to develop rapid and cost-effective tests for EAggEC.

Outbreaks caused by VTEC

In contrast to infections with EPEC, ETEC and EIEC, human disease caused by VTEC belonging to serogroup O157 (VTEC O157) has been recognized as an emerging problem in the UK. VTEC O157 and strains belonging to other serogroups are associated with a spectrum of disease, including mild diarrhoea, severe bloody diarrhoea and haemolytic uraemic syndrome, which is the most common cause of acute renal failure in children in the UK. The vast majority of data on VTEC in the UK relate to serogroup O157 because of the lack of simple tests and laboratory surveillance for VTEC of other serogroups. Outbreaks of infection caused by non-O157 VTEC have not been reported so far in the UK, but several have been investigated in the Republic of Ireland and continental Europe.

Outbreaks of VTEC O157 infection in the UK have been reported since 1985. Fig. 1 illustrates the transmission routes in 137 outbreaks of VTEC O157 infection in England and Wales between 1995 and 2003. The main transmission route in the majority of these outbreaks was contaminated food or water and the foods implicated most frequently were dairy products and meats, both raw and cooked. Person to person spread and contact with animals or their faeces were also very important routes of transmission. In the reference laboratory the investigation of outbreaks requires an integrated approach involving several different typing methods together with detailed epidemiological data. The use of phage typing of VTEC O157 and VT gene typing by PCR provide rapid methods for the identification of possible outbreak cases as well as the differentiation of 'outbreak' and 'sporadic' cases of VTEC O157 infection. Pulsed-field gel electrophoresis (PFGE) is currently the method of choice as a highly discriminatory typing technique for strains of VTEC O157 as well as several other gastrointestinal pathogens. Outbreak strains belonging to different phage types rarely share PFGE profiles generated with the enzyme *Xba*I, whereas there is significant discrimination of isolates within a phage type. In the USA and Canada PFGE typing of VTEC O157, as part of the PulseNet scheme, has been used to identify outbreaks that may have been missed or not detected so rapidly by 'traditional' epidemiology. Successful examples have included outbreaks caused by distribution of contaminated ground beef to outlets in several states. General outbreaks caused by widely distributed foods of this type have not occurred in the UK so far, although family outbreaks and sporadic cases of VTEC O157 infection result from the undercooking of beefburgers or cross-contamination at barbecues.

Outbreaks of VTEC O157 infection have been reported in all parts of the UK with the most serious being that in Central Scotland in 1996/97. This led to nearly 500 cases and 21 deaths in elderly patients and was caused by contaminated meat from a butcher's shop in Lanarkshire. After this major outbreak, a detailed investigation headed by Professor Hugh Pennington resulted in the implementation of recommendations that led to significant changes in the management, distribution and handling procedures for the preparation and sale of raw and cooked meat products. More recently the Food Standards Agency Scotland and Scottish Executive Health Department set up a Task Force on *E. coli* O157 under the chairmanship of Professor Bill Reilly. The Task Force Report reviewed the risk of infection with VTEC O157 and recommended practical measures that would help to protect public health.

The future

Several studies show that outbreaks, as well as sporadic cases, caused by diarrhoeagenic *E. coli* in the UK are significantly underestimated. Apart from VTEC O157, insufficient laboratory surveillance data are collected, largely because suitable detection methods are not available in diagnostic laboratories. Several techniques, mainly PCR-based, have been developed for the detection of the different diarrhoeagenic *E. coli* but their use has been restricted in general to reference and specialist laboratories. The wider application of suitable methods should be used in the investigation of outbreaks of diarrhoeal diseases currently reported as of 'unknown aetiology'. Progress has been made in relation to VTEC O157 infection. Examples are the introduction of improved legislation for butchers' shops, increased awareness and control measures at 'open' farms and in relation to transmission via animals and their faeces. These factors may have contributed to a decline in the numbers of VTEC O157 infections in the UK since 1999.

The surveillance in place for VTEC O157 needs to be maintained and also extended to cover non-O157 VTEC as well as other diarrhoeagenic *E. coli*. This will allow a better assessment of the public health importance of this fascinating organism.

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Further reading

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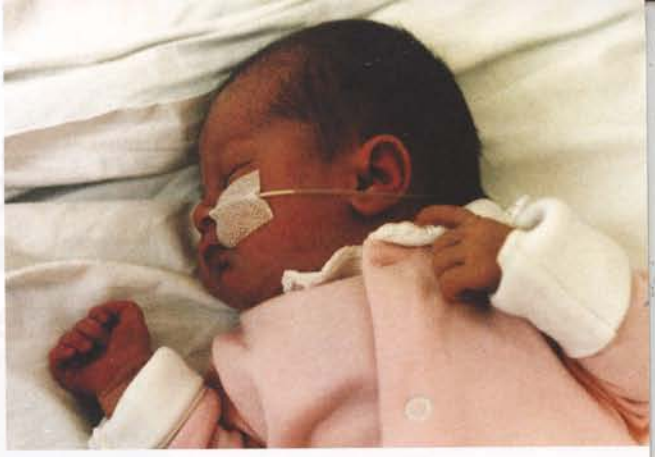
E. coli as a probiotic

Bob Rastall & Glenn Gibson



One rapidly developing area in the food microbial sciences is the use of dietary intervention to modulate the gut flora, with the consequent aim of improving health. Although probiotics have been used in human and animal nutrition for centuries, many new food products have recently become available, including fermented milks, lyophilized preparations and drinks. The most popular delivery system for human use is yoghurt, whereby additional cultures to the traditional starter strains (*Lactobacillus delbrueckii* subsp. *bulgaricus*, *Streptococcus thermophilus*) are used in the fermentation process and/or added to the product afterwards. Both bacteria and yeasts are used for their probiotic effects. The literature indicates over 50 reported human trials with a so-called 'positive' result. These have largely centred around gastrointestinal disorders, such as protection from travellers diarrhoea and alleviation of symptoms of irritable bowel syndrome. However, some systemic effects are also said to occur through the metabolic end products of probiotic growth in the gut (e.g. acetic acid is transported to muscle tissues where it can act as a source of ATP) and probiotics have been used to treat conditions such as atopic eczema and vaginosis. The annual European market for probiotics is said to be in excess of several billion euros, with new product developments occurring rapidly.

The Greek translation of probiotic is 'for life', and it is formally defined as a '*live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance*'. This has since been modified by a European working party on gastrointestinal function foods to a '*live microbial food ingredient that is beneficial to health*'. This implies that health outcomes should be defined and proven, which is not the case for all of the purported benefits of probiotics. Most research has been directed towards the use of intestinal isolates of bacteria as probiotics. Over the years, many species of micro-organisms have been used. They consist not only of lactic acid bacteria (lactobacilli, streptococci, enterococci, lactococci, bifidobacteria) but also *Bacillus* spp., yeasts such as *Saccharomyces* spp. and fungi such as *Aspergillus* spp.

Most probiotic bacteria are Gram-positive strains. This is largely because of their ability to persist within the gut ecosystem and produce organic acids such as lactate and acetate. One difficulty with many probiotics, however, is stability within the product. For example, the bifidobacteria are strictly anaerobic, leading to processing difficulties. Attention has therefore turned to less fastidious micro-organisms and recent reports have cited the use of *E. coli* as a probiotic.

Most of the work on probiotic *E. coli* centres around one particular strain, known as Nissle 1917. It was isolated in World War I from a soldier who survived a particularly severe outbreak of diarrhoea. Nissle proposed the use of *E. coli* as early as 1916 and showed in the 1930s that administration of this strain improved symptoms in patients with non-infectious bowel disorders. Subsequent work with Nissle 1917 has shown that administration to infants results in colonization of the gastrointestinal tract and a serum antibody response. Further, such colonized infants showed reduced colonization by bacterial pathogens and potentially pathogenic species. It has also been found that postnatal colonization with Nissle 1917 results in a significantly reduced incidence of allergies by the age of 10.

The use of this *E. coli* strain to treat Crohn's disease and ulcerative colitis has generated attention. In well controlled, doubly blind trials, Nissle 1917 was found to be as effective as the drug mesalazine in maintaining remission periods in patients with ulcerative colitis. In addition, it was found to inhibit adhesion of pathogenic *E. coli* strains isolated from patients with Crohn's disease to intestinal epithelial cells. As such, the use of *E. coli* as a probiotic for inflammatory bowel diseases has renewed interest in the use of microbial intervention for these conditions (established therapies include broad spectrum antibiotics like metranidazole and anti-inflammatory agents such as sulphasalazine – often, neither are especially effective).

The data on Nissle 1917 suggests that it may have some use as a probiotic, although much more data from human trials are required before firm conclusions can be safely drawn. Further research to clarify how it works is also necessary.

Use of a Gram-negative species as a probiotic is rare, but is likely to stimulate interest in other species. One aspect to consider is that within the normal gastrointestinal microflora, *E. coli* is normally present only in relatively trivial numbers, when compared to bacteroides, bifidobacteria, eubacteria, clostridia, lactobacilli, etc. In the context of colonization of the neonatal gastrointestinal tract, the 'Gold Standard' is generally held to be human milk. The result of breast feeding is a gastrointestinal microflora very much dominated by Gram-positive micro-organisms (usually bifidobacteria), more so than in formula feeding. In this light, the strategy of colonization of infants with *E. coli* should be pursued with caution.

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The use of probiotic microbes to improve health is becoming well established. Most of the bacteria in commercial preparations are Gram-positive, but as Bob Rastall and Glenn Gibson describe, *E. coli* may also prove to be a useful probiotic.

ABOVE:
A premature tube-fed baby.
PHOTO J. WESTWELL, SGM

Further reading

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The use of *E. coli* as a tool in applied and environmental investigations

Keith Jones & Richard J. Smith

Much of the publicity surrounding *E. coli* is concerned with death and disease. However, for applied and environmental microbiologists, such as those involved in the water industry, *E. coli* is regarded as an extremely useful tool.

E. coli as an indicator of faecal pollution

E. coli is found in the intestine of all warm-blooded animals and is voided in large numbers in faeces. Therefore, when faecal contamination is suspected it should be possible to isolate *E. coli*. In other words, *E. coli* acts as an indicator of faecal contamination.

It does this in two main ways.

First, because its density (number of bacteria per 100 ml water) is proportional to the amount of pollution, it acts as a quantitative indicator of faecal pollution.

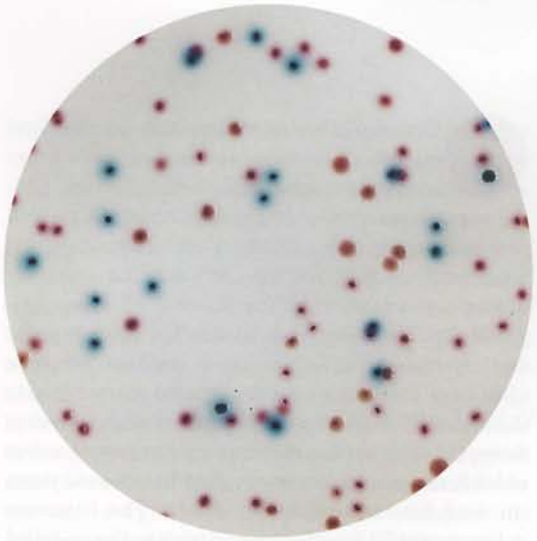
Second, it serves as a surrogate for the presence of pathogenic micro-organisms, e.g., *Salmonella*, *Campylobacter*, *E. coli* O157:H7, *Cryptosporidium*, *Giardia* and enteroviruses, which are present in faeces but in such low numbers that they are difficult and expensive to detect. As an indicator, *E. coli* should be found whenever pathogens are present and survive for as long as the hardiest pathogen.

Additionally, the tests for indicators need to be inexpensive, robust, sensitive, technically easy and work in all types of water. This is exemplified by *E. coli* which uses a selective medium and incubation at 44 °C. The selective isolation medium, containing peptone, lactose, bile salts and a pH indicator is familiar to anyone who has done microbiology. The lactose provides a substrate for fermentation to lactic acid that changes the colour of a pH indicator and the bile salts select for bacteria adapted to an intestinal habitat. There is a range of selective media for isolating and identifying *E. coli*. One such, developed by CHROMagar, is shown in Fig. 1.

Table 1. The effect of installation of a secondary sewage treatment and a long sea outfall on *E. coli* numbers (per 100 ml sea water) at Morecambe North

	New treatment works	*n**	No. of *E. coli*
(a) During the bathing season	Before	30	2535
	After	30	908
(b) Non-bathing season	Before	60	4004
	After	42	3565

**n*, Number of triplicate samples.



E. coli microbial standards

E. coli has been used as an indicator of faecal pollution for over 100 years. Indeed, its use is so widespread that it is enshrined in EU and World Health Organization standards for the safe limits of *E. coli* in foods, drinking water and bathing waters.

(a) Drinking water. There should be no *E. coli* in drinking water. When *E. coli* is found during routine monitoring, boil water advisory notices are issued until the problem is solved.

(b) Bathing waters. The current EU Bathing Water Directive (1976) says that there should be no more than 2000 faecal coliforms (this in reality means *E. coli* of animal origin) in 100 ml bathing water. A more stringent Directive of 500 *E. coli* per 100 ml water is currently under discussion in the EU parliament and, as suggested in an article in the November 2002 issue of *Microbiology Today*, and this has implications for future compliance of the UK's bathing waters.

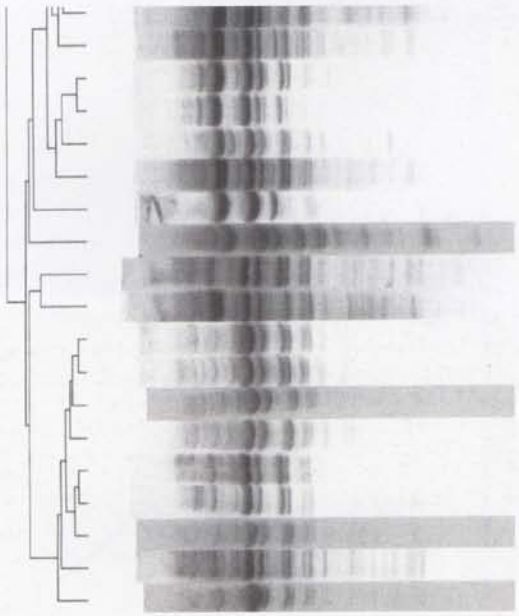
(c) Food. The Health Protection Agency guidelines for the microbiological quality of ready-to-eat foods, fresh fruit, vegetables and salad vegetables have three categories for the presence of *E. coli* (number per gram): satisfactory, <20; acceptible, 20–<100; unsatisfactory, >100.

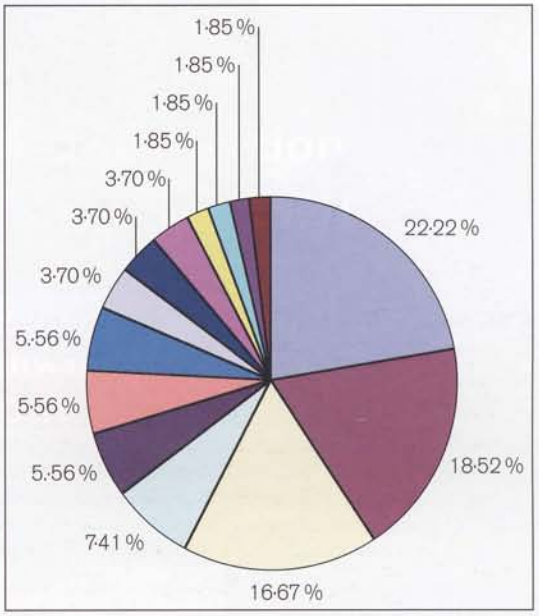
The use of faecal coliform (*E. coli*) counts in Morecambe Bay bathing waters

This is an illustration of how *E. coli* can be used as both an indicator of pollution levels and to track the source of that pollution.

A. Testing water quality

At Lancaster University we were involved in the microbial testing of bathing waters at three beaches in Morecambe Bay. One investigation was to quantify the effects of the installation of secondary sewage treatment and a long sea outfall on water quality. Prior to that installation,





OPPOSITE PAGE TOP:
Fig. 1 CHROMagar ECC selective agar showing a mixture of *E. coli* (blue) and non-*E. coli* coliforms (red).
COURTESY K. JONES

OPPOSITE PAGE BOTTOM:
Fig. 2. Masahiro Aoki (Hiro), a Japanese MSc student who worked on the DNA fingerprinting of *E. coli* in mussels, oystercatchers and seawater, taking samples at Morecambe.
COURTESY K. JONES

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Fig. 3. DNA banding patterns from *E. coli* isolates. DNA was extracted from isolates and small sections were PCR-amplified before size separation by electrophoresis, producing a pattern for isolate. Using sophisticated computer analysis, bands of similar patterns are grouped into related groups (clades) with similar patterns. Each clade is made up of closely related *E. coli* genotypes
COURTESY K. JONES

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Fig. 4. Clade composition of *E. coli* isolated from St Annes, Blackpool. Bathing waters are dominated by only three or four clades of *E. coli*.
COURTESY K. JONES

sewage was simply macerated and discharged via a short-sea outfall on the ebb tide. The results taken for approximately a year before and after installation are shown in Table 1.

Two features are immediately obvious. First, the overall effect in year one was to reduce the average coliform numbers to below the EU Directive of 2000 *E. coli* per 100 ml, but not below the proposed value of 500 *E. coli* per 100 ml. Second, there was much less effect in winter. This is probably because there are many more birds at Morecambe North in winter and less bacterial die-off at lower temperatures and in low sunlight.

The effects on the compliance of Morecambe's three bathing waters with the Bathing Water Directive were dramatic.

Prior to the installation of secondary sewage treatment none had passed the Directive. In the year after, two of the three passed. In the subsequent year there was a failure, but not the same one as in the previous year. The next, they all passed. Since then there have been sporadic failures, including Heysham in 2003. It is usually not clear why the sporadic failures occur and the accompanying bad publicity is not good for tourism.

In the 1990s it was realized that sewage treatment may not be the sole answer to cleaning up the UK's bathing waters and that diffuse sources (so-called non-point sources) may be important, especially when there are sporadic failures in compliance. Diffuse sources include run-off from agricultural land (cattle and sheep faeces), run-off from roads (dog faeces) and wild animals, including birds. This stimulated an interest in finding ways to track the origins of the faecal pollution reaching the UK's beaches. A number of methods have been tried, ranging from the Environment Agency's use of painted cucumbers, to mimic the floatation characteristics of faeces from sheep grazing on salt marshes, to the release of genetically engineered bacteriophage.

B. Use of *E. coli* in pollution source tracking

At Lancaster University we decided to concentrate on methods involving *E. coli*, largely because we wanted to exploit the immense know-how the water industry has built up over the years*.

Initially we thought we might be able to work with phenotypes of *E. coli*. This involved isolating a range of *E. coli* from bathing waters, purifying them, obtaining phenotypic, biochemical profiles using API 20E (bioMérieux) and comparing them with isolates from cattle, sheep, birds and humans. Indeed, we found that there were relatively few *E. coli* phenotypes in the bathing waters and that the dominant phenotype was common in birds, particularly gulls and oystercatchers. Unfortunately, the same phenotype was also found in humans, cattle and sheep, although it was not dominant. Most importantly, it was only a minor component in the effluent from waste water treatment works (WWTWs). We concluded that while *E. coli* is an excellent indicator of faecal pollution, it is poorly suited to tracing the source of that pollution, at least when using conventional methods. We decided, therefore, to investigate a more discriminatory method using genotyping of *E. coli*.

We developed a DNA-based typing scheme with *E. coli* that can be used to (1) identify individual genotypes and (2) identify animal/human sources.

E. coli were isolated from bathing waters and a variety of sources with the potential for polluting bathing waters:

- Effluents from WWTWs, humans
- Cattle, sheep, beach donkeys, wild birds, dogs
- Ribble estuary, tributary rivers
- Fylde bathing waters at Blackpool and St Annes

Genotypes (DNA fingerprints) from each source were matched with those from each of the bathing waters. The genotyping procedure is presented in Fig. 3.

The results show that each bathing water is dominated by only three or four clades of *E. coli*, for example, at St Annes (Fig. 4).

We can also show that genotyping reveals the relationships between sites, for example, major clades at St Annes are less common in Blackpool South and least common at Blackpool central (Fig. 5).

Recently we used genotyping to investigate whether oystercatchers' faeces are responsible for the high numbers of *E. coli* found in mussels growing in Morecambe Bay. We already know that most *Campylobacter* found in mussels comes from wild birds and the results in Fig. 6 show that at least 50 % of the *E. coli* also come from oystercatchers and not, as previously assumed, sewage.

Further reading

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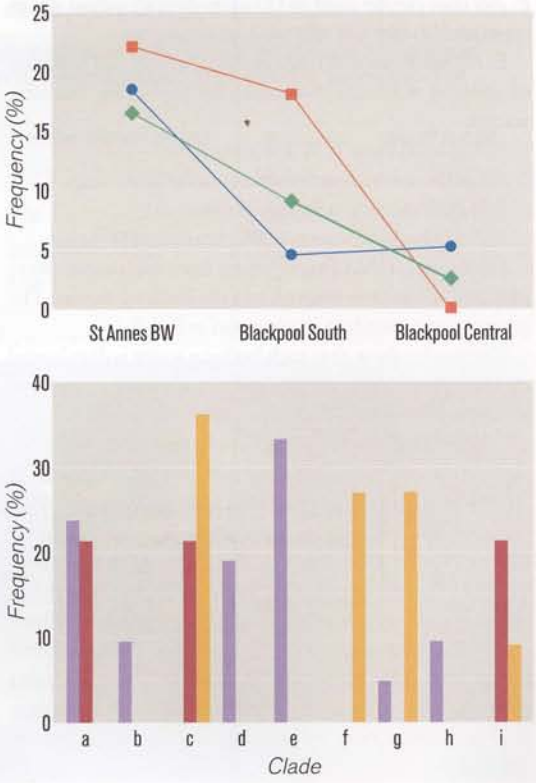
Whole of December 2003 issue of *Journal of Water and Health* devoted to microbial source tracking.

So, what can we conclude from our use of a DNA fingerprinting genotyping to trace *E. coli* in the aquatic environment?

- Groups of genotypes are associated with particular animal sources.
- Bathing waters contain *E. coli* from human, agricultural run-off and wild bird sources.
- The proportions of genotypes from a particular source are different in every bathing water.
- Genotyping is able to identify which, and in what proportion, animal or human sources contribute to faecal pollution.
- Genotyping is able to distinguish *E. coli* strains better than conventional techniques.
- It can, therefore, assist in tracing the source.

The phenotypes and genotypes of all the *E. coli* isolates from all sources and the bathing waters are put onto a reference computer database to form a library. Thereafter, when bathing waters fail the EU Directive, *E. coli* can be isolated from the positive faecal coliform counts, genotyped and compared with the library strains with a view to tracking the source of the pollution.

Research on pollution source tracking using a variety of genotype-based molecular methods with *E. coli* and other bacteria is being done by microbiologists in several countries and the pros and cons of particular methods can be accessed from the further reading section.



RIGHT:
Fig. 5. Genotyping reveals relationships between Fylde coast bathing waters. Major clades found at St Annes are less common at Blackpool South and least common at Blackpool Central. Clades: ■, 9.1; ●, 7; ◆, 14.

LOWER RIGHT:
Fig. 6. Distribution of *E. coli* genotypes (clades) in oystercatchers (■), mussels (■) and seawater (■) in Morecambe Bay.

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Fig. 7. Oystercatchers at Heysham.
COURTESY K. JONES

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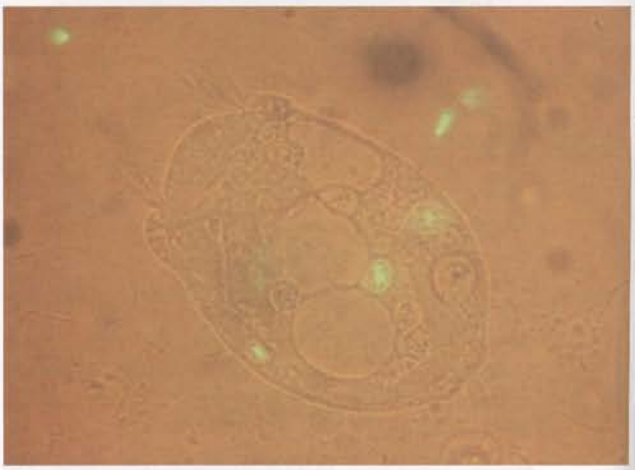
Fig. 8. GFP-*E. coli* cells inside a protozoan food vacuole.
COURTESY DR JACKIE PARRY, DEPARTMENT BIOLOGICAL SCIENCES, LANCASTER UNIVERSITY



E. coli as a sensor

As is readily apparent from other articles in this issue of *Microbiology Today*, *E. coli* is a pre-eminent tool for molecular biology, biotechnology and bioengineering.

In environmental microbiology, *E. coli* has been modified to respond to a variety of stimuli by switching on genes (reporter genes) that make them easily detectable. Such strains tend to be used to detect particular chemicals or to track bacteria in the environment. For example, *E. coli*, engineered to contain luciferase genes, is able to luminesce and will 'light up' quantitatively in response to different concentrations of particular pollutants. *E. coli* cells, labelled with GFP (green fluorescent protein), can be detected as individual bacteria in biofilms and even within grazing protozoa (Fig. 8).

The use of *E. coli* as a tool in the ways described above is not of course restricted to environmental microbiology. It is used in industry, particularly the food industry, not only to detect contamination and spoilage, but also as a means of tracking the source of that contamination.

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Comparative genomics of *E. coli*

Jeremy D. Glasner & Nicole T. Perna

As more genome sequences of different strains of *E. coli* are completed, researchers are finding a surprising variability.

E. coli is notorious for two reasons; first, many people have encountered one or more of the nasty strains responsible for gastrointestinal disease or urinary tract infection, and second, tamed to the Petri dish in the 1920s, the K-12 strain became a favourite of geneticists and molecular biologists who discovered and elaborated fundamental genetic and biochemical processes by studying this organism. The realization that basic cellular activities such as metabolism, DNA replication and gene expression are achieved using homologous systems in organisms as different as bacteria and man led to extensive investigation of their molecular basis in *E. coli*, owing to its easy manipulation in the lab. In this way, *E. coli*, along with other experimentally tractable organisms such as fruit flies and yeast, became premier 'model organisms'; systems where scientists could extract maximal information about critical processes with minimal experimental effort.

Not surprisingly, *E. coli* K-12 was among the first organisms targeted for complete genome sequencing due to its prominent role as a model organism and industrial tool. Genomes of additional strains of *E. coli* have been sequenced because of their impact on human health. Comparisons of these genomes revealed the genetic diversity underlying the phenotypic diversity of this species. Gene gain and loss is extensive, providing different lineages with distinct metabolic, pathogenic and other capabilities. The variable regions identified through comparative genomics are serving as candidates for further research on the evolution, epidemiology and molecular biology of *E. coli*. As more *E. coli* genome sequences accumulate, we continue to discover new genes in the population. Ongoing genome projects directed at additional distinct pathogenic *E. coli* will provide an even richer data set. Perhaps the future of *E. coli* as a model organism is *E. coli* as a model bacterial species.

The *E. coli* K-12 strain MG1655 genome sequence was published in 1997. It marked the culmination of a project that spanned the transition from tedious radioactive methods to automated fluorescent sequencing and other technological innovations, advancing genome sequencing in general and the efficient completion of additional *E. coli* genomes. In 2001, two sequences were published for enterohaemorrhagic *E. coli* strains of the serogroup O157:H7, one isolated from a contaminated ground beef lot associated with a disease outbreak in the US and the other from the single largest reported outbreak of all time, a 1996 incident involving school lunches in Japan. In 2003, genome sequences were published for an *E. coli* strain (CFT073) associated with urinary tract infections and two strains of *Shigella flexneri* serotype 2a (2457T and 301).

Radical differences among genomes

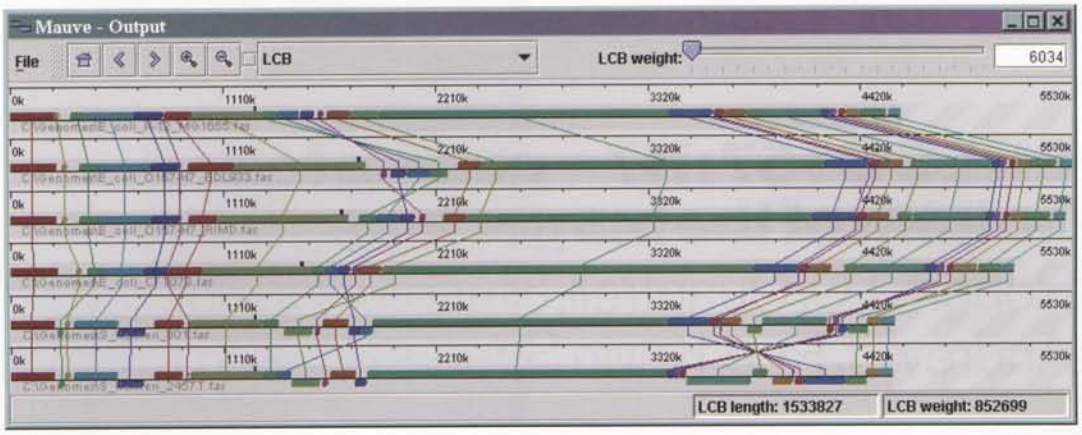
A comprehensive understanding of the commonalities and differences among these genomes has not yet been achieved, in large part because of the massive amount of genomic variability within the species. Even before the first *E. coli* genome was complete there was substantial knowledge of conservation in function, regulation and chromosomal positions of genes involved in core processes like central metabolism, transcription and translation as well as examples of genes responsible for differences between strains, often contained on mobile genetic elements such as plasmids. As larger pieces of the K-12 DNA sequence became available, examination of patterns in DNA sequence composition and codon usage revealed evidence of atypical 'islands' nestled among well studied genes. Despite evidence hinting at the variability within this species most researchers did not expect the magnitude of changes observed when compared with the next *E. coli* genomes.

The two *E. coli* O157:H7 genomes come from very closely related strains and, as expected, their genomes are extremely similar. However, comparison of either O157:H7 sequence to *E. coli* K-12 reveals that an extraordinary amount of gene loss and gain has occurred since these strains last shared a common ancestor roughly 5 million years ago. The 5·5 million base pair (Mbp) O157:H7 genome is nearly 1 Mbp larger than the 4·6 Mbp *E. coli* K-12 sequence. This much was evident in advance of genome sequencing. What was more surprising was while roughly 4·1 Mbp of the chromosome was very similar (~98·5 % identical) between either O157:H7 and K-12, this conserved 'backbone' was punctuated with hundreds of 'islands' of sequences specific to one strain or the other.

For example, O157:H7 strain EDL933 has over 1·4 Mbp of DNA without a counterpart in the K-12 genome, and these sequences are found clustered into 177 regions ranging from 50 to nearly 90,000 bp in length. Among more than a thousand genes encoded in these islands are some that were previously associated with O157:H7 virulence and many new candidate pathogenicity factors, such as iron utilization and host-cell adherence-associated genes, that are now under active investigation. A surprising discovery was two large islands, each containing (nearly identical, apparently functional) genes encoding urease – and this in a strain typically characterized by its lack of urease activity in clinical assays. A large fraction of the genomic differences can be accounted for by the activity of mobile genetic elements. Nearly 40 % of the O157-specific elements are found in one of at least 18 cryptic prophage or the one intact bacteriophage (933W). Interestingly, some of the most characteristic virulence genes of O157:H7, those for the Shiga-like toxins, are encoded within phages and evidence is mounting for additional phage-associated virulence determinants.

Horizontal gene transfer

If we consider the comparison from the *E. coli* K-12



ABOVE:
Linear diagram comparing the six complete *E. coli* and *S. flexneri* genomes using a software tool called Mauve.
COURTESY J.D. GLASNER & N.T. PERNA

perspective, it is important to note that many of the regions of the K-12 chromosome without counterpart in O157:H7 correspond to those previously noted islands of atypical base composition. It is believed that these odd sequences come from the occasional transfer of DNA from other species and integration into the *E. coli* chromosome, known as horizontal transfer. The strange base composition of these sequences is due to a high degree of variability in this characteristic between bacterial families. It is also significant that many of the K-12 islands are found at the same position in the chromosome as O157:H7-specific islands, and these also have atypical base composition. Taken together, these observations suggest that the elements specific to each strain accumulated over time by repeated horizontal gene transfer, frequently with successive transfers of different elements into the same slot of the core chromosome, descended from the common ancestor of all *E. coli* strains.

The fate of horizontally transferred sequences depends on their cost or benefit to the bacteria, with those that provide an obvious advantage under a wide variety of conditions expected to increase in frequency in the population and over long periods of time to evolve a base composition typical of the species, a process referred to as amelioration. The fact that we can recognize so many atypical sequences in the islands differentiating these closely related *E. coli* strains suggests that many of these horizontally transferred regions are temporary residents of the genome or provide an advantage specific to conditions encountered by particular strains.

More *E. coli* genomes

The publication of a 5·2 Mbp genome of the pyelonephritis-associated *E. coli* strain CFT073 cemented these views, and comparisons with an O157:H7 and K-12 genome easily reveals close to 3,000 genes encoded in stretches of the chromosome common to all three strains. However, the comparison also reveals more than another million base pairs of DNA not found in either of the other strains. Here, a phylogenetic perspective is helpful. *E. coli* K-12 and O157:H7 are more closely related to each other than either is to this extraintestinal strain. Again, although the island contents differ, we find many of the same chromosomal sites reused to house these strain-specific elements. Among the most notable observations is the lack of a type III secretion system encoded in this genome, given the apparent ubiquity of these systems in Gram-negative pathogens. There are, however, a number of previously unknown toxins and adhesions to fuel further research on the molecular basis of pathogenesis in the human urogenital tract. There is an ongoing project to sequence the genome of RS218, a quite different pathogen closely related to CFT073. RS218 is associated with neonatal septis and meningitis, and comparisons with existing sequences should reveal genes common to both extraintestinal pathogens, but not found in diarrhoeagenic or commensal strains, and identify genes responsible for distinct aspects of their diseases.

The year 2003 also saw the publication of two genomes from *S. flexneri*. Molecular phylogenetics has clearly demonstrated, and it is now widely accepted, that *Shigella* are members of the species *E. coli*. This is clearly borne out by comparisons of the *S. flexneri* sequences with the other sequenced genomes. However, one thing was quite different – the rate of genome rearrangement is much higher than observed in previous comparisons. There are at least 15 rearrangements between the two *Shigella* genomes, and nearly all inversions are bounded by insertion sequences which are abundant in these genomes. In contrast, among all previous comparisons, there is only one apparent inversion event bounded by cryptic prophage in one of the two O157:H7 genomes.

Even more *E. coli* genomes?

There is no reason to think that interest in sequencing additional *E. coli* genomes is waning. There are a number of important pathogen lineages, such as those with a K1 capsular polysaccharide, enteroaggregative *E. coli*, enteropathogenic *E. coli*, and other *Shigella* species with sequencing projects underway and other significant groups remaining. The existing data raise important questions about the levels and mechanisms generating and maintaining genome variability within and between *E. coli* populations that will require substantial genome-scale sequence information to resolve. The abundant genetic, biochemical and physiological data for *E. coli*, emerging results from high-throughput microarray and proteomic experiments and computational models of whole-cell physiology promise future development of this system. By leveraging the strength of *E. coli* as a model organism and comparing processes across strains of varying levels of relatedness and different lifestyles we can adopt *E. coli* as a 'model bacterial species' where we can begin to dissect the complex processes involved in diversification of bacterial species.

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Further reading

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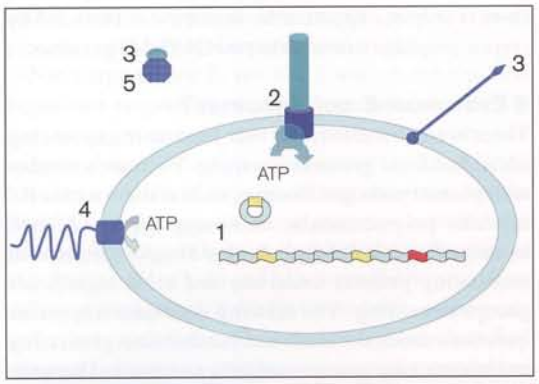
EHEC O157:H7 – getting to the bottom of the burger bug

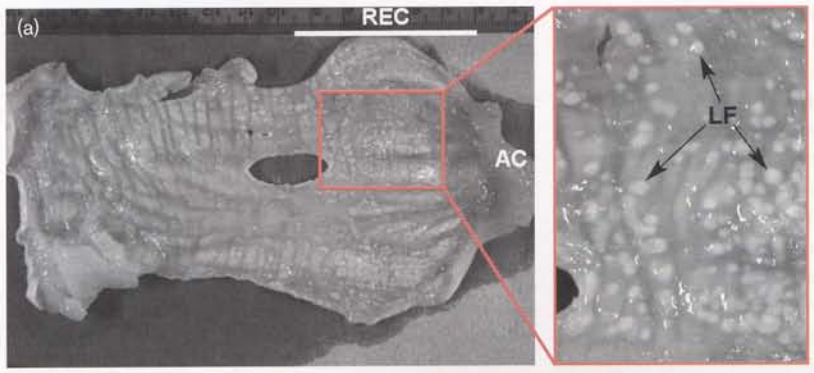
Robert J. O. Quantrell, Stuart W. Naylor, Andrew J. Roe, Kevin Spears & David L. Gally

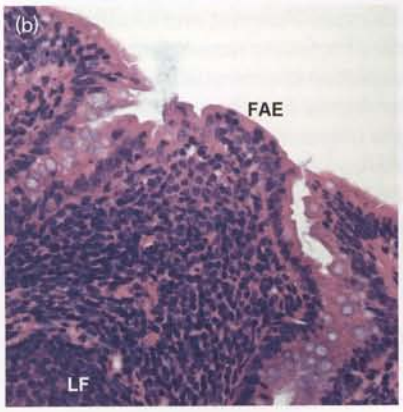
E. coli O157:H7 is a nasty human pathogen, yet it does not harm its cattle host. Dave Gally and his colleagues are finding out why.

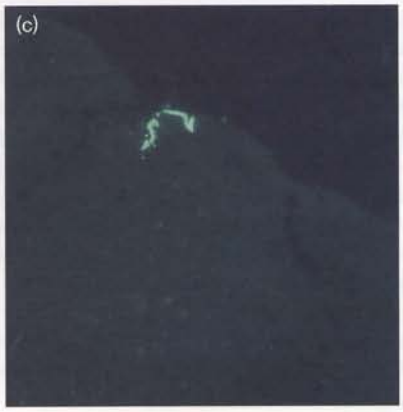
Enterohaemorrhagic *E. coli* (EHEC) emerged as a human pathogen in the 1980s through a series of food-borne outbreaks. Its notoriety stems from the severe disease it can cause, especially in the very young and the elderly. EHEC contain integrated bacteriophage genomes capable of expressing a potent toxin known as verotoxin (VT) or shiga-like toxin (SLT) that destroys blood vessels by killing endothelial cells. Damage to blood vessels in the gastrointestinal tract leads to the characteristic bloody diarrhoea associated with this infection. Kidney damage and failure can also be precipitated by the toxin and the very young are more susceptible, due in part to a higher toxin receptor level in the kidney. Fig. 1 outlines the key virulence-associated factors produced by the organism.



RIGHT (TOP DIAGRAM):
Fig. 1. Diagram illustrating some of the major virulence factors of EHEC O157. (1) Chromosomal DNA contains pathogenicity islands (red and yellow) such as the locus for enterocyte effacement (LEE) that is largely responsible for the attaching and effacing phenotype. Additional virulence traits are carried by the large pO157 plasmid. (2) The LEE encodes a type III secretion system that allows the injection of bacterial proteins into target cells, thereby allowing intimate attachment. (3) Initial bacterial binding to host cells or bacterial spread following attachment may be mediated by fimbriae. (4) Bacterial motility is driven by the presence of flagellae that may enhance penetration of host defences, including mucus, thereby aiding initial attachment to host tissue. (5) Finally, *E. coli* O157 carries a phage-encoded AB toxin known as Shiga-like toxin (SLT) or verotoxin (VT), which can have multiple effects dependent on host and cell type. These include inhibition of pro-inflammatory responses and apoptosis.
COURTESY D.L. GALLY







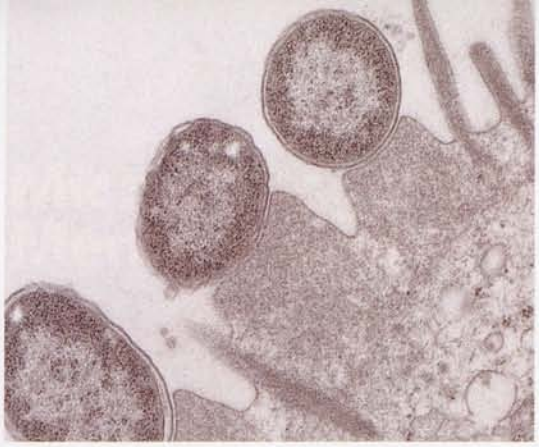
RIGHT:
Fig. 2. Lymphoid follicles at the bovine terminal rectum. (a) Location of lymphoid follicles (LF) after acetic acid treatment of terminal rectal mucosa. AC, anal canal; REC, region of bacterial colonization. (b) H&E stain of a lymphoid follicle (LF) and follicle-associated epithelium (FAE) at the terminal rectum. (c) Microcolony of EHEC O157:H7 (green) situated on FAE.
COURTESY D.L. GALLY

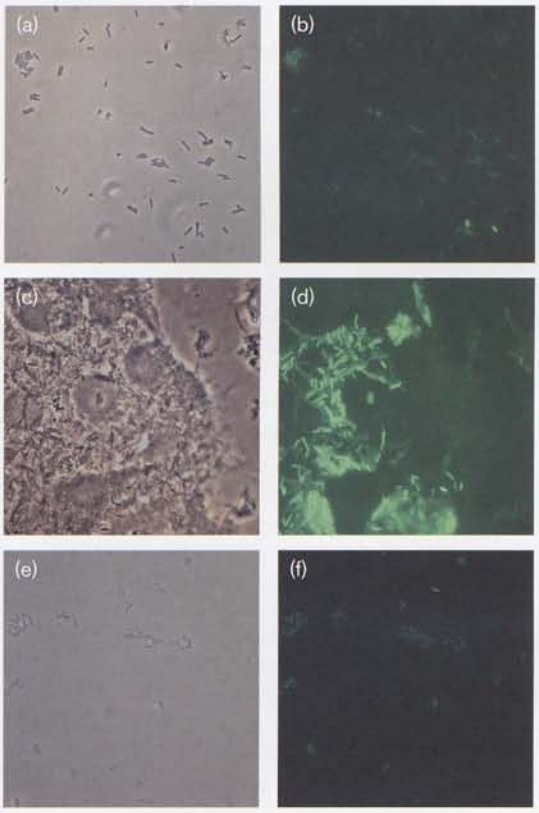
EHEC in cattle

There is now considerable evidence that ruminants, particularly cattle, are the direct or indirect source of most human infections. In the UK, North America and Japan, the main serogroup associated with disease is EHEC O157:H7. Unlike in humans, EHEC O157:H7 does not cause overt disease in cattle and can be considered a commensal. The overall aim of our research is to understand how EHEC O157:H7 colonizes cattle so that interventions can be designed to remove it from this primary host and therefore prevent transmission to humans. A key requirement is to determine where and how EHEC O157:H7 persists in the bovine gastrointestinal tract, as this is a prerequisite to finding the factors involved in bacterial persistence and designing interventions.

The bottom line

Cattle orally dosed with 10^9 EHEC O157:H7 shed up to 10^6 bacteria per gram faeces for at least 4 weeks. In our work to localize the bacterium in cattle, the first few post-mortems of animals shedding high levels of EHEC O157:H7 in their faeces failed to find significant levels at any site within the gastrointestinal tract, including the contents. As a result of this observation, attention turned to the terminal rectum of the animal, with subsequent work demonstrating that the bacteria were really only colonizing the final few centimetres of the gut at the terminal rectum adjacent to the anal canal. EHEC O157:H7 was coating the faeces as the animal defaecated and this was proven by sampling the surface versus the core of the faecal stool (when such separation is possible). The bacteria are therefore being taken in orally and more or less ignore metres of gastrointestinal tract and then colonize in a narrow band adjacent to the anus (this research was supported by a Veterinary Fellowship from DEFRA and was subsequently known as *The Fellowship of the Ring*!). This remarkable tropism explained why others had missed the site in the past and opened up the possibility of simple interventions to remove the bacteria from colonized animals.





TOP LEFT:
Fig. 3. A/E lesions in the bovine spiral colon induced by a human EHEC O111:H- strain (E43035N) at 4 days post-inoculation.
REPRODUCED WITH PERMISSION FROM *MICROBIOLOGY* **148**, 3767–3778.

LEFT:
Fig. 4. Expression of *tir*::*egfp* in *E. coli* O157:H7 on contact with cultured EBL cells. Cells were incubated with bacteria before fixation at the time points indicated. (b), (d) and (f) show expression of *tir*::*egfp* at 0 min (b), 15 min with EBL contact (d) and 15 min without EBL contact (f). (a), (c) and (e) show bacterial phase contrast images at 0 min (a), 15 min with EBL contact (c) and 15 min without EBL contact (e).
COURTESY D.L. GALLY

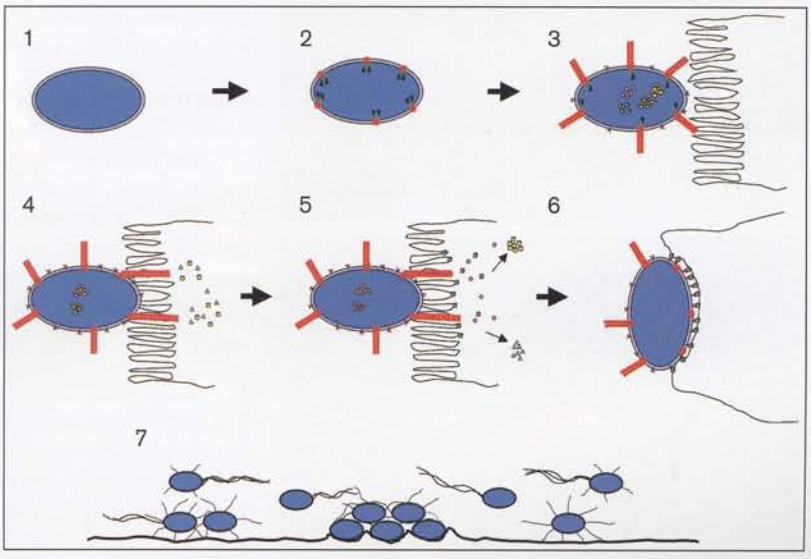
The molecular basis of colonization

Attention then turned to the molecular basis of this tropism. Examination of the site of EHEC O157:H7 colonization was not shared by the generic *E. coli* population and revealed a region containing a high concentration of sub-mucosal lymphoid follicles (Fig. 2a). These follicles contain B and T lymphocytes that signal alterations to the epithelium above these structures. This follicle-associated epithelium (FAE) is characterized by a reduction in the levels of mucus-secreting goblet cells and the presence of cells with shortened microvilli. These cells are similar to M-cells found in the small intestine that sample lumenal antigens. In conjunction with work carried out using human gastrointestinal explants, this research indicates that EHEC O157:H7 is likely to interact initially with M or M-like cells in both humans and cattle. Similarly, members of the *Enterobacteriaceae* – *Salmonella*, *Shigella* and other pathotypes of *E. coli* – have been shown to use M-cells as an initial point of interaction with their host.

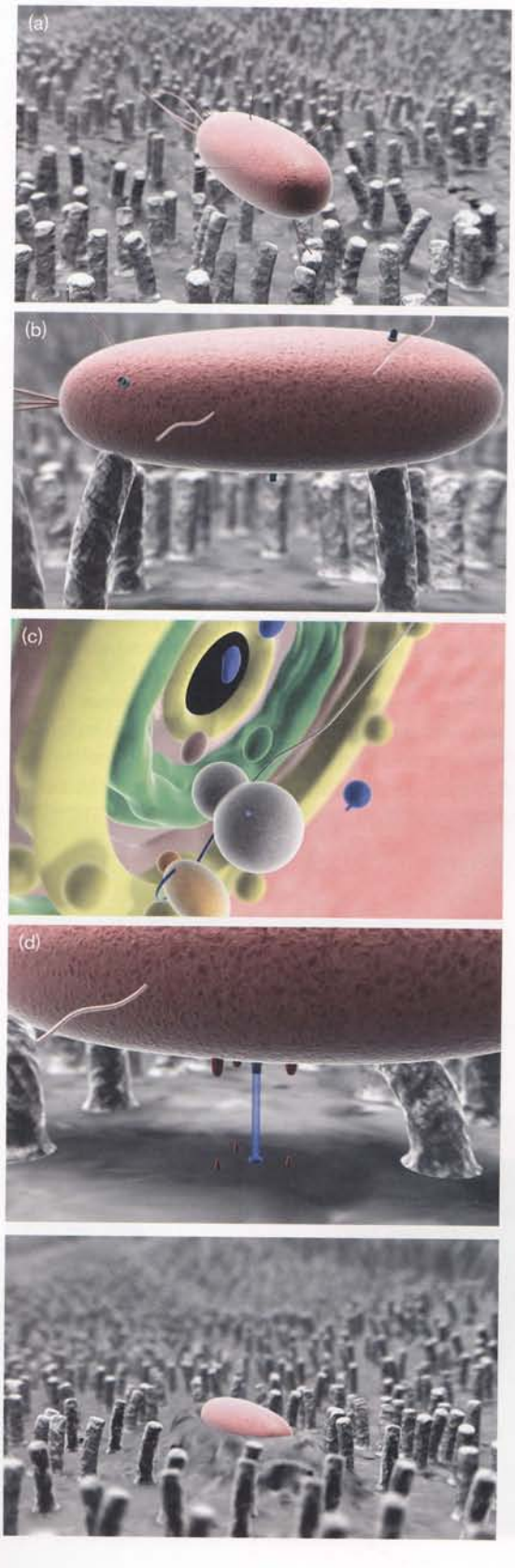
The obvious downside to contacting M-cells is that their usual function is to take up foreign particles. Bacteria such as *Salmonella* have the capacity to take advantage of this internalization, but this does not appear to be the case for EHEC O157:H7 as it is predominantly extracellular. In common with these other enteric pathogens, EHEC has a type III secretion system that enables the injection of bacterial proteins into host cells (see Figs 1, 5 and 6). The most obvious consequence of this is the formation of attaching and effacing lesions (Fig. 3) and this secretion system is essential for colonization and persistence in cattle. Another fundamental role for this system could be in disabling the M-cell on contact to then allow colonization of the epithelium in that area. This is analogous to the type III secretion system of *Yersinia* spp. that is able to rapidly disable macrophages and prevent phagocytosis. One hypothesis to explain the EHEC O157:H7 tropism is that the type III secretion system is only primed for action by signals present in the lower gastrointestinal tract, thus allowing this specific region to be colonized rather than FAE at higher sites in the gastrointestinal tract. Subsequent spread and persistence of the bacteria at the terminal rectal site will require other components such as flagellae and fimbriae as well as the capacity to multiply in the mucus layer.

EPEC vs EHEC in cattle

In contrast to the related but non-toxigenic enteropathogenic *E. coli* (EPEC), EHEC O157:H7 does not cause disease in cattle and can colonize and potentially recolonize animals for long periods (weeks). This long-term shedding relies on preventing both an



LOWER LEFT:
Fig. 5. Model illustrating primed expression of type III secretion on colonization of the bovine terminal rectum. (1) Transition through the majority of the bovine gastrointestinal tract without epithelial interaction. (2) In the lower gastrointestinal tract a combination of environmental cues, including higher bacteria levels and quorum sensing, lead to expression of the basal type III secretion apparatus. At this time the mRNA for the EspADB translocon may also be produced. (3) With a further signal, such as cell contact, the mRNA is translated and EspA filaments are produced. Transcription of certain type III secreted effector proteins occurs and intimin is expressed and inserted into the bacterial outer membrane (4 & 5). Secretion of effector proteins may occur in a co-ordinated manner, controlled by both expression patterns and differential affinities of effector proteins for shared chaperones that escort the secreted proteins to the apparatus and out of the bacterial cell. (6) Cytoskeletal rearrangements occur as a consequence of the activities of the injected effector proteins and the interaction of intimin with the translocated intimin receptor (Tir). The result is an intimately attached bacterium and an attaching and effacing (A/E) lesion. (7) From this initial binding site the bacteria spread to colonize the surrounding epithelium using a combination of flagellae, fimbriae and type III secretion. This includes possible bacterium–bacterium binding via type IV pili.
COURTESY D.L. GALLY



RIGHT:
Fig. 6. (a) EHEC O157:H7 responds to host environmental signals and expresses adhesins on its outer membrane. (b) EHEC O157:H7 binds to microvilli on the host-cell surface. (c) LEE4 (EspADB translocon) mRNA (shown in blue) is translated *in situ* at the inner membrane of the TTSS. The resultant Esp proteins are then exported through the needle complex. In this way translation and secretion are coupled. (d) EHEC O157:H7 produces a long EspA filament that allows the injection of the translocated intimin receptor (Tir) into the host cell where it inserts into the membrane. EHEC O157:H7 then binds tightly to the host cell via this Tir–intimin interaction. (e) Host-cell cytoskeletal rearrangements result in EHEC O157:H7 embedding in the host-cell membrane as part of the formation of an attaching and effacing (A/E) lesion.
COURTESY BIOVISUAL

inflammatory response and an adaptive immune response on colonization. Multiple factors contribute to this biology.

1. The very restricted site of colonization may limit responses in comparison to generalized colonization of the gut, or gastrointestinal tract.
2. *In vitro*, most EHEC isolates limit expression of important surface antigens such as the type III translocation filaments and intimin; this is in stark contrast to EPEC strains characterized to date that show less restricted expression.
3. The regulation in EHEC O157:H7 has evolved to allow rapid expression of these type III secretion-related factors on contact with host cells (Fig. 4).
4. Other EHEC factors such as VT/SLT appear to inhibit pro-inflammatory cytokine expression.

Having described EHEC O157:H7 as a commensal in cattle earlier in the article, it is clear that this belies a complex multifactorial interaction with the bovine host that leads to colonization by stealth. Transfer this bacterium to humans as an incidental host and the consequences can be devastating. This difference primarily lies with the receptor distribution for the VT/SLT in the two hosts, but also is likely to reflect their differences in colonization patterns, gene expression and signalling pathways. Fig. 5 illustrates the initial sequential interactions envisaged currently

EHEC O157:H7 – the movie

We have worked with a UK-based animation company Biovisual (www.biovisual.co.uk) to produce a full-length animation representing the key stages of EHEC O157:H7 interaction with the host. Biovisual produces custom animations that aim to summarize complex microbiological processes in a 3D environment. Still images illustrating steps in the process are shown in Fig. 6 and the full animation can be viewed at the Biovisual website or at our laboratory homepage (www.vet.ed.ac.uk/zap/research/movie.htm).

Acknowledgments

Research discussed in this article was predominantly funded by a DEFRA Research Fellowship to D. G. and was carried out in a consortium with Professor David G. E. Smith at the Moredun Research Institute, Penicuik and Dr J. Christopher Low at the Scottish Agricultural College (SAC) Veterinary Sciences Division. R. Q. & A. R. are based at UoE and funded by DEFRA. K. S. is based at UoE and funded by the BBSRC. S. N. is funded by DEFRA and based at SAC.

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Microbiology in the Regions – Member's report

3rd Workshop on Microbiology, Genetics and Molecular Mechanisms of the *Archaea*

St Andrews University, 5–6 February 2004

These are exciting times for archaeal molecular biology. Genome sequencing has highlighted the unique biology of the archaea. They are now known to be a major component of the biosphere, common in temperate seawater and soil, as well as the more familiar extreme environments such as volcanic pools, deep-sea vents and salt pans. Archaeal methanogens, living symbiotically in ruminants (and also humans), are an important source of the greenhouse gas methane. An archaeal parasite, *Nanoarchaeum equitans*, recently found in association with another species of archaeon, encodes almost no genes for metabolic proteins but a full set of 'informational' genes for DNA replication, repair, transcription and translation.

The focus of this meeting was on the molecular basis for informational processes in archaea, where there are striking differences from bacteria, and similarities to the equivalent pathways in *Eukarya*. These similarities have made the *Archaea* an attractive model system for studies of DNA replication and transcription. However, archaeal molecular biology also has many unique features that we are only just beginning to appreciate and explore.

Highlights of the meeting included the opening talk by Dr Rolf Bernander (Uppsala), who described the

construction and characterization of whole-genome microarrays for two species of *Sulfolobus*. These were used to demonstrate the existence of three separate DNA replication origins in these species – in marked contrast to the situation in bacteria where only a single origin exists. Dr Steve Bell (Cambridge) presented a very elegant set of biochemical experiments demonstrating the roles of multiple cdc6 proteins in replication origin binding and suggesting a mechanism for their coordinate control. Continuing the theme of DNA replication, Dr Dale Wigley (CRC-UK) outlined recent work on the clamp-loading complex RFC, combining structural biology and protein biochemistry to tease out some fascinating insights into the structure and mechanism of the protein.

DNA repair processes in archaea are also coming under scrutiny. Dr Thorsten Allers (Nottingham) presented intriguing data on the effect of deletion of key repair genes in *Haloferax*, whilst Dr Ed Bolt described the identification of a novel DNA repair complex from *Methanothermobacter thermoautotrophicum*.

The meeting included a poster session and workshop dinner, giving the participants from Sweden, France, Italy and all parts of the UK an opportunity to mix in an informal atmosphere. Dr Clare Jelinska (St Andrews) was awarded the Microbiology Communication Prize for her oral presentation on the archaeal chromatin proteins Alba1 and Alba2.

Thanks to the SGM, SfAM, Genetics Society and New England Biolabs for their support of this meeting. The 4th Workshop will take place in Cambridge in February 2005, and will be organized by Dr Stephen D. Bell (sdb@mole.bio.cam.ac.uk).

Dr Malcolm White, Centre for Biomolecular Science, University of St Andrews, North Haugh, St Andrews, Fife KY16 9ST, UK.
email mfw2@st-andrews.ac.uk

SGM/SfAM Joint Regional Meetings Grants aim to promote microbiology in the UK at a local level. Information on the scheme is available at **www.sgm.ac.uk/grants**

LEFT:
Delegates at the Workshop brave a windy St Andrews.

BELOW LEFT: Dr Stuart MacNeill awards the Communication Prize to Dr Clare Jelinksa

PHOTOS COURTESY M. WHITE

Alexander Fleming is interviewed for the 1934 RAE

Milton Wainwright

This is a long-lost transcript of the meeting between Alexander Fleming and his boss Almroth Wright about the forthcoming 1934 RAE to be submitted by the Inoculation Department at St Mary's Hospital, London.

The views in this humorous article are the author's and do not represent SGM opinion.

ABOVE:
Portrait of Sir Alexander Fleming (1881–1955) in his lab.
COURTESY SCIENCE PHOTO LIBRARY

AW: As you are aware, Alex, the next RAE is upon us and we need to get our submission ready in good time. Last time we got top marks and we need to maintain this standard, otherwise our income will plummet and we will have to engage in that dreaded activity – teaching.

AF: But what is the point of the RAE?

AW: Well Alex, money is tight and the Government needs to make sure that the 'Golden Triangle' of Imperial and Oxbridge get most of it.

AF: But why don't they just give it to them?

AW: Because, Alex, decisions must be seen to be accountable. Now, let's look at your submission. I see you have given me the required four papers. All in low impact factor journals. Could you start thinking about publishing more of your work in *Lancet* or the *BMJ*?

AF: But I publish in specialized journals in my field, medical bacteriology.

AW: I know that, Alex. But these are now deemed to be rubbish journals and we don't want St Mary's name to be associated with rubbish, do we? As far as I can see all that you are publishing on at the moment is this penicillin stuff.

AF: Well there is lysozyme.

AW: Yes, but you did that work outside the relevant dates. Lysozyme doesn't count any more. I don't see much future in the penicillin stuff. Have you purified it yet? You say in your paper it could be used as a curative. Have you got any industrial partners interested?

AF: I tried collaborating with Raistrick, but they were only interested in the yellow pigment. We did some tests on patients, but as you know, penicillin is very unstable. Do you mind if I smoke?

AW: What about grants, Alex?

AF: Well, we applied to the MRC but they rejected the penicillin work as a waste of time.

AW: Alex, you need to get some grant income. What about dropping this penicillin stuff and working on the ketogenic diet?

AF: You're not telling me, Almroth, that you believe that feeding patients masses of fat to change the pH of their urine is the way ahead for medicine?

AW: Of course not, but Foresight committees have deemed the ketogenic diet the way forward, and that's where the grant money's going.

AF: All this is extremely anti-academic and philistine, Almroth. Can't we take on these bean counters?

AW: No, right or wrong, Alex, we have to fight for our own slice of the cake. Times have changed.

AF: But real science hasn't. Anyway, penicillin has a great future.

AW: Look, I've taken advice from my friends on this. They think that your first penicillin paper is weak and badly written. And more importantly, no one cites any of these penicillin papers, so they can't be important, can they? The RAE committees will probably laugh if I submit them. What's more worrying, this penicillin stuff might adversely affect their decisions.

AF: Well leave me out of the RAE, I don't mind.

AW: Sorry, Alex, everybody goes in. No opportunity this time for fiddling the books.

AF: Look, Almroth, if penicillin is as important as I think, it will revolutionize medicine and save millions. We might even get an Institute named after us –imagine, the Wright–Fleming Institute.

If only the Department could provide me with a few mice, I could test it.

AW: Alex, all I want is to get top marks in the RAE. I'm not interested in revolutionizing medicine and saving lives. And I am certainly not going to waste Departmental funds providing you with mice.

AF: So, Almroth, what do you want me to do?

AW: Simple. Stop wasting your time on penicillin and work on the ketogenic diet. This will allow you to get grants. Who knows you might even get invited to meetings abroad and develop some markers of esteem.

AW: One last thing, Alex.

AF: Yes?

AW: The Departmental Safety Officer has asked me to insist that you wear a lab coat.

Postscript

Fortunately, Alexander Fleming ignored his boss. He continued working with penicillin and searching for new antibiotics throughout the 1930s. St Mary's did get its Wright–Fleming Institute and penicillin did save millions of lives. The ketogenic diet, as a means of treating infections, slipped into oblivion. Finally, most of the photographs of Fleming, as a famous laboratory scientist, show him wearing a shining white lab coat!

Unfortunately, the minutes do not record the result of the St Mary's bid to the 1934 RAE.

● *Dr Milton Wainwright, Department of Molecular Biology and Biotechnology, University of Sheffield, UK.*
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SocietyNews

May Council Meeting

Inspector of Microbiology

● Recently **Professor Brian Duerden** has been appointed by the government as the first Inspector of Microbiology, a post based in the Department of Health. The need for an Inspector of Microbiology was identified in the strategy for infectious diseases *Getting Ahead of the Curve* and was designed to ensure a high quality, integrated microbiology service across the country. Council was pleased to receive a letter from Brian saying how pleased he was with the positive attitude the Society was taking to help him in his new role.

Education and career activities

● The President expressed pleasure at the extent of activities being undertaken by members of the Marlborough House staff in these areas, which were highlighted in the Education Officer's report to Council. Ranging from careers fairs, new resources for schools, training courses for teachers and technicians to a communications workshop for PhD students and postdocs as well as helping to judge the MISAC composting leaflet competition. An impressive record of achievement for SGM.

New management structure for SGM journals

● Council was told of the implementation of a new management structure, bringing the four journals and the symposium series under a single overall manager with responsibility for strategic decisions, with each journal having a Senior Staff Editor for oversight of day-to-day production matters. There was warm approval for the appointment of **Dr Robin Dunford** as overall Manager and his team of Senior Staff Editors: **Lesley Hoyles** (*International Journal of Systematic and Evolutionary Microbiology*), **Melanie Scourfield** (*Journal of Medical Microbiology*), **Chris Sinclair** (*Microbiology*) and **Natalie Wilder** (*Journal of General Virology*).

● *Alan Vivian, General Secretary*

Address Book 2004

A new edition of the Address Book, containing a list of names and contact details of Society members and other useful information about the Society, is being compiled and will be distributed with the November issue of *Microbiology Today*.

Please let the Membership Office have any changes to your address, telephone/fax numbers or email details as soon as possible, but **no later than 13 August**. Send them to members@sgm.ac.uk

Also if anyone wishes to have their details omitted from the Address Book and has not already notified the Membership Office of this, they should do so immediately.

Elected Fellows of the Royal Society

Congratulations to the following SGM members who were elected Fellows of the Royal Society recently. Fellows are elected for their contribution to science, both in fundamental research resulting in greater understanding and also in leading and directing scientific and technological progress in industry and research establishments. A maximum of 42 new Fellows are elected each year.

Bland James Finlay

Leading Scientist, NERC Centre for Ecology and Hydrology, Winfrith Technology Centre, Dorset

He is distinguished for his many discoveries in protozoan ecology. He discovered seasonal migrations by protozoa in lakes, their integrated perception of gravity, blue light and oxygen tension. He discovered new methanogenic endosymbionts and showed that they increased the growth rate of their protozoan hosts.

David William Holden

Professor of Molecular Microbiology, Imperial College London

He is distinguished for genetic studies of microbial pathogenicity. He made a seminal breakthrough by inventing signature-tagged mutagenesis (STM), an *in vivo* genetic screen for identifying virulence genes.

News of Members

Nigel Brown, Professor of Molecular Genetics and Microbiology and Head of the School of Chemistry at the University of Birmingham, will take over as BBSRC Director of Science and Technology with effect from 1 September 2004.

Professor Brown has worked with BBSRC since the Council's formation in 1994, when he served as a member of the newly formed Genes and Developmental Biology Committee. He became Chairman of the Committee and a member of BBSRC's Strategy Board in 1997. In 2000 he became Chair of BBSRC's Studentships and Fellowships Committee.

Congratulations to **Dr Martin Adams**, University of Surrey, on his appointment as Professor of Food Microbiology.

Student member **Bibi Rehana Jauhangeer**, University of Westminster, has won one of the 15 L'Oreal UNESCO awards for the best young female scientists worldwide. The prize comprised a grant to support work on anaerobes in diabetic foot ulcers in Mauritius and media training in Paris.

Annual General Meeting 2004

The AGM of the Society will be held on **Tuesday 7 September** at the Society meeting at Trinity College Dublin. Agenda papers, including reports from Officers and Group Conveners, the accounts of the Society for 2003 and a special resolution to amend Article 25 of the Articles of Association, are in the separate Annual Report booklet distributed to all members with this issue of *Microbiology Today*.

Council

Dr Ulrich Desselberger, Cambridge, has accepted Council's invitation to be the next General Secretary of the Society. He will start his term of office in September.

Following the call for nominations to fill three vacancies for elected members of Council, the following have been elected unopposed to serve for four years from 7 September 2004:

Professor Iain Hagan, Paterson Institute for Cancer Research, Manchester

Professor Bert Rima, The Queen's University of Belfast

Dr Katherine Smart, Oxford Brookes University

Biographies of the new Officer and Council Members will be published in the November issue of *Microbiology Today*.

Grants

International Research Grants

This scheme allows scientists to travel from or to the UK/Republic of Ireland to carry out a defined piece of research in any field of microbiology. Applicants must be of senior postdoctoral level or above. The visits may be from one to three months duration. The awards cover the costs of return travel, a subsistence allowance and a contribution towards the costs of consumables in the host laboratory. The closing date for applications is **11 October 2004**.

International Development Fund

Members are reminded that funding is again available for competition this year. The purpose of the Fund is to assist microbiologists in countries where microbiology is inadequately developed. Members may apply for funding to run training courses in developing countries appropriate to the needs of those countries, or for any other small project to assist in technology transfer from developed countries. The closing date for applications is **11 October 2004**.

Seminar Speakers Fund

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

Watanabe Book Fund

Members who are permanently resident in a developing country are reminded that they may apply for funding to acquire for their libraries books, or possibly journals, relating to microbiology. These annual awards are available as a result of a generous donation from Professor T. Watanabe of Japan. The closing date for applications to the Grants Office is **11 October 2004**.

Education Development Fund/PUS Awards

Grants are available from this fund to members for projects intended to lead to an improvement in the teaching of any aspect of microbiology relevant to education in the UK. This might include the development of teaching materials (e.g. videos, slides, posters, CAL packages) or novel practical exercises. Funding is also available for small projects to promote the public understanding of microbiology, such as workshops, talks, demonstrations, leaflets, activities at science festivals. Applications will be considered on a first come, first served basis during the calendar year 2004.

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

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

Vacation Studentships

These enable undergraduates to work on microbiological projects during the summer vacation before their final year. They are intended to provide undergraduates with experience of research and to encourage them to consider a career in a laboratory-based science. Support is provided at the rate of £160 per week for a maximum period of 8 weeks. Up to £400 may also be awarded towards the cost of consumables. Students are required to submit a brief report of their research on the completion of the studentship. The scheme has proved to be very successful. This year 68 applications were received (nine more than in 2003) and studentships were offered to 44 applicants. A list of awardees is available from the SGM Grants Office on request.

Council has set aside a further sum to fund vacation studentships next year. Full details of the scheme will be announced in the next issue of *Microbiology Today* and published on the SGM website.

Retired Member Conference Grants

Retired members are reminded that they may now apply for a grant to attend one SGM conference each year. The award covers en-suite accommodation and the Society dinner, up to a maximum of £250. Applications for grants to attend the SGM meeting at Trinity College Dublin are now invited.

SGM Undergraduate Prizes

Nominations are invited from higher education institutions for the undergraduate student who performs best in microbiology in their penultimate BSc year. Each student is awarded £100, a certificate and a free year's undergraduate membership of the Society. The prizes are intended to encourage excellence in the study of microbiology by undergraduates and to promote scholarship in, and awareness of, microbiology in universities. Nomination forms were sent out to departments in early June, but further copies may be downloaded from the SGM website.

The closing date for the receipt of applications by the Grants Office is **31 August 2004**.

Staff News

We are pleased to welcome **Mrs Josie Underhill** as our afternoon receptionist, in place of **Diane James** who retired at Easter. Josie has had a career in various administrative posts, including a long stint in the offices at Reading Magistrates' Court.

The duties of the morning receptionist have been taken over by **Karen Turner**, who has been part-time membership assistant for some years. Currently Karen is also assisting Josiane with the arrangements for the SGM meeting in Dublin. She will be back in the Membership Office in September, ready for the annual subscriptions round.

Congratulations to Senior Staff Editor **Natalie Wilder** on her recent marriage to James McGuire in Reading. We wish the couple every future happiness. They will make their home in Reading.

Dr John Brimelow, Managing Editor of *Journal of General Virology*, has resigned his post. John has worked on the Society's journals since 1985.

SGM Prizes and Lectures

Peter Wildy Prize for Microbiology Education

Dr Nick Thomson

Title of Lecture: *Taking an educated guess: the ART of whole genome analysis*

Nick Thomson completed his PhD at Warwick University, studying bacterial molecular biology, and then went on to conduct a postdoctorate study on quorum sensing in the enteric bacteria at the Department of Biochemistry, Cambridge University. He has worked as a Senior Computer Biologist at the Pathogen Sequencing Unit (PSU) of the Wellcome Trust Sanger Institute in Cambridge since 1999, and is currently a project manager for bacterial whole-genome sequence projects of many important microbial pathogens, including *Chlamydiaceae*, *Salmonella typhi* and *Yersinia pestis*.

Nick is being presented with this prize for his efforts in organizing the highly successful SGM-sponsored genomics workshops. Their popularity has meant that they are now running for the third consecutive year with over 5 % of SGM members estimated to have already attended one of these regional events. Central features of the workshops are the widely acclaimed and freely available genome analysis software Artemis (ART) and its sister program ACT, which facilitates whole-genome comparison. The virtues of these tools have been enthusiastically demonstrated by researchers from the PSU, including the author of the software Kim Rutherford, who are keen to show how the ever-increasing amorphous mass of genomic data can be displayed and manipulated in a more easily interpreted format.

Marjory Stephenson Prize Lecture

Professor Stanley Falkow

Title of Lecture: *Thoughts on persistent bacterial infections*

Dr Falkow received his BSc degree from the University of Maine and his PhD from Brown University, following which he worked at the Walter Reed Army Institute of Research in the Department of Bacterial Immunology and was later named the Assistant Chief of the Department. In 1966 he joined the faculty of Georgetown University Medical School as Associate Professor of Microbiology. He later moved to Seattle to become Professor of Microbiology and Medicine of the faculty of the Department of Microbiology and Immunology at the University of Washington Medical School. In 1981 he became Chairman of the Department of Medical Microbiology at Stanford University School of Medicine. Since 1985, he has been Professor of Microbiology and Immunology and Medicine at Stanford University.

Dr Falkow's laboratory is recognized throughout the world for the research group's observations related to molecular mechanisms of bacterial pathogenesis. He has received numerous awards and honours in recognition of his accomplishments, including election as President of the American Society for Microbiology (1997–98). He has received honorary doctorates in Europe and the US, has served as an editorial board member of many prestigious journals and belongs to numerous professional organizations. Dr Falkow feels his greatest accomplishment has been that of mentor to many individuals who have continued their success in the study of microbial pathogenesis in universities around the world.

Industrial Member Forum

Council's initiative to promote greater interaction between the Society and industry based members took another step forward in early July when External Relations staff and Council members met with a group of microbiologists from a range of industrial sectors.

The meeting participants discussed current Society activities and gave useful feedback on how some services could be tailored to better fit the needs of members working outside academia. A full report will be given in the next issue of *Microbiology Today*.

As reported in the May 2004 magazine, Council has already voted to have an Industrial Liaison Officer to spearhead this scheme. The proposed new post will be put to the AGM in September for approval.

Medical, Dental and Veterinary Science Elective Awards

Council recently announced a new scheme offering awards to enable medical, dental and veterinary science undergraduates to work on microbiological research projects during their elective periods. The purpose of the awards is to provide students with the necessary experience to encourage them to consider a career in microbiology.

The studentships provide a maximum payment of £1,200 to support travel and living expenses for a period of up to 10 weeks. An additional sum of up to £400 for specific research costs may also awarded. Five applications were received and refereed by experts on Council. Congratulations to the following who received awards:

Gina Banks, Royal (Dick) School of Veterinary Studies, University of Edinburgh.
Project: *Studies on host–pathogen interactions of* Pasteurella multocida *A:3 in bovine lymph nodes using immunohisto/cytochemistry.*

Shauna Culshaw, Glasgow Dental Hospital and School.
Project: *A peptide vaccine to protect against dental caries.*

Kathryn Laws, University of Warwick Medical School.
Project: Methylobacterium*: a potential opportunistic pathogen?*

Dennis Ryan, Faculty of Veterinary Medicine, University of Glasgow.
Project: *Campylobacterosis and the food chain in Morogoro, Tanzania.*

Education Development Fund report

Micro-organisms and the safety and stability of foods: an electronic teaching resource for food microbiology

Alan Varnam

The philosophy and methodology of higher education teaching and learning are subject to constant flux. Changes are driven by many factors, including the outlook and aspirations of students, the needs of employers, increased quantities of data within the body of knowledge underpinning teaching and changes in the technology available for delivery of course material. One of the important consequences of change is the continuing development of new courses which may combine elements of several conventional disciplines. These include a large number of food-related courses at both undergraduate and graduate level.

Microbiology is recognized as being of fundamental importance in food science and other food-related courses. The need for students to understand the relationships between micro-organisms and food extends beyond direct teaching of food microbiology to other courses, such as technology and product development. In many cases, teaching includes problem-solving and similar student-based exercises that require application of microbiological knowledge to concerns of safety and spoilage. There are inherent difficulties where the nature of the course means that underlying student microbiological knowledge is limited. In 'real-world' exercises, inherent difficulties can be compounded by problems of obtaining relevant data. These problems can affect teaching at both undergraduate and graduate level.

The Department of Health and Human Sciences at London Metropolitan University teaches a number of food-related courses, including BSc Food Science, Food and Consumer Science and MSc Food Science. The microbiological safety and stability of foods is a common feature and knowledge of hazards and options for control is required at various levels across the range of teaching. Difficulties in identifying hazards and control cause problems. Discussions with students suggested that a custom-designed database providing information about the micro-organisms associated with different types of food would be of considerable value. At the same time, a predictive model for major spoilage organisms was developed by Dr Jane Sutherland and collaborators in a European Union-funded project. There was obvious potential synergy between the database, as a means of identifying micro-organisms likely to be present, and the predictive model for determining the probable extent of their growth. After much thought and many doubts, it was decided to develop an electronic resource combining the database and predictive model.

The resource developed is based on Microsoft Office software. The initial design comprised the original two components, the database and the predictive model entered through a 'home page'. Having made the decision to develop the resource, further thought was given to its functional use. It had been noted in earlier teaching that some students encountering micro-organisms in a problem-solving context showed a natural inclination to learn more. An extra element was therefore added to the resource: illustrated text files that provide supplementary information concerning the major food-borne pathogens and spoilage micro-organisms.

The database is in MS Access and consists of two components. The first is a file of approximately 100 food commodities listing hazards, probable spoilage microflora and microbiological standards. Alerts are included warning of possible new problems and notes supply additional information. The second file comprises food-borne micro-organisms, their basic properties and control options.

The predictive model is constructed in MS Excel and incorporates yeast, *Bacillus* spp., lactic acid bacteria, *Enterobacteriaceae*, pseudomonads and *Brochothrix thermosphacta*. The output is displayed graphically, ensuring that students work for their predictions!

The resource also includes guidance notes for users and an empty MS Excel file titled 'My results'. This file is primarily intended for use in laboratory classes.

There is considerable flexibility in how the 'functional' parts of the programme are used in exercises. Any part can be used individually, but a very effective approach is to use the database to identify potential problems. Once identified the predictive model can be used to ensure product stability and that shelf life requirements are met. At this stage, or at any other time, the student can learn more about individual micro-organisms from the text files. These are designed to be read at different levels according to student background, but are not intended as an electronic textbook, the general thrust being to target specific points of direct relevance to the database.

The resource has been well received by students, although it is currently undergoing more extensive evaluation. Beyond the immediate aims, other learning benefits, including enhanced interpretational ability and greater confidence in use of complex data are apparent.

The resource was developed with the aid of an Education Development grant from the SGM. Naaema Jawaid, an undergraduate student studying Biochemistry at London Metropolitan worked on the project and played a major role in its development.

Dr Alan Varnam, Department of Health and Human Sciences, Food Microbiology Unit, London Metropolitan University, North Campus, 166–220 Holloway Road, Holloway, London N7 8DB, UK.
Tel. 0207 133 2524; Fax 0207 133 2571
email a.varnam@londonmet.ac.uk

This fund supports developments likely to lead to an improvement in the teaching of any aspect of microbiology relevant to secondary or tertiary (including postgraduate) education in the UK. For full details of the rules and an application form see the SGM website.

Meetings

Meetings on the web

For up-to-date information on future Society meetings and to book on-line see: **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. 151 for contact details of Group Conveners.

Administration of meetings is carried out by **Mrs Josiane Dunn** 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).

Offered papers and posters

Many Groups organize sessions for the presentation of short oral papers or allow intercalated papers within their symposia. Offered posters are welcome at all Society meetings.

Offered posters

Each poster should be associated either with the Plenary Session topic or with a Group. The subject content of the latter should be relevant to the remit of a Group (see website for details); it does not have to relate to the topic of the Group Symposium taking place at a particular meeting. General Offered Posters will not be accepted.

Abstracts

Titles and abstracts for all presentations are required in a standard format and should be submitted through the SGM website. Deadlines for submissions are published in *Microbiology Today* and on the web. For further information contact the Events Administrator.

Future Meetings

AUTUMN 2004 – 155th Meeting

Trinity College Dublin, 6–9 September 2004

● Plenary: Alternative antimicrobial therapies

The City of Dublin promises to be an exciting venue for the autumn meeting, which is the first the SGM has held outside the UK for several years. A packed programme of symposia and workshops has been planned, but the format of the meeting will be different in many ways from usual.

● ACCOMMODATION

The scientific sessions will take place in Trinity College, but delegates will be responsible for booking their own overnight accommodation. Arrangements have been made with Total Stay – The Hotel Shop who are offering bed and breakfast in hotels at prices to suit all pockets. Bookings should be made directly with the agency by telephone (Tel. 0870 0112 292) or online (www.totalstay.com).

● MEALS

No meals will be available at Trinity College. There is a huge variety of cafes, bars, restaurants and pubs nearby where delegates can buy lunch and dinner.

● REGISTRATION FEES

£25 per day will be payable by SGM members for this meeting. Non-member registration fees are £70 per day. These include refreshments, the abstracts book, all conference literature and administration. Student Members, Retired Members and Honorary Members are exempt from registration fees.

● POSTGRADUATE CONFERENCE GRANTS

These will be available, subject to the usual conditions. A flat rate will be paid for accommodation of £30 per night plus daily subsistence of £10. For full details, a form and allowances for travel see www.sgm.ac.uk/grants/pg.cfm

● SOCIAL EVENTS

Welcome Reception

Get to know your fellow delegates over a glass of wine on the first evening of the conference.

Irish Night

Instead of a formal Society Dinner, there will be an evening of unlimited Irish food, drink (including Guinness, of course), music, dancing and other traditional entertainments.

Old Jameson Distillery

Find out how traditional Irish whiskey is made by touring the exhibition. Wine and a finger buffet will be served.

Trinity College

There are many attractions within the College, including the Old Library, Book of Kells and the Dublin Experience exhibition. Tickets will be available at concessionary prices for conference delegates.

● PROGRAMME BOOKLET

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

● Registration

Register for the meeting through the SGM website. You can either register online (https://www.sgm.ac.uk/regforms/155/regform.cfm) or download a PDF of the booking form and fax or post it to the Meetings Office with your payment (www.sgm.ac.uk/meetings/MTGPAGES/tcd_form.pdf).

We are no longer printing registration forms. Anyone who experiences problems with registering through the website should contact the Meetings Office (Tel. 0118 988 1805; email meetings@sgm.ac.uk)

Deadline for early registration: **Friday 6 August**. Thereafter a late booking charge will be incurred.

SPRING 2005 – 156th Meeting

Heriot-Watt University, 4–7 April 2005

● Plenary: Molecular pathogenesis of virus infections

Organizers: P.E. Digard, H.F. Jenkinson, A.A. Nash & R.E. Randall

● Speakers

J.L. WHITTON (Scripps Research Institute, USA) *Adaptive immune response*

G. SCREATON (John Radcliffe Hospital) *Immune response to Dengue virus*

S. BORROW (Jenner Institute for Vaccine Research) *Immune response to HIV*

J.K. FAZACKERLEY (Edinburgh) *Persistent RNA virus infections*

S. NICHOL (CDCP, USA) *Exotic virus pathogenesis*

S. SIDDELL (Bristol) *Coronaviruses and SARS*

J. MANSON (IAH, Edinburgh) *Transmissible spongiform encephalopathies*

R. WEBSTER (St Jude's Children's Research Hospital, USA) *Influenza virus pathogenesis*

R. ANDINO (California, USA) *Antiviral potential of RNA silencing*

D. LEIB (Washington, St Louis, USA) *HSV infections in vivo*

S.M. LEMON (Texas, USA) *Molecular pathogenesis of HCV*

S. HERRINGTON (St Andrews) *Papillomaviruses & human neoplasma*

O. HALLER (Freiburg, Germany) *Intracelluair antiviral defence mechanisms*

A. ALCAMI (Autonoma, Madrid, Spain) Poxvirus immune evasion

L. DIXON (IAH Pirbright) African swine fever

● Other symposia and workshops

● Special Symposium – Emerging diseases of wildlife and farmed animals

Organizers: G. Schild & C. Howard *et al.*

● Molecular typing and epidemiology

Clinical Microbiology/ Systematics & Evolution Groups

Organizers: S.C. Clarke, N.A. Logan & G.S. Saddler

● Antibiotic resistance

Clinical Microbiology Group/ BSAC

Organizers: P. Hawkey & M.B. Avison

- Emerging infections: dangers to human and animal health

Clinical Virology Group

Organizers: D. Paton & P. Simmonds

- Virology: is it practical?

Education & Training Group

Organizers: R.J. Cooper & B.A.B. Martin

- Microbe–pollutant interactions: ecology, function and applications

Environmental Microbiology Group

Organizers: G.I. Paton & K.T. Semple

- Evolving bacteria and emerging food-borne disease

Food & Beverages Group

Organizer: M. Peck

- Alternative models of infection

Microbial Infection Group

Organizer: J.N. Fletcher

- Bacteriophage evolution, ecology and applications

Physiology, Biochemistry & Molecular Genetics/ Cells & Cell Surfaces/ Education & Training/ Microbial Infection Groups

Organizers: M.C.M. Smith & G.P.C. Salmond

- Cell tropisms and host range

Virus Group

Organizer: L. Dixon

- Virus Group Workshops

RNA viruses – Organizers: P. Digard & J. McLauchlan

DNA viruses – Organizers: D. Blackbourn, L. Dixon & G. Wilkinson

Virus pathogenesis – Organizer: A.A. Nash

Virus, immunity and vaccines – Organizer: N. Almond

Plant viruses – Organizer: J. Carr

Prions – Organizer: J. Manson

Email addresses of all session organizers are available on the SGM website.

Irish Branch

Environmental genomics

University College Cork, Spring 2005

Organizer: J.R. Marchesi

Rapid molecular diagnostics in medical microbiology

University of Ulster, Coleraine September 2005

Organizer: C.J. Lowery

Mechanisms of microbial adherence and invasion

Trinity College Dublin April 2006

Organizer: S.G. Smith

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

Other News & Events

● Bioinformatics Workshops

Following the success of the workshops held jointly by the SGM and The Sanger Centre in 2003, Council is sponsoring further events this year. See web for details and a booking form.

Queen's University Belfast – 17 September 2004
(deadline for registration **3 September**)

Plymouth Marine Biological Association – 15 October
(deadline for registration **1 October**)

● European Federation of Biotechnology

Microbial Physiology Section Meetings
6–8 October 2004; Copanello, Southern Italy

A residential symposium *Functional Genomics of Pathogenic Bacteria*. Includes, at no extra cost, an introductory workshop on the design, use and applications of microarrays. Organized by Francesco Falciani (f.falciani@bham.ac.uk).

11–14 November, Algarve, Portugal
Symposium *Recombinant Protein Production*.

For full details, visit the Microbial Physiology Section web page at **www.efbpublic.org**. SGM members can still register for both meetings at the cost of the original registration fee.

The EFB is becoming increasingly influential in Europe and beyond as the voice speaking on behalf of European academic and industrial scientists. Anyone wishing to become involved in its activities is invited to contact the Chairman of the Microbial Physiology Section: Jeff Cole, School of Biosciences, University of Birmingham (j.a.cole@bham.ac.uk)

● IUMS Congresses (www.iums2005.org)

Microbes in a Changing World

Joint Meeting of the three Divisions of the International Union of Microbiological Societies
23–28 July 2005, San Francisco, CA, USA

Hosted by the American Society for Microbiology

Abstract deadline:	**11 February 2005**
Early registration:	**13 May 2005**
Registration & housing deadline:	**1 June 2005**

SGM travel grants will be available. Details will be posted on the SGM website soon: **www.sgm.ac.uk/grants**

● Biosciences Federation: Bioscience and business: commercializing your research

12 October 2004, The Royal Society London

The symposium's topics will include:

Forming and funding biosciences companies – what's the value of a patent?

The role of charity funders: support at the early stages – technology transfer services

Developing partnerships with industry – what do investors look for?

The researcher's perspective – is it all worth it?

Fees: Member of BSF Member Society, £40; Academic (non-member), £50; Industry (non-member), £75.

For more information and a booking form visit **www.bsf.ac.uk** or call 020 7581 8333.

The SGM sponsors and carries out a whole range of activities to promote microbiology to the general public, schools, the media and decision-makers. Members can apply for a Public Understanding of Science grant for up to £1,000 to organize relevant activities, such as the one described here by Vyv Salisbury.

Alternatively they may wish to communicate some of their own research findings to a broader audience, but are not sure how to go about it. Sue Assinder reports on a new initiative – the Society's recent Communication Workshop at Marlborough House. Sue has also been involved in the Wrexham Science Festival, while Miriam Windsor has been telling 10-year-olds at her children's school all about viruses.

Finally we need more experts on our database to handle queries from the media and to provide responses to consultation documents. Can you help?

Lighting up biomedical research

An exhibit and series of events engaging the public in dialogue with scientists and showcasing applications of microbiology research

We have known for years that our students get really excited when they enter a dark room and see a culture of *Vibrio fischeri*, producing that eerie blue-green light, but our challenge was to put on a display of glowing bacteria and flashlight fish (*Photoblepheron palpebratus*), for the general public, within the acclaimed and highly popular At-Bristol Science Centre. The flashing light organs of the fish, packed with light-emitting bacteria, are a great way to illustrate this fascinating symbiotic relationship. We also displayed two airlift fermenters full of *V. fischeri* – one fully oxygenated and the other only aerated when a button was pushed, so that it instantly 'lit-up'. Once the public were interested, we were able to explain how we use the *lux* genes from the naturally glowing bacteria to genetically modify a range of bacterial pathogens, which then act as real-time reporters of antibiotic action.

With the help of a Wellcome Trust Engaging Science 'People Award', we set up an initial collaboration with the staff at the science centre, appointed a recent microbiology graduate from UWE – Robin Thorn – to run the exhibit, and had a number of planning meetings. It rapidly became clear that we were on a very steep learning curve, but fortunately the At-Bristol staff came to the rescue with their considerable experience of graphic design and safety of public displays.

Keeping bacteria happy in an airlift fermenter so that they glowed brightly for the public each day for 5 months was a Herculean task, not without incident, most spectacularly when the *V. fischeri* contaminated 10 litres of sterile reserve medium and all the lines into the fermenter, giving a 'Blackpool Illuminations' effect to the back of the exhibit. The fish also had their moments and were initially very shy – hiding from the public on every occasion, until we discovered that we could trick them into displaying beautifully by keeping their tank light on all night and then turning it off while the public visited. We were fortunate to be running the exhibit just after the release of *Finding Nemo* at local cinemas, so many of the 5–10-year-old visitors had an added interest!

The exhibit opened during the autumn half-term 2003, with Wellcome Trust funding to run until early February 2004. The 6-month project was a great success, with the number of visitors to the exhibit exceeding 130,000. We needed additional funding to extend over the spring half-term, a highly popular time for visits to the Science Centre. We were most grateful, therefore, to the SGM for their Public Understanding of Science grant, which enabled us to keep the display running over the half-term week, when it was viewed by over 5,000 visitors a day, with 1,146 of them taking part in the daily 'meet the scientist' sessions. Our evaluation questionnaire showed 68% of visitors thought that they had learned a lot from the exhibit and 32% felt they had learned something; 100% thought it was a good way for scientists to communicate with the public. Finally, the overall verdict of the team – good fun, hard work and very worthwhile.

Dr Vyv Salisbury, Department of Biological Science, Faculty of Applied Science, University of the West of England, Frenchay Campus, Coldharbour Lane, Bristol BS16 1QY, UK
email Vyv.Salisbury@uwe.ac.uk

ABOVE:
Children viewing the exhibit.

RIGHT:
The glowing bacteria team. From left to right: *back row* Maggie Pownell, Vyv Salisbury, Penny Fidler, Julian Pilkington; *front row* Gillian Smith, Karen Croker, Robin Thorn, Austin Stevens.

PHOTOS COURTESY V. SALISBURY

Pustules, pox and pupils

How do you keep the attention of two classes of nine- and ten-year-olds? This was the rather daunting prospect that confronted me when planning a visit to Pirbright Village School. As a parent who also works at the Institute for Animal Health in Pirbright, I had been approached by their science co-ordinator to find someone to help them cover the virus section of the year-five topic of 'microbes'. Unfortunately, everyone I approached suggested that I do it myself! Luckily, as I have two children of that age and am aware of their fascination with all things gruesome, I decided to involve the children as much as possible. I opened by asking if anyone could think of any diseases caused by viruses. To my relief, they were eager to share their knowledge, and suggested everything from colds and chickenpox to SARS and bird flu. When smallpox was mentioned I took the opportunity to ask for volunteers to recreate Jenner's pioneering work on vaccination. They particularly liked being covered in smallpox pustules (actually bubble wrap and red stickers), while we acted out the story of the milkmaids, the cow horn and the cut-throat razor!

We then discussed the differences between viruses and bacteria and talked about routes of infection, choosing my words carefully, as their teacher had told me they weren't covering sexual education till the next week! I then showed a short PowerPoint animation about viruses being the 'masters of disguise' that hitch a ride on the cell's transport system. This had also been a hit with children at the Royal Agricultural Show last year. We also talked about the formation of virus factories and about how viruses target particular cell types. They were amazingly cool about the thought of certain viruses lying dormant in their nervous system for many years. Then to a chorus of '*oh, that's gross*', I showed close-up photographs of blood-filled biting midges, and discussed climate change and the spread of vector-borne diseases such as bluetongue. The children were equally disgusted by the soft ticks that carry African swine fever virus, and thoroughly enjoyed examining both ticks and midges under low-power microscopes. All this was put to shame, however, by the highlight of the afternoon – the distribution of the IAH and SGM freebies. The teachers were especially grateful for the stress relievers!

Thanks to Steven Archibald for his prize-winning midge photographs and for all his technical help. Also to Eric Denison for providing the live midges and soft ticks. If you would like to learn more about the cow horn and the cut-throat razor, see *Epidemic* by Brian Ward, a Dorling Kindersley Eyewitness Guide that I found particularly helpful for my preparation.

Miriam Windsor works in the Department of Immunology, Institute for Animal Health Pirbright Laboratory, Ash Road, Woking, Surrey GU24 0NF, UK. email Miriam.Windsor@bbsrc.ac.uk

ABOVE & LEFT:
Children at the Pirbright Village School enjoying learning about microbes.
COURTESY STEVEN ARCHIBALD

Microbiology experts required

With so many controversial microbiological issues hitting the headlines almost daily, it has never been more important for scientists to communicate with members of the public and policymakers. It is essential to promote microbiology effectively so that people can make informed decisions about topics such as GM foods and MMR vaccination.

The External Relations Office at SGM regularly deals with requests from the media to locate experts in various fields of microbiology. For each new media query, availability and willingness to respond, as well as permission to release contact details, is sought by the staff in External Relations from each relevant Expert.

In addition to media queries, the Society responds to all relevant government consultation documents and produces occasional briefing papers.

SGM is currently seeking to expand its list of experts. If you are interested in becoming an SGM Expert, please complete the Expert's Form in as much detail as possible and return it to Faye Jones, SGM, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (Fax 0118 988 5656). The form can be found on the SGM website Noticeboard (www.sgm.ac.uk/noticeboard.cfm).

A Festival of Microbiology

6th Wrexham Science Festival

18–28 March 2004

Since its humble beginnings in 1998, the Wrexham Science Festival has grown into an event of national significance. This year some 20,000 people from across Wales, North West England and beyond attended over 150 events on such diverse topics as killer whales, maths for the terrified, colour blindness, coral reefs and Chaos theory. It was good to see that there was also plenty of microbiology on offer to educate and entertain them.

A highlight was a thought-provoking talk by SGM President Hugh Pennington entitled '*BSE, Smallpox, Anthrax and E. coli – WMDs?*'. Hugh had warned his audience in advance that they would be both scared and reassured, and he delivered on both counts. With typical wry humour, he recounted what went wrong and why in a number of high-profile food-poisoning cases, drawing on his personal experiences as a scientist and expert witness during various periods of tabloid frenzy and recrimination. He also highlighted the effectiveness of some micro-organisms as agents for bioterrorism, and left his audience in no doubt that he is not a man to cross!

Each Festival culminates in 'Scientriffic', a family day of exploration and experiment centred on the North East Wales Institute for Higher Education, and there was plenty to excite the budding microbiologist in the 50 or so exhibits dotted around the campus. These included the 'Fun with Fungi' stand from the British Mycological Society, which appealed to all ages and levels of expertise with a combination of display models, informative posters and hands-on activities. Meanwhile, the Pathology Department at Wrexham Maelor Hospital illustrated the role of the biomedical scientist, with a rainbow display of Petri dishes and the chance to talk to staff about the tests used in clinical laboratories to detect pathogenic microbes.

Academic scientists are often sceptical about being involved in public outreach activities, but in my experience are usually converts within the first hour and by the end of the day are already planning what to do the following year. Events like the Wrexham Science Festival are also an excellent opportunity for postgraduates to gain confidence in explaining their work, which for my students has had very positive knock-on effects when they have then had to give more formal research talks. They also give learned societies like the SGM the chance to reach a large and diverse audience, and possibly gain a few new members along the way. Those of you in the Wrexham area have been warned!

Sue Assinder, SGM Education Officer

LEFT:
Wrexham Maelor Hospital Pathology Department and British Mycological Society exhibits at the Wrexham Science Festival.
COURTESY S. ASSINDER

Science, media and making your point

Communicating Microbiology Workshop

29 April 2004, Marlborough House, Reading

How can we alert the public to some of the amazing discoveries being made through research with micro-organisms? This was the question that the participants in the first 'Communicating Microbiology Workshop' set out to answer at an intensive training day held at Marlborough House in April.

Twelve postgraduate and postdoctoral SGM members joined Myc Riggulsford, a professional facilitator with extensive experience of writing science for the general public, to learn about the principles of effective science communication. They began by discussing what makes a good (and bad) news story, and it was then their turn to have a go at putting the theory into practice by producing a story about their own research. They all came prepared with draft articles and a lot of time was devoted to helping them develop and improve these. There was a huge diversity in topics, from microbial biodiversity and bioremediation through to comparative genomics of pathogens and the effect of surface chemistry on microbial adhesion. For each of these, the group worked with the author to identify an attention-grabbing 'hook' and to suggest ways in which complex concepts could be explained in simple terms. After time for reflection and pencil-chewing, the participants came back to the group with a revised article, and in all cases the transformation was remarkable. By eliminating jargon, focusing on getting the story 'up front' and picking out the important messages, the drafts evolved from scientific abstracts into lively news stories that communicated the key points about each piece of research and its relevance to society.

The feedback from the workshop was extremely positive. The participants enjoyed the informal style of the day, with plenty of time for debate and discussion. Many commented that they now had a much better feel for how science can be made accessible to a wide audience, and for some of the pitfalls to avoid when writing for the public. They also understood better the role of the press in science communication, and would feel confident in seizing opportunities to publicize their work through the local press and radio.

The SGM will now publish the articles as a collection of case studies in a research-focused promotional publication, which will be distributed free of charge to schools, at careers fairs and at science events for the public. The Education Officer is also preparing a factsheet summarizing the key points from the workshop, which will be posted on the SGM website for the benefit of all members. A repeat workshop is being planned for next year, and we are open to suggestions from members about providing training in other aspects of science communication.

Sue Assinder, SGM Education Officer

Gradline

Gradline aims to inform and entertain SGM members in the early stages of their career in microbiology. Contributions from undergraduate and postgraduate students or postdocs are always welcome. If you have any news or stories, or would like to see any topics featured, contact Jane Westwell (j.westwell@sgm.ac.uk).

Life Science Careers 2004

6 November
King's College London

20 November
Leeds, Manchester

27 November
Glasgow University

Aimed at life science under- and postgraduate students, each conference includes a range of talks on career choices and further training, plus a small exhibition by companies, organizations and higher education institutions. A CV review service is also available, by prior arrangement.

Cost: £10, to include refreshments and lunch

Details and a booking form are available at: **www.bsf.ac.uk/careers**

Sponsored by AstraZeneca, Biochemical Society, British Pharmacological Society, Pfizer, Physiological Society, Society for General Microbiology

A job in... University research and teaching

Profile

Name Gavin Thomas
Age 30
Present Occupation
Lecturer, Department of Biology, University of York
Previous Employment
2000–2002: *Postdoctoral Research Fellow, Department of Molecular Biology and Biotechnology, University of Sheffield*
1998–2000: *Postdoctoral Research Fellow, Department of Molecular Microbiology, John Innes Centre, Norwich*
Education
PhD Biochemistry, University of Birmingham, 1998
BSc (Hons) Microbiology, University of Bristol, 1995

Q *What attracted you to microbiology research?*

As an undergraduate, I was fascinated with the mechanisms of gene regulation, the most interesting examples of which came from microbes, primarily *E. coli*. I chose to work on *E. coli* and having enjoyed my PhD, I continued doing research. This opened my eyes to other approaches to studying the organism, much of which was driven by the timely completion of the genome sequence in 1997.

Q *How did you find the transition from postdoc to lecturer?*

This has been the most dramatic change I have experienced in my career. Having been at the bench for 8 years, I felt I was getting quite good at doing experiments. Not being able to use this experience fully as an academic can be frustrating, although I have learned a whole range of new skills. Grant writing is the biggest challenge and it carries the most pressure to succeed as a new lecturer in a research-led department. Teaching undergraduates is the other obvious new role, but slightly less obvious is the amount of administration that needs to be done. There are so many activities that keep the department running, whether this is being involved in examinations, marking, interviews, admissions, etc. Given all these other jobs that often have short deadlines, planning even the shortest experiment is difficult. The day my students look shocked when I put on a lab coat will be a sad one, but one, I fear, that is not too distant.

Q *How do you divide your time between research, teaching and admin duties?*

This mainly depends on whether or not it is term time, with some parts of the academic calendar being so busy that research does not get a look in. However, equally there are quieter times in the holidays when I can really get into the research again. I do work longer hours than I did as a postdoc – trying to be a researcher and a lecturer at the same time. I have a relatively low teaching load, but, since it is all new material, it requires a lot of preparation. I now also organize 'year in industry' placements, which can take up a lot of time. There are also my commitments with the SGM [Gavin is Editor of *Microbiology Today*]. All new academics at York and other universities have to do a Master's level qualification in Academic Practice. This involves extra time out of the lab, but should theoretically make me a better teacher and researcher.

Q *Can you describe a typical day?*

There is no typical day, but I usually start by checking my email to find out what needs my immediate attention. I try and speak to my PhD students every day and we meet formally each week. Then much of my day is spent at the computer doing a whole range of tasks relating to research, teaching and administration. If it's a quiet week, I can spend a day or so in the lab and make some progress as well as keeping in touch with what's going on.

Q *How do you see your future?*

Happily, I can see my future in York for a considerable time. I hope that this will result in an expansion of my research group as much as my other roles within the department.

Q *What advice can you offer people planning career as an academic?*

Talking to people who have recently made the transition is a good idea. Although there is much competition for academic jobs, colleagues of mine who have decided that this is what they really want to do have usually found positions. If you view being an academic as the only route to having a permanent job and still being able to do research, then I would advise you to think strongly about applying for fellowships. This would allow you to focus on developing a research group in the absence of teaching and admin duties. I would say that being a lecturer is very different from being a postdoc, but it's still a great job.

Further information

- The University of York (www.york.ac.uk)
- www.shintonconsulting.com – career progression advice & information for postdocs
- http://nextwave.sciencemag.org/cgi/content/full/2004/06/10/6 – academic careers demystified
- Rothwell, N. (2002). *Who wants to be a scientist? Choosing Science as a Career.* CUP, ISBN: 0521-52092-4

Job opportunities

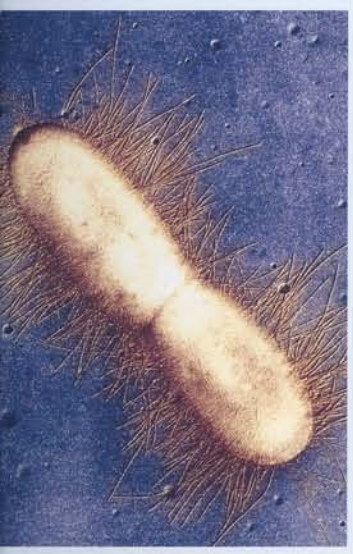
- www.jobs.ac.uk
- www.newscientistjobs.com
- www.jobs.thes.co.uk

SchoolZone

Keep up-to-date with what's happening in microbiology education. Schools Membership costs only £10 a year. For this, a named teacher representative will receive *Microbiology Today* each quarter, advance copies of new teaching resources and discounted fees on SGM INSET courses. To join see **www.sgm.ac.uk/membership**

Enquiries: education@sgm.ac.uk

Education website: www.microbiologyonline.org.uk



ABOVE:
Fig. 1. Coloured transmission electron micrograph of an *E. coli* bacterium in the early stages of binary fission.
CNRI / SCIENCE PHOTO LIBRARY

TOP RIGHT:
Fig. 2. A nutrient agar plate streaked with an *E. coli* K-12 strain after overnight growth at 37 °C.
COURTESY G. THOMAS

E. coli K-12 – model NOT menace in schoolwork

E. coli *is a microbe used in a number of school practicals, but recently there have been concerns about its safety.* Microbiology Today *Editor Gavin Thomas clears up these issues.*

Escherichia coli K-12 is a great organism to use in the school lab for a variety of different experiments. This is because it has actually been developed as a tool in research labs to study basic principles of biology. In this article I will introduce the species and general properties of *E. coli* and compare the strains that are used in the lab to the pathogenic ones that cause disease in an attempt to convince the reader that they are certainly not the same beast.

What are *E. coli*?

E. coli are Gram-negative bacteria that belong to the *γ-Proteobacteria*. As they primarily live in the mammalian gut they have been grouped with other related bacteria as 'enteric' bacteria. They are straight rod-shaped cells of about 2 μm long and 0·5 μm wide, which can grow and divide rapidly by binary fission (Fig. 1).

There are many different types of *E. coli* and the chief way they are distinguished is immunologically using serotyping. The current typing system is based mainly on three types of antigen: the somatic (O) antigen which corresponds to terminal sugars on the cell surface lipopolysaccharide (LPS), the capsular (K) antigens and the flagellar (H) antigen. There are over 170 O antigens, over 100 K antigens and over 50 H antigens. Hence, when we refer to pathogenic strain O157:H7, it means that this *E. coli* has O antigen 157 and H antigen 7. Many other strains cause disease as well, like O26:H11.

Why do we use *E. coli* K-12?

While there is a great diversity of strains in the environment, only a few are used in the lab. The majority are a derivative of a commensal strain called K-12, described in the article by Joshua Lederberg on p. 116. One of the main reasons why this microbe is a key research tool is that it is safe to handle; you could drink a culture of the stuff and not notice any effect (not to be recommended, however!). As well as being safe to use, K-12 is ridiculously easy to grow. It is usually cultured in the lab on a rich nutrient broth or agar, which supplies plenty of goodies for rapid growth. Whilst it is often said to be able to divide every 20 minutes, that is really only under absolutely optimal conditions. However, it still grows very quickly compared to other microbes. This is a big advantage in school as a culture can be set up one evening and by the following day nice clear and distinct colonies are visible on an agar plate (Fig. 2).

Growing *E. coli* in nutrient broth is a quick and simple way of propagating this microbe, but does not exploit one of *E. coli*'s most important properties. Unlike humans and many other microbes, it doesn't need lots of complex chemicals, like vitamins, to grow. Just provide a solution of some sugar (glucose is best), ammonium sulphate, salt and phosphates and grow it aerobically at the 37 °C used in research laboratories and it's perfectly happy. Such

incubation temperatures are not allowed in schools, but even at the permitted maximum of 25 °C, K-12 still grows well. Basically, it can synthesize everything it needs to make a completely new cell from these few simple molecules, which is a seriously impressive feat.

All *E. coli* are not the same

While K-12 and B strains are safe microbes, we know that there are other *E. coli* out there, like O157:H7, that can kill people. However, these are quite different from K-12 even though they have the same species name. This is illustrated very clearly when the DNA sequences (genomes) that make up K-12 and O157:H7 are compared. They are 25 % different from each other! As humans share about 99 % of their DNA with chimps, this gives an indication of how much evolution and movement of genes have occurred in the environment since these two strains of *E. coli* last had a common ancestor.

Scientists now know why K-12 is not harmful. Many of the known properties of the bacteria that allow them to cause disease, called virulence factors, are seen in pathogenic strains but not in K-12. In fact, the K-12 strain used in the laboratory is even less dangerous than a commensal strain living in your own gut that you might isolate from your stools. K-12 has been grown in the lab for many generations and so has adapted to live there rather than the intestine. It wouldn't stand a chance in the hugely competitive environment that is your gut where bacteria are constantly evolving to keep their 'cutting edge' and not be pushed out by other microbes. Getting K-12 to establish itself in the gut would be like trying to qualify for a Formula 1 race with a car from 1922 (which is when K-12 was taken from the somebody's gut)! It was competitive at the time, but is now way off the pace.

E. coli K-12 is a friendly bacterium

The article by Rastall and Gibson (p. 119) reports some interesting studies that suggest *E. coli* could be used as a probiotic, but when you browse the web for information about commensal *E. coli* you will find a statement something like '*E. coli is a friendly bacterium as it can produce vitamins that we require, especially vitamin K*'. Not trusting the internet as a particularly reliable source, I searched for experimental data that supports this assertion. To see what I found, look at the longer online version of this article at www.microbiologyonline.org.uk

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Dariel Burdass, Education Projects Administrator, rounds up some recent microbiology education activities.

Basic Practical Microbiology Courses

September 2003 saw the start of the third year of Basic Practical Microbiology, the Society's one-day course for school science teachers and technicians. The aims of the programme are to instill confidence and to support teachers and technicians in carrying out all aspects of practical microbiology safely and at the appropriate level within their laboratory. This comment from a teacher in Lincoln highlights the positive feedback the SGM have been receiving:

'*The course was excellent. I have a lot of useful ideas to take back to the workplace. I feel my practical skills have improved a great deal.*'

The SGM has been extremely fortunate, as members have continued to allow us to use their university laboratories. The teachers and technicians have appreciated being able to use their excellent, often state-of-the-art, facilities. We have received only positive responses from the universities, with many offering to host subsequent courses. It is hoped that this partnership approach will continue giving universities the opportunity to showcase their facilities. This was reflected in the comments made by Ron Dixon, principal lecturer in the Department of Biological Sciences, University of Lincoln, to the press:

'*This is the first time we have been invited to host this event. The fact that we are staging the course shows that the University of Lincoln is building a reputation as an excellent venue for science-based events.*'

Course leaders John Schollar and John Grainger have once again travelled far and wide to deliver courses at the University of Reading (2), University of Surrey (2), University of Wales Aberystwyth (2), University of Leicester, University of Lincoln, University of Plymouth and Yale FE College Wrexham. They have continued to be immensely popular and 220 teachers/technicians have been successfully trained.

For the first time this year we offered at the University of Aberystwyth a dedicated course to 21 secondary school science PGCE students. The education department was able to incorporate the day into their course timetable. The SGM is keen to run more of these dedicated courses.

In response to more than 65 % of the delegates requesting an advanced microbiology course, the SGM has developed *Microbes, Maths and ICT*. This workshop supports the A2 microbiology option and provides a range of microbial investigations for statistical analysis. It was successfully trialled at the University of Reading and will be launched September 2004.

MISAC Competition 2004

MiSAC
MICROBIOLOGY IN SCHOOLS ADVISORY COMMITTEE

Composting: not just a load of old rot but a way to save the planet

This year's secondary schools competition invited students to produce an illustrated information leaflet suitable for distribution by a local authority to the general public to encourage the use of composting as an important contribution to the recycling of waste. As well as highlighting the role of microbes in the composting process students also needed to include materials suitable for composting, the technology of the process and the uses and value of composting. The judges looked for original eye-catching designs that presented the scientific information in an accurate and engaging manner.

Once again the competition proved to be popular, attracting 370 entries involving over 400 students from 46 schools. As usual there were more entries from the 11–14 age group (over 80 %); however, the number of GCSE entries was significantly reduced. This was particularly disappointing, as these students have to study the role of decomposers in the breakdown of organic matter.

A panel of microbiology education experts, comprising MISAC members and officers of the Society for Applied Microbiology, the competition sponsor, carried out the judging. Many entries were of high quality. They demonstrated a good grasp of the scientific principles and environmental issues involved in composting. Although the judges felt unable to award prizes in the GCSE age group this year, several entries were highly commended and it was decided to give money awards to them and their schools.

The winner of the 11–14 age range was Charlotte Matthews from Sandbach High School & Sixth Form College; SfAM Treasurer Dr Val Edwards-Jones presented the cash prizes and certificates to the school. Further details of the winners are available on the SGM education website (www.microbiologyonline.org.uk/misac). A selection of the posters will be displayed on the MISAC stand at the ASE Annual Meeting at University of Leeds, 6–8 January 2005.

Every school entering the competition received a pack of microbiology teaching resources and each student was sent a certificate of entry.

MISAC wishes to express its sincere thanks to the Society for Applied Microbiology for sponsoring the 16th competition.

Next year's competition *Fungi in your Shopping Basket*, sponsored by the British Mycological Society, asks students to create a poster to inform the public of the importance of fungi in the production of foods, drinks and other goods they buy. A competition entry form can be downloaded from www.microbiologyonline.org.uk

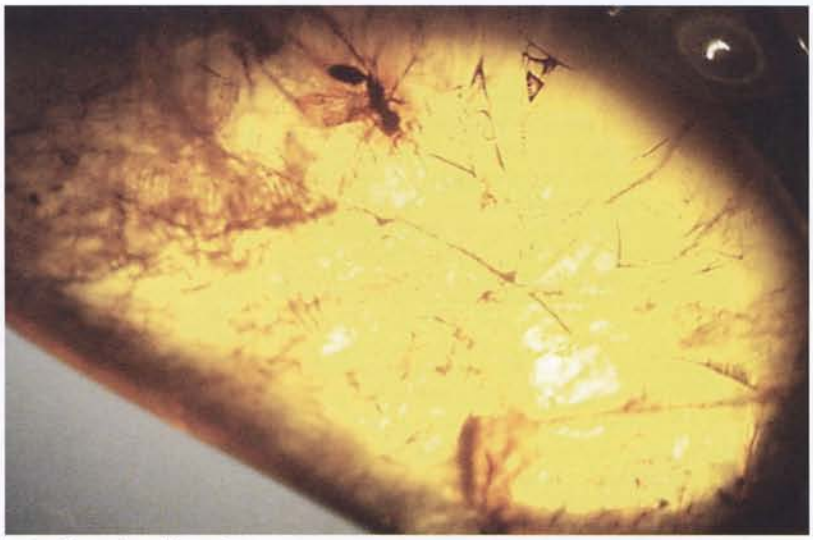
ABOVE:
A selection of the winning entries in the MISAC 'Composting' leaflet competition.

LEFT:
John Schollar (far left) next to Ron Dixon and John Grainger (right) with participants at an SGM Basic Practical Microbiology Course.
PHOTO UNIVERSITY OF LINCOLN

Hot off the Press

Science writer 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.

Ancient yeast genes



The science of molecular palaeontology, where researchers examine ancient DNA from fossils, has developed far enough for commercial firms to sell kits for isolating ancient DNA. Considerable skill is still needed to obtain DNA that has been preserved in rock for millions of years. One favoured source is the semi-precious stone amber, where the mixture of sugars, alcohols, terpenes and organic acids provides an excellent dehydrating and embedding environment for all sorts of insects, pollen and micro-organisms.

Researchers at the University of Santiago de Compostela in Spain have been looking at genes from the common baking and brewing yeast, *Saccharomyces cerevisiae*, that has been embedded in amber. To do this, they picked out pieces of amber in which ants had been trapped, because the insects pick up yeast cells as they clamber around in the sugary nectar of flowers. The amber came from 15–30-million-year-old rocks in the Santiago de Los Caballeros Mountains in the Dominican Republic and from slightly older Polish sources. Researchers used a standard procedure to decontaminate the surfaces, to remove all traces of modern DNA, and then they ground the stones to a powder. Rather than trying to extract individual strands of ancient molecules, they used the polymerase chain reaction (PCR) to make multiple copies that are much easier to detect. They also checked that the data came from short pieces of DNA, since only small fragments will survive the chemical degradation that occurs over millions of years. Any long DNA molecules will originate from contamination with modern DNA.

The researchers focused on several essential genes in *Saccharomyces cerevisiae* that can be easily recognized and compared with modern sequences. They managed to put together a complete sequence of some genes as they existed in the Miocene and Oligocene. They discovered that the sequence of each gene had been conserved to a different extent between these epochs and the present. Comparisons with gene sequences in modern yeasts have allowed the researchers to discover more about the evolution of yeasts. Although molecular palaeontology is still far from routine, it is providing exciting information about fossil organisms from our past.

Veiga-Crespo, P., Poza, M., Prieto-Alcedo, M. & Villa, T.G. (2004). Ancient genes of *Saccharomyces cerevisiae*. *Microbiology* **150**, 2221–2227.

ABOVE:
Ancient insects trapped in a piece of amber.
COURTESY T.G.VILLA

Underdiagnosis of UTIs

Hospital microbiology laboratories analyse samples from patients using standard procedures that have been proven to be the best way to detect and identify pathogens. Staff at the Chang Gung Memorial Hospital-Kaohsiung, a 2,500-bed medical centre in southern Taiwan, now wonder whether these procedures miss a potential pathogen. They had four cases of urinary tract infections (UTI) in otherwise healthy women. All cleared up after antibiotic therapy, but the results of tests on urine and blood were puzzling. All the urine cultures contained few, or no, bacteria, but the blood cultures revealed a *Methylobacterium* species. This genus is normally found in the environment, particularly soil and sewage. It has been reported from some infections, but always in people who were immunocompromised. The question was: how did it get into the blood of these four immunologically normal women?

The clinical microbiologists suspected that the routine urine cultures had not given a complete picture, so tested exactly how to detect *Methylobacterium* in urine. They discovered that it needed at least 40 hours, rather than the standard 24, to become visible on culture media. In addition, its growth was completely suppressed if the usual cause of UTIs, *Escherichia coli*, was present. The researchers therefore suspect that UTIs caused by *Methylobacterium* are under-reported. A good test for it in urine needs to be devised to check this. They also investigated the antibiotic sensitivity of the *Methylobacterium* isolates and confirmed that, as expected, aminoglycoside-type antibiotics killed them all. Their recommendation is therefore to switch to this type of antibiotic if a UTI is not cleared up promptly by other treatments. This should end the infection even if its cause has not been positively identified.

Lee, C.-H., Tang, Y.-F. & Liu, J.-W. (2004). Underdiagnosis of urinary tract infection caused by *Methylobacterium* species with current standard processing of urine culture and its clinical implications. *J Med Microbiol* **53**, 755–759.

Virologists look to Merlin for help

Infection with human cytomegalovirus (HCMV) is widespread throughout the world. In the UK, 60 % of adults have been infected by the age of 40. There are only two situations when HCMV infection causes problems. It can be serious for babies of mothers who become infected during their pregnancy, causing hearing loss, vision impairment and varying degrees of mental retardation. The other occasion is if the immune system is not working effectively. Then, HCMV can cause pneumonia and gastrointestinal disease.

There are no cures for HCMV infection, although some antiviral drugs are used to treat at-risk patients. Like all viruses, HCMV can only reproduce within a living cell and researchers would obviously like to know all about its life history. In 1990, the complete genome of the virus was sequenced, and this listing of all its genes has helped researchers. However, the strain of the virus that was sequenced (AD169) had been grown in cell cultures for many years. It has became obvious that this strain has accumulated many mutations that make it different from wild strains. Researchers have therefore been studying more recently isolated HCMV strains, and, led by Andrew Davison at the Medical Research Council's Virology Unit in Glasgow, UK, they have now sequenced a strain called Merlin that has been grown in culture for only a short period. They have also sequenced substantial regions from other isolates, two of which were taken directly from infected humans.

Comparisons between all the sequences made the researchers confident that the Merlin strain contains the full complement of 165 genes from the wild virus, with only one obvious mutation that probably shortens one protein. A surprisingly large number of genes had variations from strain to strain. Many of these genes specify proteins associated with the surface of the virus or infected cell, or that are secreted. This variation might be the consequence of the human immune system permitting survival of new viral variants that escape detection for a while. All the strains that had been passaged through cell culture had mutations in genes that are thought to be involved in the ability of the virus to live in many types of cell. This was not unexpected, since the virus is cultured in a very limited range of cells compared with the number that it encounters in the wild. Further investigation of these genes may give the researchers a clearer idea of how the virus grows in different types of cell during infection.

Dolan, A., Cunningham, C., Hector, R.D. & 12 other authors (2004). Genetic content of wild-type human cytomegalovirus. *J Gen Virol* **85**, 1301–1312.

Communication blackout?

The conventional idea of bacteria as single-celled organisms floating around oblivious to other bacteria in the environment is fading. All bacteria have sophisticated systems to sense and respond to their environment, and researchers have realized that some secrete chemical signals to communicate with individuals of the same species. The concentration of the chemical informs the bacterial cell of the number of others in its surroundings. Once a threshold level is passed, the bacteria collectively do something. The actions are as diverse as synthesizing chemicals that glow in the dark or starting to behave as pathogens. The latter is, of course, one reason why researchers are very interested in these systems. Methods of disabling the system, which is called quorum sensing, could prevent diseases.

One interesting question is what happens to the chemicals after the signal has been received. They do not build up in the environment, and indeed, would be useless as a signal if they did. So how are the chemicals destroyed? In a recent issue of *Microbiology*, Martin Welch and his colleagues at Cambridge University, UK, have reviewed information about the enzymes that degrade one class of these communication chemicals, the *N*-acylhomoserine-lactones (AHLs). These chemicals undergo partial spontaneous chemical degradation in the environment. However, several species of bacteria secrete enzymes that either inactivate or completely destroy AHLs. There are even strains of *Variovorax paradoxus* that can live with AHLs as the sole energy source. The genes for several of the enzymes have been detected in many bacteria, suggesting that the ability to metabolize AHLs is widespread. The race is therefore on to develop AHL-degrading enzymes as so-called 'quorum-quenchers' for treating disease.

However, even though an enzyme can degrade AHLs and disrupt quorum-sensing-related activities in carefully designed laboratory experiments, this may not be their role in real life. When researchers test the activities of the enzymes, several chemicals are degraded with different speeds and efficiencies and there is no easy way to identify which occurs in nature. Bacteria are always ready to exploit new sources of food, and so the AHL-degrading enzymes might have this rather mundane role.

In 2002, researchers discovered that the pathogenic species *Agrobacterium tumefaciens*, which uses quorum sensing to time the transfer of its genes into plant cells, has an enzyme that can degrade AHLs. This was the first time that researchers had found an AHL-degrading enzyme in a bacterial species that was known to produce AHLs. The enzyme, AttM, was a potent blocker of AHL accumulation. However, cells without AttM were not pathogenic, exactly the opposite behaviour expected of cells that are free to accumulate AHLs without restraint. More recent discoveries of AHL-degrading enzymes in bacteria that use quorum-sensing have revealed further counter-intuitive effects, adding to a picture that degradation may have a role in fine-tuning AHL levels rather than simply clearing them away. Individual bacteria can produce several enzymes with potential to degrade AHLs and only some may have this role *in vivo*. Researchers have focused on AHL-degrading enzymes to develop new anti-bacterial therapies. However, an understanding of the complex roles these enzymes play in bacterial life may clarify which have most potential and reveal further therapeutic opportunities, as well as being intrinsically interesting.

Roche, D.M., Byers, J.T., Smith, D.S., Glansdorp, F.G., Spring, D.R. & Welch, M. (2004). Communication blackout? Do *N*-acylhomoserine-lactone-degrading enzymes have any role in quorum sensing? *Microbiology* **150**, 2023–2028.

Phytoplasma taxonomy

Several hundred plant diseases are caused by organisms that are a big problem for taxonomists. The organisms cause serious diseases with symptoms including leaf yellowing, abnormal leaf and shoot growth and a general decline in vigour, so that correct detection and identification is important for plant health protection. Diseases with names like Nigerian lethal decline of coconut, Australian grapevine yellows, rice yellow dwarf and loofah witches'-broom give a flavour of the variety and severity of the infections. The difficulty is that the organisms, which look like rounded to filamentous wall-less bacteria, will not grow outside living tissue. They are found in the phloem cells of plants, and in the gut, haemolymph, salivary gland and other organs of sap-sucking insects. The insects transmit the disease between plants, but may also suffer premature death.

The organisms were first detected in the late 1960s, but were very poorly characterized until the advent of molecular biological methods. From 1992 their official trivial name has been 'phytoplasma', by analogy with similar organisms called mycoplasmas that are found in animal cells. Collaboration between researchers in nine countries over the last few years has resulted in a description and a series of rules to advise researchers on naming conventions for phytoplasma species. The Phytoplasma/Spiroplasma Working Team of the International Research Project for Comparative Mycoplasmology has comprehensively examined all the available information. As they point out, there has been firm evidence for a single taxon descended from one ancestral group within the class *Mollicutes* for these organisms for over 15 years. Several distinct taxa have been described, but until now, there has not been a general description of the comprehensive taxon '*Candidatus* Phytoplasma', abbreviated as '*Ca.* Phytoplasma'.

The information needed to support a valid species name leaps directly into the 21st century. The sequence of a piece of DNA that provides an essential component of the cell's protein synthesis machinery is the best piece of unambiguous identification, and so the 16S rDNA sequence has to be provided from the reference strain for all future descriptions of '*Ca.* Phytoplasma' species. In principle, this sequence must be more than 97.5 % similar in all individuals of a '*Candidatus*' species. However, some phytoplasmas share more than 97.5 % of their 16S rRNA gene sequence, but clearly represent separate species. The phytoplasmas concerned may cause different plant diseases and are subject to different quarantine regulations. The IRPCM Phytoplasma/Spiroplasma Working Team has thought through how to decide whether these phytoplasmas really constitute different species. There must be evidence for differences in the insect vectors, natural plant hosts and/or symptoms, and for diversity in other genes before two phytoplasmas can be described as different species.

The inability to grow phytoplasmas outside their host plant provides a special difficulty for maintaining reference strains. Dr Assunta Bertaccini from the Università di Bologna maintains an international collection of phytoplasmas within micropropagated plants. The Working Group has given thought to this and advises anyone who names a new species to deposit the reference strain with her. For species that cannot be preserved in this way, reference DNA from infected plants has to be maintained by whoever defined the species. This comprehensive review of the status of an important group of plant pathogens will provide basic information for researchers in this area for decades.

The IRPCM Phytoplasma/Spiroplasma Working Team – Phytoplasma taxonomy group (2004). '*Candidatus* Phytoplasma', a taxon for the wall-less non-helical prokaryotes that colonize plant phloem and insects. *Int J Syst Evol Microbiol* **54**, 1257–1269.

ABOVE:
A healthy (left) and a phytoplasma-infected (right) *Zinnia elegans*, showing a symptom known as virescence. As plant pathogens, the phytoplasmas cause severe physiological changes and dramatic morphological modifications to their hosts.
COURTESY ALBERTO LOSCHI, UNIV. DEGLI STUDI DI UDINE, ITALY

Working safely with SARS

The new disease severe acute respiratory syndrome (SARS) erupted into the news in late 2002 as it spread from China around the world. It is transmitted very rapidly, has a high mortality rate and there is still no effective therapy. Nevertheless, within a remarkably short period of time the causal agent had been identified and researchers had discovered a surprisingly large amount of information about it.

SARS turned out to be caused by a coronavirus, a group that produces respiratory and enteric disease in animals and humans. Human coronaviruses are one of the causes of the common cold, with generally mild symptoms. The general principles of coronavirus biology, including how the virus replicates, are known, but SARS means that there is a new urgency for discovering how to stop virus replication. However, the infection of laboratory workers and their contact persons in Taiwan and Singapore in 2003, and in Beijing in 2004, means that there is real concern for the safety of anyone involved in this research and the fear that laboratory infections may give rise to a new epidemic.

Researchers from the Cantonal Hospital St Gallen, Switzerland, the University of Würzburg, Germany and the University of Bristol, UK, have now developed what should be a safe method for testing drugs that might provide effective anti-SARS therapy. Viruses consist of an outer coating surrounding the nucleic acid genome that contains all the instructions for making new viruses. The researchers reasoned that, if the virus lacked several of the proteins required for the exterior coating, it would be unable to cause an infection, but could still replicate while being trapped within cultured human cells. Adding the gene for a fluorescent protein in place of a missing one would provide an easy way to tell if the virus was really replicating. If it was, the cells should fluoresce.

To test this idea, the researchers used a harmless human coronavirus, rather than the SARS virus. To their satisfaction, it worked and they were even able to show that addition of a drug with antiviral activity made the fluorescence die away as virus replication slowed. Once this methodology is transferred to SARS, it should allow researchers to screen hundreds of compounds safely for anti-SARS activity, and speed development of an effective treatment.

Hertzig, T., Scandella, E., Schelle, B., Ziebuhr, J., Siddell, S.G., Ludewig, B. & Thiel, V. (2004). Rapid identification of coronavirus replicase inhibitors using a selectable replicon RNA. *J Gen Virol* **85**, 1717–1725.

The SGM publishes four journals, ***Microbiology***, ***Journal of General Virology*** **(JGV)**, ***International Journal of Systematic and Evolutionary Microbiology*** **(IJSEM)** and ***Journal of Medical Microbiology*** **(JMM)**.

They are all available online with full-text HTML, and other features such as CiteTrack, Email-a-Friend and Most-cited/Most-read listings. For further information visit the journal website: **www.sgmjournals.org**

Members may purchase SGM journals at concessionary rates. See p. 113 or contact the Membership Office for details. Information on commercial subscriptions is available from the Journals Sales Office.

Letter

Wound botulism in the UK and Ireland

Wound botulism was unknown in the UK and Ireland before 2000, but since then the Food Safety Microbiology Laboratory (FSML) of the Health Protection Agency has tested 33 suspected cases. This lab is the specialist botulism reference laboratory for the UK and Ireland and Moira Brett, Gill Hallas and Obioma Mpamugo have recently reviewed these cases in the *Journal of Medical Microbiology*.

Wound botulism is caused by neurotoxins produced by *Clostridium botulinum*, a spore-forming bacterium that is always present in soil, but only multiplies in anaerobic conditions. The toxins bind to neurons, blocking their action, which results in a progressive paralysis. Provided the nerves have time to sprout new terminals in the absence of the toxin, patients can make a slow recovery.

All the recent cases seen by the FSML came from drug users who were injecting heroin into muscle or by 'skin-popping' and were probably caused by bacterial spores that had contaminated the drugs. A particular danger of injecting heroin in this way (rather than intravenously) is that it damages muscle and causes scarring, reducing blood-flow and encouraging an oxygen-free environment in which *C. botulinum* can thrive. It is not known how many *C. botulinum* spores are needed to cause illness in humans, but a mere 25 can be fatal to a guinea pig. Since very small amounts of bacteria and toxins can cause disease, the levels in blood or tissue samples can easily be too low to detect. Nevertheless, the lab detected either bacteria, toxin or both in samples from 19 of the 33 possible cases, and in all of them the patients had symptoms that were typical of wound botulism. Treatment included antibiotics to kill *C. botulinum* to prevent further toxin production and antitoxin to counter the effects of the toxin. However, several of the patients needed support on a ventilator for days or even months because the toxin had weakened the respiratory muscles. All the patients fortunately recovered.

The classic symptom of wound botulism is a symmetrical flaccid paralysis that descends the body with effects such as slurred speech, difficulty with swallowing, vision or breathing and weakness of the limbs, although the order in which the symptoms appear may vary. Wound botulism must now be considered in drug users presenting with these symptoms, particularly if they have been injecting into muscle or 'skin-popping'. As a result, this has implications for the care of drug users and can add to the requirement for long-term intensive care facilities.

Brett, M.M., Hallas, G. & Mpamugo, O. (2004). Wound botulism in the UK and Ireland. *J Med Microbiol* 53, 555–561.

An arsenic-resistant *Bacillus* sp.

Researchers from India have identified a new species of bacterium in arsenic-contaminated soils of the Bengal Basin. Several bacterial genera, such as *Bacillus*, *Deinococcus*, *Desulfitobacterium* and *Acidithiobacillus* contain species that can survive the toxic effects of arsenic. To see if any of these bacteria were present in sand from a contaminated aquifer in the Chakdah district of West Bengal, the researchers spread it over a conventional laboratory growth medium supplemented with 5 % sodium arsenate. A host of smooth, circular yellow-orange bacterial colonies grew, even in 20 mM arsenate. Using a microscope, the researchers could see that many of the cells were slightly swollen because they had turned into an endospore. These survival structures are a characteristic of the genus *Bacillus*, but were an unusual combination of an oval shape and cell wall composition. Many more physical and biochemical characteristics were tested to compare the bacteria with the many identified *Bacillus* species. The new bacteria were sufficiently different to be classified as a new species and the researchers have proposed the name *Bacillus indicus* to signify the country in which this arsenic-resistant species was first found.

Suresh, K., Prabagaran, S.R., Sengupta, S. & Shivaji, A. (2004). *Bacillus indicus* sp. nov., an arsenic-resistant bacterium isolated from an aquifer in West Bengal, India. *Int J Syst Evol Microbiol* 54, 1383–1389.

Veterinary microbiology

I read with interest the letters in the recent edition of *Microbiology Today*, concerning veterinary microbiology. As a longstanding member of SGM and someone actively involved in this area I would like to contribute to this valuable discussion. It is true that in recent years veterinary microbiology has not been well catered for by the learned societies. The Society for Applied Microbiology (SfAM) has taken this point on board and we are now seeing some of our initiatives coming to fruition. As President of SfAM I will outline our involvement in this area.

One of the frustrations has been that until recently we have not been able to make public the really exciting news of our involvement in MED-VET-NET and so there are few who are aware of just what was happening.

MED-VET-NET is a 'Network of Excellence' funded under the EU Framework 6 Directive and with 16 partners made up of veterinary and public health institutes across 10 European countries. All partner institutes have national reference laboratory-based responsibilities for the prevention and control of zoonoses. The management structure is based on that of a virtual institute and is designed to generate durable interactions between partners. Over 300 key scientists, with complementary expertise and skills, will be incorporated into the network. Organizational work packages will develop activities to enable integration, including structured and systematic communications, both electronically and through meetings, and training/continuous professional development. A management project will investigate the strengths and weaknesses of, and barriers to, integrated scientific collaboration. Scientific work packages will undertake jointly executed research on zoonotic agents selected on their importance in Europe and covering four thematic areas: epidemiology, host–microbe interactions, detection and control and risk analysis. Given the network structure, the technical resources and the scientific excellence it is expected that MED-VET-NET will undertake strategically-driven, state-of-art zoonoses research of world-renowned quality. The overall objective of the network is to integrate veterinary, medical and food sciences, in the field of food safety, at the European level, in order to improve research on the prevention and control of zoonoses including food-borne diseases, while taking into account the public health concerns of consumers and other stakeholders throughout the food chain.

SfAM is taking a pivotal role in this exciting venture as we have the responsibility of heading up one of the work packages, namely *Spreading Excellence*.

For more information on MED-VET-NET why not have a look at the web site at **www.medvetnet.org/**

● ***Dr Peter Silley, Honorary President, Society for Applied Microbiology, MB Consult Limited, The Triangle, 52 Moorbottom Lane, Bingley, West Yorkshire BD16 4HA, UK.***
Tel. 01274 551818; Fax 01274 551818

Reviews

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

A list of publishers' website addresses is given opposite.

Vaccines for OIE List A and Emerging Animal Diseases. Developments in Biologicals, Vol. 114

Edited by F. Brown & J.A. Roth
Published by Karger (2003)
Euro200.00/CHF280.00/US$243.50, pp. 306
ISBN: 3-8055-7577-7

This book comprises the proceedings for an international symposium on vaccines for the List A diseases identified by the Office International Des Epizooties (OIE) and also selected emerging diseases such as West Nile Fever. List A diseases are considered to have serious socio-economic or public health implications and to present severe threats to international trade in food animals. This is a very useful source book, not only on the important role of the OIE but with chapters on individual diseases, regulatory concerns, available vaccines and their source. It provides an up-to-date reference. Topically, FMD vaccines are well to the fore in a number of chapters and this helps illustrate the complexities involved in decisions to use or not to use vaccination during outbreaks. Anybody with an interest in how and when vaccines should be deployed against List A diseases should get a copy of this book.

■ ***Willie Donachie***
Moredun Research Institute

Modern Medical Microbiology: The Fundamentals

By S.C. Clarke
Published by Arnold (2003)
£19.99, pp. 239
ISBN: 0-340-81044-0

This introduction to medical microbiology is intended for students, clinical microbiologists and academic researchers. It gives an interesting overview of many infectious diseases and provides the important basic facts regarding acquisition of an infection, clinical signs and treatment. Readers are expected to have an understanding of physiological and pharmacological processes as often they are alluded to but not explained. The book achieves what it sets out to do – to provide an introduction to infectious diseases and their cause, but due to the extent of this topic, the depth of field for each example is sadly lacking. At best the reader can gain a surface understanding of a particular disease, which may stimulate enough interest to seek further literature on the subject. However, I am not sure that this is exactly why the intended audience would read such a book. There are some diagrams/figures present, but it would benefit from pictures of the various infectious agents or diseases which would grab the reader's attention and spark further interest.

■ ***Georgina Hold***
University of Aberdeen

Medical Implications of Biofilms

Edited by M. Wilson & D. Devine
Published by Cambridge University Press (2003)
£65.00/US$90.00, pp. 314
ISBN: 0-521-81240-2

The increasing recognition that micro-organisms frequently attach themselves to surfaces and adopt a sedentary lifestyle has led to a huge expansion in the literature pertaining to biofilms. This book focuses on the role played by biofilms in human infections. It appears to be based largely on a symposium of the same name organized by the Editors for SGM in September 2000. The book is divided into four parts, each containing three or four chapters. The opening section provides an introduction to gene expression, quorum sensing and antimicrobial resistance in biofilms. The remaining sections deal with biofilm involvement in infections of implanted devices, teeth and mucosal surfaces. All of the chapters represent concise, readable and reasonably current overviews by experts from North America and Europe. The book is well produced, with a central section of colour plates. Curiously, the plates are also reproduced in black and white at the appropriate place in the text. Overall, the book will serve as a valuable reference both for biofilm aficionados and anyone, including final-year undergraduates, with an interest in infectious diseases.

■ ***Julia Douglas***
University of Glasgow

Microbial Diversity and Bioprospecting

Edited by A.T. Bull
Published by American Society for Microbiology (2003)
US$129.95, pp. 524
ISBN: 1-55581-267-8

I do not know what the opposite of 'a curate's egg' might be, but this book is an example. Like the curate's egg it is good in parts, but in the case of this book the rest is even better. I was a sceptical reviewer, put off by the title, but I was hooked from the introductory chapter ('the Rationale') which set out the intention to examine current understanding of microbial diversity from both a systematics and an ecological perspective, and the result is a collection of splendid reviews which will be of interest to those in the field and an oft-consulted work for the busy, essay-writing student. The authors keep the book's objective of bioprospecting in mind, but treat it liberally, focussing more on the questions of what is out there, how does it do what it does, and how can we bring the process into the laboratory?

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

Micro-Facts: The Working Companion for Food Microbiologists. Fifth Edition

Revised by L. Curtis & R. Lawley
Published by Royal Society of Chemistry (2003)
£50.00, pp. 279
ISBN: 1-904007-54-6

This is a very useful and thorough book for food microbiologists. Its format is detailed, yet the size is small. Each chapter is therefore compact and allows easy access to usable data.
Most food-borne pathogens and other food-associated bacteria are included. Moreover, there are sections on spoilage organisms, viruses and protozoa. The breakdown for each micro-organism described is similar in that description of the organism is followed by sections on sources, incidence, survival and control. This makes the various characteristics easy to compare. There are few illustrations, but this is intended to be more of a factual book. Key references are cited throughout.
The authors are to be congratulated for bringing together such a concise and up-to-date volume. Moreover, new information on HACCP and legislation add to the value of the book. Perhaps future editions may include more information on fermented food organisms like probiotics and starter cultures?

■ ***Glenn Gibson***
University of Reading

Bacillus thuringiensis: A Cornerstone of Modern Agriculture

Edited by M. Metz
Published by Haworth Press, Inc. (2003)
US$59.95, pp. 237
ISBN: 1-56022-109-7

This comprehensive collection of reviews and articles examines many aspects of the use of *Bacillus thuringiensis* in modern agriculture, but focuses primarily on the introduction of insecticidal protein genes into crop plants, the advantages and disadvantages of this for agriculture and the economic and ecological consequences of this technology. The contributions are well researched (with references up to 2003, but it is gratifying to see that groundbreaking earlier work is also acknowledged). Each piece can be read as an individual review, so that there is inevitably a little bit of overlap between articles, but not unduly so. Although the general reader

can easily assimilate most of the chapters, some are essentially very specialized research articles, which, whilst not without interest, may not have found their true niche in this book. The quality of some of the figures is rather poor, which does dilute the impact when the benefits of Bt protection are being illustrated. Probably a book for the library rather than a personal must-have.

■ ***Peter Morris***
Heriot-Watt University

Molecular Microbiology: Diagnostic Principles and Practice

Edited by D.H. Persing, F.C. Tenover, J. Versalovic, Y.-W. Tang, E.R. Unger, D.A. Relman & T.J. White
Published by American Society for Microbiology (2004)
US$124.95, pp. 748
ISBN: 1-55581-221-X

As one of the authors points out, molecular methods have come of age, and techniques once confined to research laboratories should now have a role in clinical microbiology. The publication of this book is therefore timely. Its 53 chapters comprise two sections, the former outlining the underlying principles of current molecular methods, and the latter focusing on their application to a range of bacterial, viral, fungal and parasitic pathogens. The first section should prove useful for clinical microbiologists unfamiliar with some of this new technology, and many of the chapters have effective diagrams that help explain how the techniques work. The Editors specifically included personal experiences of molecular biology, and I particularly enjoyed reading David Pershing's reflections on PCR and the O.J. Simpson murder trial in 1994. Given the potential impact of molecular biology on the practice of clinical microbiology, I recommend this book to hospital microbiologists.

■ ***Alan Johnson***
Health Protection Agency, Colindale, London

Prions: A Challenge for Science, Medicine and the Public Health System. 2nd Revised and Extended Edition. Contributions to Microbiology Vol. 11

Edited by H.F. Rabenau, J. Cinatl & H.W. Doerr
Published by Karger (2004)
CHF178.00/Euro127.00/US$162.00, pp. 222
ISBN: 3-8055-7656-0

A series of excellent reviews, but of a limited range of aspects of prion science. Despite the huge budgets that have been put into the subject, what we find is beefed up versions of reviews and official data: the most important factors might be found missing. We are beginning to understand the diseases fairly well, but are now watching the growth of an epidemic of BSE in humans. Surely now is the time to review the prion science of diagnostics, treatment and public health? Well, these are largely missing. As a regularly stabbed scientist myself from the 1990s it rather sticks in my throat to read a very clear explanation that vCJD is due to BSE coming from researchers spending years denying that it would ever happen. I suppose I should be impressed by such a good re-review, but you will need more information than this for a now massive field.

■ ***Steve Dealler***
Royal Lancaster Infirmary

Management of Multiple Drug-Resistant Infections

Edited by S.H. Gillespie
Published by Humana Press (2004)
US$125.00, pp. 403
ISBN: 1-58829-230-4

Although the title suggests this book would primarily be of interest to clinicians, it is suitable for a wider readership, as many chapters cover a broad brief, encompassing topics such as drug resistance mechanisms, pharmacodynamics and susceptibility testing. Related topics, such as molecular epidemiology and infection control are also covered. The complexity of the therapeutic dilemmas posed by some highly multi-drug-resistant pathogens (not only bacteria, but fungi, viruses and parasites) are such, that this book does not necessarily provide definitive clinical solutions. However, this is not meant as an adverse criticism, as the book provides a wealth of information about current options for approaching the problem of multi-drug resistance, as well as giving pointers for what the future may hold in the way of new drugs and vaccines. It is recommended for clinicians working in microbiology or infectious diseases and all those with an interest in anti-infective therapy.

■ ***Alan Johnson***
Health Protection Agency, Colindale, London

Molecular Genetics of Bacteria, Second Edition

By L. Snyder & W. Champness
Published by American Society for Microbiology (2002)
US$99.95, pp. 582
ISBN: 1-55581-204-X

This is a wonderful book. The authors have managed to reach out to both introductory level and advanced level microbiologists with this text book. The presentation and the organization of the information is excellent and the use of problems and 'Questions for thought' is great for both teacher and student. Text boxes are frequently used to highlight recent discoveries or technological breakthroughs. This book should be essential reading for microbiology undergraduates, postgraduates and lecturers. It is also an information resource for the thousands of researchers in other fields of biology who use bacterial genetics every day. It is well worth the investment in the second edition as it incorporates new material such as *B. subtilis* sporulation and greatly expands on new and exciting fields, including chromosome segregation and cell division, the relationship between DNA replication, recombination and repair, and many other topics. Preparing lectures on bacterial genetics without this book would be substantially more time-consuming. I can only thank the authors for making my life a lot easier.

■ ***Maggie Smith***
University of Aberdeen

Protein Expression Technologies: Current Status and Future Trends

Edited by F. Baneyx
Published by Horizon Bioscience (2004)
US$180.00/£90.00, pp. 532
ISBN: 0-9545232-5-3

This book covers an often neglected, however integral, aspect of the biotechnology sector. The book outlines various prokaryotic and eukaryotic methodologies that could be adopted to enhance and optimize protein production. Each chapter includes a concise introduction that leads the reader into the practical approaches of the various subjects covered. The figures and tables are clearly presented and well defined. Furthermore, if greater detail is required, the comprehensive and up-to-date reference list allows further specifics to be obtained. This overall layout means that the chapters flow well, without hindering understanding with excessive minutiae. Consequently, the book is suitable for both postgraduate and postdoctoral research scientists. The book will prove to be extremely useful in any molecular biology lab.

■ ***Andy Walker***
University of Cambridge

A History of Beer and Brewing

By I.S. Hornsey
Published by Royal Society of Chemistry (2003)
£39.95, pp. 742
ISBN: 0-85404-630-5

General histories of brewing have been a bit like buses in the last 12 months. You wait for ages (actually since 1975) and nothing appears, and then three come along at once. The latest addition by the brewer and botanist Ian Hornsey is the most impressive of the three. His book will appeal to anyone with an interest in the application of microbiology, but is more than just a chronicle of technological change. It is a magisterial account covering 8,000 years, which sifts the historical evidence with skill and care in charting the change in the role of beer from cult social drink to essential element of diet, and now branded recreational beverage. All is put into context, with an informed analysis of the literature and quotes *in extenso*. If you only have room for one book on brewing, historical or otherwise, on your shelves then buy this one.

■ ***Ray Anderson***
Marchington, Uttoxeter

Publisher's website addresses

American Society for Microbiology	www.asmpress.org
Arnold	www.arnoldpublishers.com
Cambridge University Press	www.cambridge.org
Haworth Press, Inc	www.haworthpressinc.com
Horizon Bioscience	www.horizonbioscience.com
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Karger	www.karger.com
Royal Society of Chemistry	www.rsc.org
Wiley	www.wileyeurope.com

Medical Research Council Laboratories
The Gambia

MRC Medical Research Council

Head of Bacterial Diseases Programme

Established over 54 years ago, the Medical Research Council in The Gambia employs around 700 staff from 20 countries and hosts many visiting researchers. Its main base in Fajara comprises laboratories, a hospital, computer centre, offices, workshops and residential accommodation. There are also field stations upcountry – Basse, Farafenni, Keneba, Bansang, Walikunda and Caio (Guinea Bissau) – each in a different ecological setting, providing varied research opportunities.

The Unit has a long and established history of research in the area of bacterial diseases. MRC Gambia has hosted several major vaccine trials, including those for Haemophilus influenzae type B and the pneumoccocal conjugate vaccine. The TB group is currently engaged in identifying surrogate markers for infection and disease and the Unit's sexually transmitted infections laboratory is a WHO – referenced laboratory. The Unit's current programme of research in bacterial diseases includes acute respiratory infections, pneumoccocal disease, tuberculosis, sexually transmitted infections and chlamydia. Investigations range from the genetics of chronic infection, through interventional studies with new vaccines, to surveillance studies exploring the genetic risk factors for disease susceptibility.

The Head of the Bacterial Diseases Programme will be in charge of one large component of the Unit's research portfolio, play an important role in the drawing up of the Unit's next quinquennial plan and will contribute to MRC Gambia's future scientific direction. The successful applicant should be a scientist of international status and be experienced in one or more of the major areas of research, such as microbiology, bacterial genetics, immunology, epidemiology, clinical research or large-scale vaccine trials. S/he must have proven leadership skills.

Previous experience of working in developing countries will be advantageous.

Salary will be within the MRC Band 2 range and will be commensurate with qualifications and experience. Overseas allowances, furnished accommodation, flights and other benefits will also apply. The appointment, which we would like to be taken up as soon as possible, will initially be for a 5-year period.

Further details and application forms are available from Samantha Smith, Human Resource Advisory Group, Medical Research Council, 20 Park Crescent, London W1B 1AL, 24 hour answerphone service: +44(0)20 7637 6005. Fax: +44 (0)20 7637 0361. Email: Samantha.smith@headoffice.mrc.ac.uk

Closing date: 2 August 2004. Interviews: 12 August 2004.

For further information about MRC visit www.mrc.ac.uk

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Microarray Bioinformatics

By D. Stekel
Published by Cambridge University Press (2003)
£28.00/US$45.00, pp. 263
ISBN: 0-521-52587-X

The microarray process is complex, including target identification, reporter generation, array manufacture, data collection and analysis. The author begins with chapters describing the experimental techniques used to manufacture and use microarrays, and the informatics required to select and generate reporters to target genes. These initial chapters provide good summaries of the approaches generally taken, although they draw heavily from experience with eukaryotic microarrays and largely ignore the considerations required for their microbiological application. The subsequent chapters are the strength of this book; they provide a detailed summary of the approaches and techniques used in experimental design, data normalization and data analysis. The author concentrates on examples of usage of the different analysis methods, and largely ignores implementation details; referring the interested reader to a good list of links and further reading at the end of each chapter. The book would be ideal for biologists who wish to gain a grasp of the different analysis techniques available to the microarray user.

■ ***Adam Witney***
St George's Hospital Medical School, London

Protein Purification Protocols, Second Edition, Methods in Molecular Biology, Vol. 244

Edited by P. Cutler
Published by Humana Press (2004)
US$115.00, pp. 512
ISBN: 1-58829-067-0

Eight years on this is a welcome new edition which retains the same overall format of a strategies chapter followed by some 43 chapters, each dealing with individual techniques. Updating ranges from new introductions, to additional references and modified protocols. The final six chapters are new and include a useful comparison of detection methods and guides to proteomics and mass spectrometry. The larger format and hard binding make this edition appear less of a bench book, but the Editor has wisely retained the readily approachable format and enhanced its overall value as a practical manual, collating a wide range of protocols useful for both less and more experienced practitioners.

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

Nanobiotechnology: Concepts, Applications and Perspectives

Edited by C.M. Niemeyer & C.A. Mirkin
Published by Wiley-VCH (2004)
Euro149.00/SFr 220.00, pp. 469
ISBN: 3-527-30658-7

Nanobiotechnology has recently been receiving growing attention as an evolving area of research fusing biotechnology with the nanosciences. Perhaps, for many biologists, they are aware of the nomenclature, but understand less about the real applications of nanobiotechnology. This book is the first serious attempt to define current applications. The 27 chapters outline different aspects of nanobiotechnology, each written by one or more experts in the field. The book is divided into four sections. First, interphase systems, that includes biological coatings and microcontact printing of proteins. The second section covers protein-based nanostructures and has an excellent chapter on S-layers as building blocks for generating functional nanostructures, bacteriorhodopsin for photochromic applications and also chapters on protein nanopores and biomolecular motors. The third section covers the interesting area of DNA-based structures and finally a final section covering nanoanalytics and includes the majority of commercial products in nanobiotechnology now under development. This book is clearly presented with each chapter carrying an overview, introduction, a brief synopsis of applications, finishing with conclusions and outlook, and every chapter is richly illustrated. For those wanting to know more about this emerging scientific area, this is an excellent starting point.

■ ***Simon M. Cutting***
Royal Holloway, University of London

Principles of Virology: Molecular Biology, Pathogenesis, and Control of Animal Viruses

By S.J. Flint, L.W. Enquist, V.R. Racaniello & A.M. Skalka
Published by American Society for Microbiology (2004)
US$109.95, pp. 944
ISBN: 1-55581-259-7

This is an excellent text which gives a comprehensive and beautifully illustrated guide to modern virology. Everything is here, from descriptions of how experiments are performed to real data reproduced from seminal papers. The aspects of cell biology which virologists need but may have forgotten since graduate days are covered here in admirable detail making this a useful book to have around the lab. There are also some lovely touches in the boxes where ground-breaking advances relevant to the section are highlighted. The book could prove useful as a teaching aid; although the information given extends well beyond the undergraduate level in breadth and detail, final-year students will find its easy reading a good way to consolidate their advanced virology lectures. Overall, *Principles of Virology* is a completely up-to-date and accurate aid for anyone who thinks of themselves as a molecular virologist.

■ ***Wendy Barclay***
University of Reading

Diary

september 04

ALTERNATIVE AND CONVENTIONAL ANTI-FOULING STRATEGIES. INTERNATIONAL CONFERENCE OF THE BIODETERIORATION AND BIODEGRADATION SOCIETY

Aquatorium, Mülheim, Germany
13–15 September 2004

CONTACT: Prof. Dr Hans-Curt Flemming, Secretariat Ingelore Pinders, IWW, Moritzstr. 26, D-45476 Mülheim, Germany (Tel. +49 208 40303401; email HansCurtFlemming@compuserve.com *or* i.pinders@iww-online.de; www.iww-online.de)

BMS ANNUAL SCIENTIFIC MEETING: FUNGI IN THE ENVIRONMENT

Nottingham
13–15 September 2004

CONTACT: BMS Meetings Manager (email john.peberdy@nottingham.ac.uk; www.britmycolsoc.org.uk)

HEALTH PROTECTION AGENCY ANNUAL CONFERENCE 2004

University of Warwick
13–15 September 2004

CONTACT: email hpaconference@hpa.org.uk (www.hpaconference.org.uk)

11TH BIENNIAL CHALLENGER CONFERENCE FOR MARINE SCIENCE 2004

Liverpool
13–17 September 2004

CONTACT: Dr Judith Wolf, Proudman Oceanographic Laboratory, Bidston Observatory, Prenton, CH43 7RA (Tel. 0151 653 8633; Fax 0151 653 6269; email jaw@pol.ac.uk; www.pol.ac.uk/ms2004/)

NSF INTERNATIONAL COURSE – WATERBORNE PATHOGENS: MINIMIZING RISK ASSOCIATED WITH BUILDING WATER SYSTEMS (IN CONJUNCTION WITH HC INFORMATION RESOURCES INC.)

NSF Headquarters, Ann Arbor, Michigan, USA
14 September 2004

CONTACT: Tel. +1 800 673 6275 (www.nsf.org/cphe)

ACINETOBACTER 2004: 6TH INTERNATIONAL SYMPOSIUM ON THE BIOLOGY OF *ACINETOBACTER*

Dublin, Ireland
15–17 September 2004

CONTACT: Kevin Towner, Department of Microbiology, University Hospital, Nottingham NG7 2UH (Tel. 0115 970 9163; Fax 0115 942 2190; email Kevin.Towner@mail.qmcuh-tr.trent.nhs.uk)

EURESCO CONFERENCE – CELLULAR AND MOLECULAR BASIS OF REGENERATION

San Feliu de Guixols, Spain
18–23 September 2004

CONTACT: Corinne Le Moal, Publicity Officer & Conference Organizer, EURESCO Office, 1 quai Lezay-Marnésia, 67080 Strasbourg, France (Tel. +33 388 767 135; Fax +33 388 366 987; email clemoal@esf.org; www.esf.org/ euresco/04/lc04177)

BIOTECHNOLOGY FOR THE NON-BIOTECHNOLOGIST

Harrington Hall Hotel, London
23 & 24 September 2004

CONTACT: Management Forum Ltd, 48 Woodbridge Road, Guildford GU1 4RJ (Tel. 01483 570099; Fax 01483 536424; email registrations@management-forum.co.uk; www.management-forum.co.uk)

JPGM GOLD CON: 50 YEARS OF MEDICAL WRITING – INTERNATIONAL CONFERENCE ON JOURNAL WRITING AND PUBLISHING

Mumbai, India
23–26 September 2004

CONTACT: Dr Atul Goel, Dept of Neurosurgery, Seth G.S. Medical College, Parel, Mumbai-400 012, India (Tel. +91 22 24129884; Fax +91 22 25032398; email goldcon@jpgmonline.com; www.jpgmonline.com/goldcon.asp)

AN INTRODUCTION TO THE IMMUNOLOGY OF VACCINES: A BASIC ONE-DAY INTERACTIVE COURSE

The Rembrandt Hotel, London
28 September 2004

CONTACT: Management Forum Ltd, 48 Woodbridge Road, Guildford GU1 4RJ (Tel. 01483 570099; Fax 01483 536424; email registrations@management-forum.co.uk; www.management-forum.co.uk)

THE IMMUNOLOGY OF VACCINES AND VACCINE DEVELOPMENT: AN INTERMEDIATE COURSE PROVIDING AN IN-DEPTH ANALYSIS

The Rembrandt Hotel, London
29 September 2004

CONTACT: Management Forum Ltd, 48 Woodbridge Road, Guildford GU1 4RJ (Tel. 01483 570099; Fax 01483 536424; email registrations@management-forum.co.uk; www.management-forum.co.uk)

october 04

FUNCTIONAL GENOMICS OF PATHOGENIC BACTERIA

Copanello, Italy
6–8 October 2004

CONTACT: Jeff Cole, Chairman, Microbial Physiology Section, European Federation of Biotechnology (email j.a.cole@bham.ac.uk; www.efbpublic.org)

FRONTIERS OF CELLULAR MICROBIOLOGY AND CELL BIOLOGY – SPATIAL AND TEMPORAL DYNAMICS OF THE ENDOMEMBRANE SYSTEM

San Feliu de Guixols (Costa Brava), Spain
16–21 October 2004

CONTACT: Corinne Le Moal, Publicity Officer & Conference Organizer, EURESCO Office, 1 quai Lezay-Marnésia, 67080 Strasbourg, France (Tel. +33 388 767 135; Fax +33 388 366 987; email clemoal@esf.org; www.esf.org/euresco)

XIII BOTRYTIS SYMPOSIUM

Antalya, Turkey
25–31 October 2004

CONTACT: Dr Yigal Elad (email elady@volcani.agri.gov.net.il; www.agri.gov.il/events/BotrytisSym/BotrytisSymposium.pdf)

november 04

EMERGING AND RE-EMERGING ZOONOSES: A MEDICAL CRISIS AND VETERINARY PERSPECTIVE

The Royal College of Pathologists, London
11 November 2004

CONTACT: Michelle Casey, The Royal College of Pathologists, 2 Carlton House Terrace, London, SW1Y 5AF (Tel: 020 7451 6740; Fax 020 7451 6701; email: michelle.casey@rcpath.org; www.rcpath.org)

RECOMBINANT PROTEIN PRODUCTION

Algarve, Portugal
11–14 November 2004

CONTACT: Jeff Cole, Chairman, Microbial Physiology Section, European Federation of Biotechnology (email j.a.cole@bham.ac.uk; www.efbpublic.org)

GENETICS AND MOLECULAR BIOLOGY OF INDUSTRIAL MICRO-ORGANISMS/ BIOTECHNOLOGY OF MICROBIAL PRODUCTS (GMBIM/BMP)

Hilton San Diego Resort, San Diego, California, USA
14–18 November 2004

CONTACT: SIM, 3929 Old Lee Highway, Suite 92A, Fairfax, VA 22030-2421, USA (Tel. +1 703 691 3357; Fax +1 703 691 7991; email info@simhq.org; www.simhq.org)

january 05

15TH EUROPEAN SOCIETY FOR ANIMAL CELL TECHNOLOGY-UK (ESACT-UK) CONFERENCE

Leicester University
6–7 January 2005

CONTACT: email meetings@esactuk.org.uk; www.esactuk.org.uk

february 05

4TH INTERNATIONAL CONFERENCE AND TRADE SHOW: GREEN TECH 2005 WITH 9TH 'SYMPOSIUM ON RENEWABLE RESOURCES'

Potsdam, The Netherlands
2 & 3 February 2005

CONTACT: Ms Marieke Bouman, PO Box 822 3700 AV Zeist, The Netherlands [Tel. +31 (0) 30 6933 489; Fax +31 (0) 30 691 394; email mbouman@europoint-bv.com; www.europoint-bv.com/greentech2005]

may 05

MICROBIAL CELLS AT THE SINGLE CELL LEVEL

Semmering, Austria
26–29 May 2005

CONTACT: Jeff Cole, Chairman, Microbial Physiology Section, European Federation of Biotechnology (email j.a.cole@bham.ac.uk; www.efbpublic.org)

Comment

Codes of practice in research

Some UK government bodies have recently issued a code of practice for research carried out by their fund-holders. Superficially this seems a good move, but as Tony Minson describes, the policy also heralds some pitfalls for microbiologists.

We are all aware that operating standards – method validation, sample documentation, record keeping – vary in different laboratories. To a large degree this reflects the fact that errors have different consequences in different circumstances, and this is perhaps particularly true in microbiology laboratories. The detection and characterization of SARS, BSE or FMDV may impact immediately and dramatically on government policy and action. Work in clinical diagnostic laboratories determines hospital practice and patient treatment. Research leading to the compilation of large databases impacts quickly on large numbers of users who are dependent on the accuracy of the information. Nevertheless, most basic research in academic laboratories has no immediate practical consequences. A piece of work may, of course, change the way we think, but such research is expected to stand the test of time before being established as scientific dogma. This does not mean that standards in academic research laboratories are, or should be, low, but very few work to 'Good Laboratory Practice' (GLP: the industry standard) and most of us will at some time have received plasmids or antibodies that are not quite what was claimed, or cell lines contaminated with mycoplasma. This happens very rarely, but most of us operate on the basis of 'receiver beware'!

The current *laissez-faire* situation in academic research laboratories looks set to change. The Food Standards Agency and DEFRA (together with the devolved Regional counterparts) have issued a code of practice for research with which laboratories must comply if they wish to hold contracts from these agencies. Compliance with the same code of practice is also a condition of BBSRC support, but is required of BBSRC institutes only. As the Biosciences Federation has noted (April 04 newsletter) this arrangement may be difficult to sustain. It is hard to see how work funded by different organizations in the same laboratory can be performed using different operating standards. And is it reasonable that BBSRC Institutes, which often compete for funds with universities and other organizations, should be obliged to operate higher and more costly standards? The implications are that there will be a drive towards uniformity of standards applied by all funding agencies to all laboratories. And in any drive to uniformity, there will be demands that the highest standards become the norm.

The code of practice to be imposed by DEFRA, FSA and BBSRC from June 2004 does not look particularly alarming (www.foodstandards.gov.uk/multimedia/pdfs/QACOPRes.pdf) though it includes phrases that are not entirely familiar to all academic laboratories – 'validated standard operating procedures', 'countersigned note books'. The devil will, however, be in the detail. What is meant by '*records must be retained in a form that ensures their integrity and security and prevents unauthorized modification*'? We should all be using hard-cover laboratory notebooks with properly dated pages, but must every original image (Western blot, acrylamide gel, confocal image) be stored in an annotated, secure, tamper-proof central database? The costs of implementing such procedures, and of demonstrating that they are in place, would be very high. The statement '*In the longer term it is expected that most research organizations will assure the quality of their research processes by means of a formal system that is audited by an impartial and competent third party against an appropriate internationally recognized standard*' gives some indication of the bureaucratic burden and likely cost. Equally important, would such measures suppress the spontaneity and immediacy associated with the best hypothesis-driven experimental research? Would the quality of process become more important than the value of the output? The challenge is not, perhaps, to achieve high uniform standards, but to identify the purpose of different kinds of research and to apply standards that are relevant to purpose.

To be against improvement in standards is like being against motherhood, but we should be alert to the dangers of universal codes of practice imposed for administrative tidiness. The fact is that the great scientific leaps of the past 50 years have not been made in laboratories using validated standard operating procedures, well defined line-management systems, and 6-monthly milestones.

● ***Professor Tony Minson, Division of Virology, Department of Pathology, University of Cambridge, Tennis Court Road, Cambridge CB2 1QP, is a member of SGM Council. email acm@mole.bio.cam.ac.uk***

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